

Q.P



Industria y Comercio
SUPERINTENDENCIA

Delegatura de Propiedad Industrial

División de Nuevas Creaciones

PCT

SOLICITUD

PATENTE DE INVENCION

FASE NACIONAL PCT

21. EXPEDIENTE No.

05-12002

54. TITULO

COMPOSICIONES QUE COMPRENDEN UN UNIDOR DE GRASA DIETETICAY
METODOS PARA SU USO

51. CLASIFICACION INTERNACIONAL

71. SOLICITANTE

ART JEN COMPLEXUS, INC.

DOMICILIO

ONTARIO, CANADA

74. APODERADO

CAMILO ALVAREZ

22. BOGOTA, D.C.,

PETITORIO



SUPERINDUSTRIA Y COMERCIO
 Radicación : 05010002 00000000 Folios: 119
 Fecha (ARM): 2005-02-10 13:11:28
 Trámite : 011 PCT-PATENT 379 FASE NACI 411 PRESENTAR
 Dependencia: 2020 DIVISION DE NUEVAS CREACIONES

FORMULARIO ÚNICO DE SOLICITUD DE PATENTE

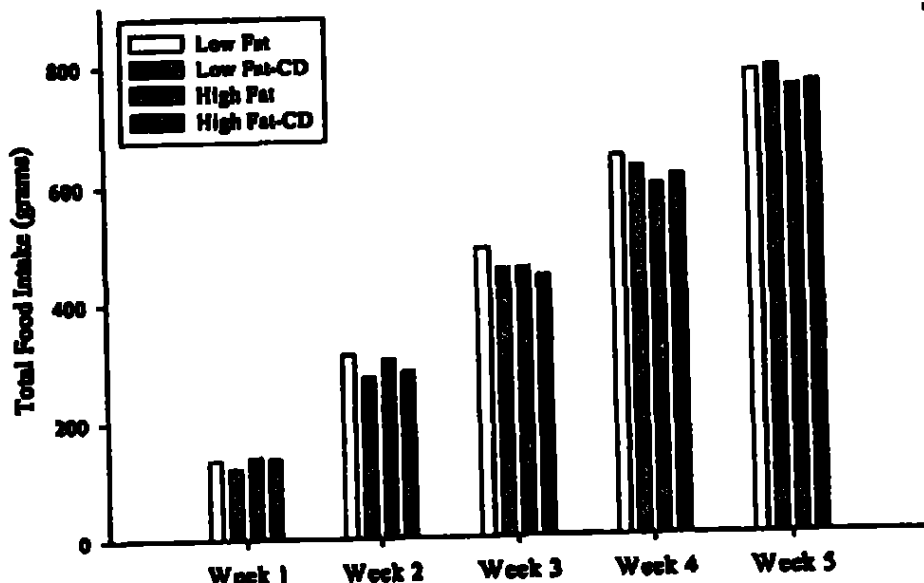
PCT ENTRADA EN FASE NACIONAL

1 SOLICITUD DE : ☒ Patente de Invención. ☐ Patente de Modelo de Utilidad, ☐ Capítulo I. ☒ Capítulo II			
2 SOLICITANTE (71)	Nombre: Art Jen Complexus, Inc. Dirección: 510 Westcourt Place, 251 Goyeau Street, Windsor, Ontario, Canada Nacionalidad o Domicilio: Ontario, Canada Lugar de Constitución: Canada Teléfono: Fax: E-mail:	IDENTIFICACIÓN C.C. ☐ NIT ☐ C.E. ☐ Otro ☒ Cual _____ Número _____	
3 REPRESENTANTE O APODERADO	Nombre: Camilo Alvarez Dirección: Calle 68A No. 4 - 64, Bogotá, D. C. Colombia Teléfono: 636 7334 Fax: 636 7650 E-mail: calvarez@alvarezbernate.com	IDENTIFICACIÓN C.C. ☒ , NIT ☐ C.E. ☐ Otro ☐ Cual _____ Número <u>19219008</u> TP <u>20343</u>	
4 INVENTOR (ES) (72)	Nombre: Ver documento adjunto. Dirección: Nacionalidad o Domicilio		
5 PCT (88) Solicitud Internacional No. <u>PCT/US03/023291</u> Fecha <u>Julio 29, 2003</u> Publicación Internacional No. <u>WO 2004/016101 A3</u> Fecha <u>Febrero 28, 2004</u>			
6 Título (54) <u>Composiciones que comprenden un unidor de grasa dietética y metodos para su uso.</u>			
7 Clasificación Internacional (51) <u>A23L A61K47/00</u>			
8 Prioridad SI ☒ NO ☐	(33) País de Origen <u>E.U.A.</u> <u>E.U.A.</u> <u>E.U.A.</u>	(32) Fecha <u>Agosto 19/02</u> <u>Abril 11/03</u> <u>Julio 14/03</u>	(31) Número de Solicitud <u>60/404,366</u> <u>60/461,847</u> <u>60/466,440</u>
9 Comprobante de pago No. <u>05 - 8,491</u> Fecha <u>Febrero 4, 2005</u>			

- ☒ Comprobante de pago de la tasa de representación de la solicitud.
- ☒ Documento que acredite la existencia y representación legal cuando el solicitante sea persona jurídica.
- ☒ Poderes, si fuere el caso.
- ☒ Documentos de cesión del inventor al solicitante o a su causante.
- ☐ Declaraciones.
- ☒ Copia de la solicitud internacional. (Resumen, descripción, reivindicaciones, dibujos).
- ☒ Traducción de la solicitud internacional al castellano. (Resumen, descripción, reivindicaciones, dibujos).
- ☒ Copia del examen preliminar internacional efectuado por la Autoridad Internacional de Examen Preliminar (IPEA)
- ☐ Traducción del examen preliminar internacional efectuado por la IPEA.
- ☐ De ser el caso, copia del contrato de acceso.
- ☐ De ser el caso, documento que acredite la licencia o autorización de uso de conocimientos tradicionales de las comunidades indígenas.
- ☐ De ser el caso, certificado de depósito del material biológico.
- ☒ Arte final 12x12.
- ☐ De ser el caso, información sobre otras solicitudes de patente o títulos obtenidos en el extranjero por el titular o su causante, relacionadas parcial o totalmente con la invención de esta solicitud.
- ☒ De ser el caso, modificaciones efectuadas a la solicitud internacional.
- ☒ Otros.

11

FIGURA CARACTERÍSTICA:



12

Solicito la concesión de la patente.

NOMBRE: Camilo AlvarezFIRMA: *Camilo Alvarez*

C.C. 19219009 de Bol.

T.P. 20343 del CSJ

Instrucciones para la presentación del os anexos, ver reverso de esta pagina.

ANEXO 1

4. INVENTOR(ES) (72)	Nombre:	Catherine Jen
	Dirección	5159 Provincial Drive Bloomfield Hills, Michigan 48302 Estados Unidos de América
	Nacionalidad:	Estados Unidos de América
	Nombre:	Joseph D. Artiss
	Dirección	3117 Curry Avenue Windsor, Ontario N9E 2T2 Canada
	Nacionalidad:	Canadiense

4

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

SUPERINDUSTRIA Y COMERCIO
Radicacon : 05012002 00000000 Folios: 119
Fecha (AMD): 2005-02-18 13:11:28
Tramite : 011 PCT-PATENT 379 FASE NACT 411 PRESENTA
Dependencia: 2028 DIVISION DE NUEVAS CREACIONES
MIT : 80017606

RECIBO OFICIAL DE CAJA : 05 - 8,491
FECHA : FEBRERO 4 DE 2005

***** CONSIGNACION *****

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PGO	Vr. PAGO
CANILO ALVAREZ	CONSIGNACION	BANCO POPULAR	050-00110-6	30610335	04/02/2005	7,223,000.00

***** CONCEPTO *****

CANT.	RENTISTICO	CONCEPTO	TOTAL CONCEPTO
1	50005-01-01	SOLICITUDES	
		1 TRAMITES DE SOL. DE PATENTE DE IN	443,000.00
		TOTAL :	\$ 443,000.00

SON: CUATROCIENTOS CUARENTA Y TRES MIL PESOS

RESPONSABLE : 

RECIBO DE CAJA APLICADO AL EXPEDIENTE No. _____

5

**ALVAREZ BERNATE ASOCIADOS
PODER/POWER OF ATTORNEY**

Nosotros/we, **ART JEN COMPLEXUS, INC.**
una sociedad de/s company of the _____
domiciliada en/domiciled in 510 Westcourt Place, 251 Goyeau Street, Windsor, Ontario N9A 6V2, Canada

Por el presente documento conferimos Poder, amplio y suficiente, a **CAMILO HERNANDO ALVAREZ BERNATE**, identificado con la cédula de ciudadanía número 19.219.009 de Bogotá, portador de la Tarjeta Profesional de Abogado No. 20.343 del Consejo Superior de la Judicatura, domiciliado en la ciudad de Bogotá, D.C., para que nos represente en todos los asuntos relacionados con nuestros derechos de propiedad intelectual.

De conformidad con este Poder **CAMILO HERNANDO ALVAREZ BERNATE** queda ampliamente facultado para representarnos en todo asunto relacionado con marcas de producto y/o servicio, nombres y enseñas comerciales, lemas comerciales, indicaciones geográficas, patentes, fase nacional de patentes solicitadas de conformidad con el Tratado de Cooperación en Materia de Patentes (PCT), modelos de utilidad, diseños industriales, esquemas de trazado de circuitos integrados, licencias y permisos sanitarios, estando expresamente facultado para representarnos ante autoridades o personas que ejerzan o no jurisdicción, autoridades del orden administrativo, contencioso administrativo y judicial, especialmente en todo lo relacionado con los siguientes asuntos:

- a) Solicitar, tramitar y obtener registros, sus renovaciones, cancelaciones, modificaciones, oclusiones, cambios de nombre.
- b) Acciones de cancelación, oposición, nulidad, medidas cautelares, concesión de licencias, y en general, para representarnos en acciones civiles, comerciales, penales, administrativas o contencioso administrativas relacionadas con nuestros registros o licencias sanitarias, incluyendo procesos por competencia desleal.

CAMILO HERNANDO ALVAREZ BERNATE queda facultado para sustituir, transigir, recibir, desistir, comprometer, renunciar y ratificar los actos realizados por agentes oficiales.

By this document, we grant a broad and ample Power of Attorney to **CAMILO HERNANDO ALVAREZ BERNATE**, identified with citizenship card No. 19.219.009 of Bogotá, holder of professional attorney card No. 20.343 of Consejo Superior de la Judicatura, resident at the city of Bogotá, D.C., to represent us in all matters related to our intellectual property rights.

In furtherance of this Power of Attorney, **CAMILO HERNANDO ALVAREZ BERNATE** is broadly authorized to represent us in all matters related to trademarks and/or services marks, commercial names and logos, slogans, geographical indications, patents, national phase of patent applications filed under the patent Cooperation Treaty (PCT), utility models, industrial designs, layout designs of integrated circuits, sanitary permits and sanitary licenses, being expressly authorized to act in our name and behalf before any authorities or individuals having or not jurisdiction, before authorities of the administrative, contentious administrative or judicial levels, specially in the following matters:

- a) Filing, prosecuting and obtaining the registration, the renewal, cancellation, amendments, assignments, change of name.
- b) Cancellation actions, oppositions, annulment, precautionary measures of licenses, and in general, to act in our behalf in civil, commercial, penal, administrative or contentious administrative processes related to our trademarks, slogans, sanitary licenses, slogans, and competition procedures.

CAMILO HERNANDO ALVAREZ BERNATE is authorized to substitute this Power of Attorney, to settle, to receive, to withdraw, to compromise, to waive and to ratify the actions of agents.

Dado en/granted on 10.4.25/04

En la ciudad de/in the city of _____

Por/by Arthur Barga - Chief Executive Officer of ArtJen Complexus, Inc.

State of Michigan



DEPARTMENT OF STATE

APOSTILLE

(Convention de La Haye du 5 Octobre 1961)

1. **Country:** **UNITED STATES OF AMERICA**

This public document

2. *has been signed by:* **Deborah A. Lombardi**

3. *acting in the capacity of:* **Michigan Notary Public**

4. *bears the seal of:* **Deborah A. Lombardi**
Macomb County, Michigan

CERTIFIED:

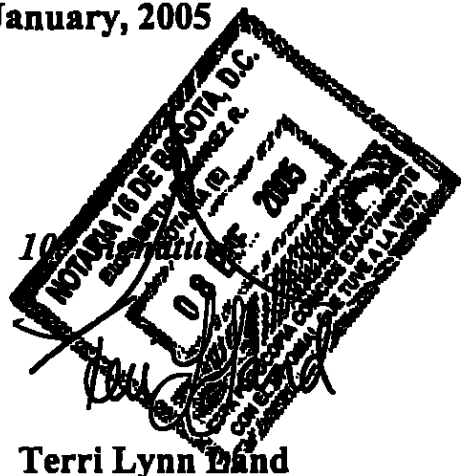
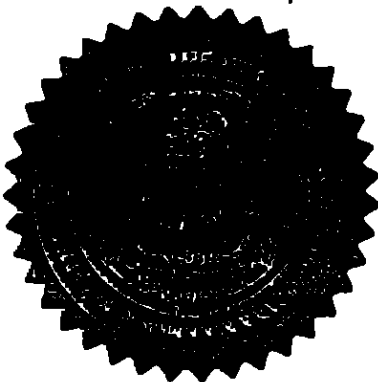
5. *at Lansing, Michigan*

6. *the 19th of January, 2005*

7. *by Secretary of State, State of Michigan*

8. **NO. 02548F-05**

9. *Seal/Stamp:*



This certification relates only to the authenticity of the signature of the official who signed the attested document, the capacity in which that official acted, and where appropriate, the expiry of the seal or stamp which the document bears. The certification is not intended to imply that the contents of the document are correct, nor that they have the approval of the State of Michigan.

CANADA)
STATE OF MICHIGAN) SS.
COUNTY OF WAYNE)

CANADA)
ESTADO DE) SS.
CONDADO DE)

DEBORAH A. LOMBARDI
I, _____, a Notary Public in and
for the above mentioned County and State,

Yo, _____, Notario Publico
en y para el Condado y Estado arriba
señalado,

CERTIFY:

On the 4 day of December, 2004, before
me appeared Arthur Bell to me known
to be the individual who signed the
foregoing instrument as Charles Bell Officer
of ART JEN COMPLEXUS, INC., a
corporation duly organized and legally
existing under the laws of the State of
Ontario, Canada, with home office located
at 510 Westcourt Place, 251 Goyeau Street,
city of Windsor, State of Ontario N9A 6V2,
Canada.

CERTIFICO:

El día 4 de December, 2004, compareció ante
mi Arthur Bell, a quien conozco y
quien me consta que es la persona que firmo
el instrumento que antecede en su calidad de
_____ de ART JEN
COMPLEXUS, INC., sociedad debidamente
constituida y legalmente existente de
conformidad con las leyes del Estado de
_____, Canada, con domicilio situado en
el 510 Westcourt Place, 251 Goyeau Street,
ciudad de Windsor, Estado de Ontario,
Canada.

I further certify that said individual is
duly authorized to sign the foregoing
instrument in the name of said corporation,
and that the purposes for which said
instrument are granted are encompassed
within the corporate purpose of said
corporation.

Además certifico que dicho individuo
se encuentra debidamente facultado para
firmar el instrumento que antecede en
representación de dicha sociedad, y que el
objeto para el que dicho instrumento es
otorgado está comprendido dentro del objeto
social de la sociedad.

In certifying the aforementioned I was
based in the following documents:

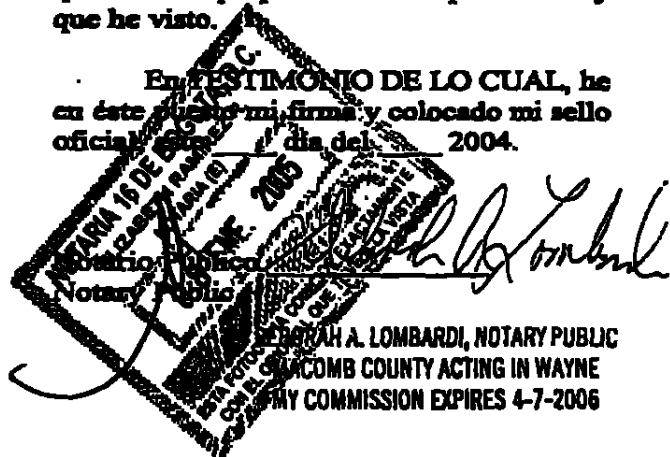
1.- Book of Certificates dated March 22
1993 which for such a purpose was
presented to me and which I have seen.

Certifico lo anterior basado en los
siguientes documentos: 1. - _____
de fecha _____ de 19____,
que con tal propósito me fue presentada y
que he visto.

IN WITNESS WHEREOF, I have
hereunto set my hand and affixed my official
seal this 17 day of Dec, 2004.

En TESTIMONIO DE LO CUAL, he
en éste puesto mi firma y colocado mi sello
oficial este 17 día del 2004.

NOTARIAL SEAL



(Requires legalization by the Consulate of
Colombia)

En conformidad con lo preceptuado por el artículo 8 de la Decisión 486 de la Comisión de la Comunidad Andina y la Resolución 210 del 2001 de la Superintendencia de Industria y Comercio, es esta una TRADUCCION SIMPLE de sellos y legalizaciones en inglés, que aparecen a continuación de un Poder escrito en español e inglés, otorgado por ART JEN COMPLEXUS, INC., sociedad del Estado de Ontario, Canada, al Dr. Camilo Hernando Alvarez Bernate, para asuntos relacionados con derechos de propiedad industrial.

dado en, Octubre 25/04
Por Arthur Barat
 Dignatario Ejecutivo Jefe de Art Jen Complexus, Inc.

Certificado Notarial (Sociedad)

Escrito en inglés y español por un Notario Público del Condado de Macomb, Estado de Michigan, quien certifica que el firmante del documento, Arthur Barat, lo hace en representación de ART JEN COMPLEXUS, INC., sobre la existencia, objeto y domicilio de la sociedad, y sobre los documentos vistos para emitir tal certificación. Fechado el 4 de diciembre, 2004.

Deborah A. Lombardi
Condado de Macomb actuando en Wayne
Mi comisión vence 4-7-2006

APOSTILLE

(Convención de La Haya del 5 de octubre 1961)

1. País: Estados Unidos de América
 El presente documento publico
2. ha sido suscrito por Deborah A. Lombardi
3. actuando en su calidad de Notario Público de Michigan

4. llevando el sello/timbre de Deborah A. Lombardi
Condado de Macomb, Michigan
CERTIFICADO
5. en Lansing, Michigan 6. El 19 de enero, 2005
7. por el Secretario de Estado, Estado de Michigan
8. No. 02548F-05
9. Sello/impresión (Sello)
10. Firma (Firmado)
Terry Lynn Land
-

10

CONTRATO DE CESIÓN / ASSIGNMENT CONTRACT

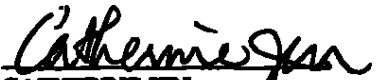
Por el presente documento, CATHERINE JEN, de nacionalidad de los Estados Unidos de America, domiciliada en el 5159 Provincial Drive, Bloomfield Hills, Michigan 48302, Estados Unidos de America y JOSEPH D. ARTISS, de nacionalidad Canadiense, domiciliado en 3117 Curry Avenue, Windsor, Ontario N9E 2T2, Canada (en adelante y para efectos de este contrato denominado "El Cedente"), inventores del invento denominado "COMPOSICIONES QUE COMPRENDEN UN COMPLEJO GRASO DIETETICO Y METODOS PARA SU USO" (en adelante y para efectos de este contrato denominado "El Invento") por el presente cede y transfiere a la sociedad ART JEN COMPLEXUS, INC. (en adelante y para efectos de este contrato denominada "La Cesionaria"), sociedad constituida y existente de conformidad con las leyes del estado de _____, Canada, domiciliada en 510 Westcourt Plaza, 251 Goyeau Street, ciudad de Windsor, estado de Ontario, Canada, todo dominio y derecho de propiedad y todo y cada uno de los derechos y prerrogativas resultantes o que puedan resultar de El Invento, incluyendo el derecho a solicitar, registrar y obtener patente del mismo, así como todo otro derecho de propiedad intelectual que pudiera resultar de El Invento, y todo derecho y privilegio, sin excepción de ninguna clase, sobre El Invento.

En conformidad con lo anterior, La Cesionaria debe ser considerada, a partir de la fecha de este documento, como única propietaria de El Invento, pudiendo explotarlo o disponer del mismo, como mejor quisiera, sin que pueda ser sujeto a reclamo o demanda alguna por parte de El Cedente, en ningún caso y en ningún tiempo, como resultado de esta cesión.

Conste solemnemente, por el presente documento, que La Cesionaria expresamente acepta la cesión y transferencia de El Invento referido.

Para constancia de lo anterior, se suscribe el presente documento por las partes correspondientes, debidamente representadas y autorizadas para hacerlo, este ____ día del mes _____, 2004.

EL CEDENTE/THE ASSIGNOR


CATHERINE JEN
U.S. Passport No. 152323804 USA

 JH139505
JOSEPH D. ARTISS
Canadian Passport No.

By this document CATHERINE JEN, a national of the United States of America, domiciled at 5159 Provincial Drive, Bloomfield Hills, Michigan 48302, United States of America and JOSEPH D. ARTISS, a national of Canada, domiciled at 3117 Curry Avenue, Windsor, Ontario N9E 2T2, Canada (hereinafter and to the effect of this Contract called "The Assignor"), the inventors of the invention called "COMPOSITIONS COMPRISING DIETARY FAT COMPLEXES AND METHODS FOR THEIR USE" (hereinafter and for the effects of this contract called "The Invention"), herewith assigns and transfers to the company ART JEN COMPLEXUS, INC. (hereinafter and to the effects of this Contract called "The Assignee"), a company organized and existing in furtherance of the state of _____, Canada, domiciled at 510 Westcourt Plaza, 251 Goyeau Street, city of Windsor, state of Ontario, Canada, all dominion and all right of ownership and all and every right and privilege resulting of or that could result from the Invention, including the right to file, process and obtain a patent for it, as well as all other intellectual property right that could result of The Invention, and all and every right and privilege, without exception, in The Invention.

In furtherance of the aforementioned, The Assignee must be considered, as of the date of this document, as sole owner of The Invention, being entitled to exploit or transfer it, in any manner that it would wish, not being the subject of any claim or complaint by The Assignor, in any case or time, by reason of this assignment.

It is also attested, by this document, that The Assignee expressly accepts the assignment and transfer of The Invention herein mentioned.

To attest as to the aforementioned, the document is executed by the corresponding parties, duly represented and authorized to do so, this ____ day of the month _____, 2004.

EL CESIONARIO/THE ASSIGNEE

ART JEN COMPLEXUS, INC.


Per By Arthur Barat

Cargo/Position Chief Executive Officer

State of Michigan



DEPARTMENT OF STATE

APOSTILLE

(Convention de La Haye du 5 Octobre 1961)

1. Country: **UNITED STATES OF AMERICA**

This public document

2. has been signed by: **Deborah A. Lombardi**

3. acting in the capacity of: **Michigan Notary Public**

4. bears the seal of: **Deborah A. Lombardi**
Macomb County, Michigan

CERTIFIED:

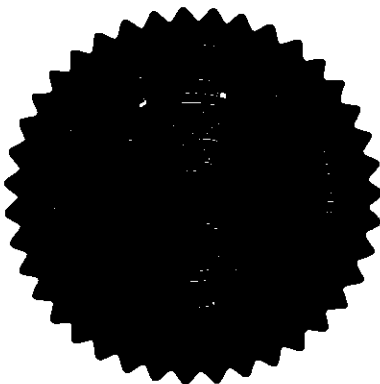
5. at **Lansing, Michigan**

6. the **19th of January, 2005**

7. by **Secretary of State, State of Michigan**

8. NO. **02549F-05**

9. Seal/Stamp:



10. Signature:

A handwritten signature in cursive script, reading "Terri Lynn Land".

Terri Lynn Land

This certification attests only to the authenticity of the signature of the official who signed the attested document, the capacity in which that official acted, and where appropriate, the identity of the party or parties to which the document bears. This certification is not intended to imply that the contents of the document are correct, nor that they have the approval of the State of Michigan.

CANADA)
STATE OF MICHIGAN) SS.
COUNTY OF WAYNE)

CANADA)
ESTADO DE) SS.
CONDADO DE)

DEBORAH A LOMBARDI
I, , a Notary Public in and
for the above mentioned County and State,

Yo, , Notario Publico
en y para el Condado y Estado arriba
señalado,

CERTIFY:

On the 17 day of December, 2004, before
me appeared Arturo Beron, to me known
to be the individual who signed the
foregoing instrument as Chief Executive Officer
of ART JEN COMPLEXUS, INC., a
corporation duly organized and legally
existing under the laws of the State of
Ontario, Canada, with home office located
at 510 Westcourt Place, 251 Goyeau Street,
city of Windsor, State of Ontario N9A 6V2,
Canada.

CERTIFICO:

El día 17 de December, 2004, compareció ante
mi Arturo Beron, a quien conozco y
quien me consta que es la persona que firmo
el instrumento que antecede en su calidad de
Chief Executive Officer de ART JEN
COMPLEXUS, INC., sociedad debidamente
constituida y legalmente existente de
conformidad con las leyes del Estado de
Ontario, Canada, con domicilio situado en
el 510 Westcourt Place, 251 Goyeau Street,
ciudad de Windsor, Estado de Ontario,
Canada.

I further certify that said individual is
duly authorized to sign the foregoing
instrument in the name of said corporation,
and that the purposes for which said
instrument are granted are encompassed
within the corporate purpose of said
corporation.

Además certifico que dicho individuo
se encuentra debidamente facultado para
firmar el instrumento que antecede en
representación de dicha sociedad, y que el
objeto para el que dicho instrumento es
otorgado está comprendido dentro del objeto
social de la sociedad.

In certifying the aforementioned I was
based in the following documents:

- 1.- Birth Certificate dated March
22 1924 which for such a purpose was
presented to me and which I have seen.

Certifico lo anterior basado en los
siguientes documentos: 1. - Birth Certificate
de fecha March 22 de 1924,
que con tal propósito me fue presentada y
que he visto.

IN WITNESS WHEREOF, I have
hereunto set my hand and affixed my official
seal this 4 day of Dec, 2004.

En TESTIMONIO DE LO CUAL, he
en éste puesto mi firma y colocado mi sello
oficial, este 4 día del Dec 2004.

NOTARIAL SEAL

Notario Público
Notary Public

DEBORAH A. LOMBARDI, NOTARY PUBLIC
MACOMB COUNTY ACTING IN WAYNE
MY COMMISSION EXPIRES 4-7-2006

(Requires legalization by the Consulate of
Colombia)

State of Michigan

13



DEPARTMENT OF STATE

APOSTILLE

(Convention de La Haye du 5 Octobre 1961)

1. Country: **UNITED STATES OF AMERICA**

This public document

2. has been signed by: **Brenda S. Batts**

3. acting in the capacity of: **Michigan Notary Public**

4. bears the seal of: **Brenda S. Batts**
Wayne County, Michigan

CERTIFIED:

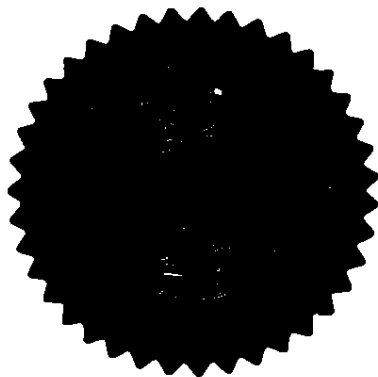
5. at **Lansing, Michigan**

6. the **26th of January, 2005**

7. by **Secretary of State, State of Michigan**

8. NO. **03799W-05**

9. Seal/Stamp:



10. Signature:

A handwritten signature in cursive script, reading "Terri Lynn Land".

Terri Lynn Land

This certification attests only to the authenticity of the signature of the official who signed the enclosed document, the capacity in which that official acted, and where appropriate, the identity of the seal or stamp which the document bears. This certification is not intended to imply that the contents of the document are correct, nor that they have the approval of the State of Michigan.

CANADA)
STATE OF MICHIGAN) SS.
COUNTY OF WAYNE)

BRENDA SUE BATTIS
I, , a Notary Public in and
for the above mentioned County and State,

CERTIFY:
On the 20th day of December, 2004, before
me appeared JOSEPH D. ARTISS, to me
known to be the individual who signed the
foregoing instrument, residing at 3117 Curry
Avenue, Windsor, Ontario N9E 2T2,
Canada.

I further certify that said individual is
duly authorized to sign the foregoing
instrument in his own name.

In certifying the aforementioned I was
based in the following documents:
1. Canadian Passport No. JH139505, dated
March 22, 2004 which for such a purpose
was presented to me and which I have seen.

IN WITNESS WHEREOF, I have
hereunto set my hand and affixed my official
seal this 20th day of December 2004.

NOTARIAL SEAL

BRENDA SUE BATTIS
Notary Public, Wayne County, MI
My Commission Expires Mar. 7, 2006

(Requires legalization by the Consulate of
Colombia)

16
CANADA)
ESTADO DE) SS.
CONDADO DE)

Yo, , Notario Publico
en y para el Condado y Estado arriba
señalado,

CERTIFICO:
El día ___ de ___, 2004, compareció ante
mi JOSEPH D. ARTISS, a quien conozco y
quien me consta que es la persona que firmo
el instrumento que antecede, residente en el
3117 Curry Avenue, Windsor, Ontario N9E
2T2, Canada.

Además certifico que dicho individuo
se encuentra debidamente facultado para
firmar el instrumento que antecede en su
propio nombre.

Certifico lo anterior basado en los
siguientes documentos: 1. - Pasaporte
Canadiense No. ___ de fecha ___
de 19___, que con tal propósito me fue
presentada y que he visto.

En TESTIMONIO DE LO CUAL, he
en éste puesto mi firma y colocado mi sello
oficial, este ___ día del ___ 2004.

Notario Público _____
Notary Public

State of Michigan



DEPARTMENT OF STATE

APOSTILLE

(Convention de La Haye du 5 Octobre 1961)

1. Country: **UNITED STATES OF AMERICA**

This public document

2. has been signed by: **Brenda S. Batts**

3. acting in the capacity of: **Michigan Notary Public**

4. bears the seal of: **Brenda S. Batts**
Wayne County, Michigan

CERTIFIED:

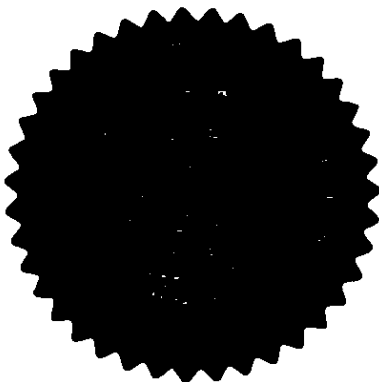
5. at Lansing, Michigan

6. the 26th of January, 2005

7. by Secretary of State, State of Michigan

8. NO. 03800W-05

9. Seal/Stamp:



10. Signature:

A handwritten signature in cursive script, reading "Terri Lynn Land".

Terri Lynn Land

This certification attests only to the authenticity of the signature of the official who signed the official document, the capacity in which that official acted, and where appropriate, the identity of the seal or stamp which the document bears. This certification is not intended to imply that the contents of the document are correct, nor that they have the approval of the State of Michigan.

UNITED STATES OF AMERICA)
STATE OF MICHIGAN) SS.
COUNTY OF WAYNE)

I, BRENDA SUE BATTS,
a Notary Public in and
for the above mentioned County and State,

CERTIFY:

On the 20 day of December, 2004, before
me appeared CATHERINE JEN, to me
known to be the individual who signed the
foregoing instrument, residing at 5159
Provincial Drive, Bloomfield Hills,
Michigan 48302, United States of America.

I further certify that said individual is
duly authorized to sign the foregoing
instrument in her own name.

In certifying the aforementioned I was
based in the following documents:

1.- United States Passport No.
211983344, dated Oct 25,
2004 which for such a purpose was
presented to me and which I have seen.

IN WITNESS WHEREOF, I have
hereunto set my hand and affixed my official
seal this 20th day of December, 2004.

NOTARIAL SEAL
BRENDA SUE BATTS
Notary Public, Wayne County, MI
My Commission Expires Mar. 7, 2008

(Requires legalization by Apostille)

18
ESTADOS UNIDOS DE AMERICA)
ESTADO DE) SS.
CONDADO DE)

Yo, _____, Notario Publico
en y para el Condado y Estado arriba
señalado,

CERTIFICO:

El día 20 de December, 2004, compareció ante
mi CATHERINE JEN, a quien conozco y
quien me consta que es la persona que firmo
el instrumento que antecede, con domicilio
situado en el 5159 Provincial Drive,
Bloomfield Hills, Michigan 48302, Estados
Unidos de América

Además certifico que dicho individuo
se encuentra debidamente facultado para
firmar el instrumento que antecede en su
propio nombre.

Certifico lo anterior basado en los
siguientes documentos: 1. - Pasaporte
de los Estados Unidos de
América No. _____ de fecha _____
de 19____, que con tal propósito me fue
presentado y que he visto.

En TESTIMONIO DE LO CUAL, he
en éste puesto mi firma y colocado mi sello
oficial, este _____ día del _____ 2004.

Notario Público _____
Notary Public _____

En conformidad con lo preceptuado por el artículo 8 de la Decisión 486 de la Comisión de la Comunidad Andina y la Resolución 210 del 2001 de la Superintendencia de Industria y Comercio, es esta una TRADUCCION SIMPLE de sellos y legalizaciones en inglés, que aparecen a continuación de un Contrato de Cesión, escrito en español e inglés, celebrado entre Catherine Jen y Joseph D. Artiss (cedentes) con por Art Jen Complexus, Inc., sociedad del Estado de Ontario, Canada.

El cedente

(firmado)

Catherine Jen

Pasaporte de los E.U. 152323804

(firmado)

Joseph Artiss

Pasaporte Canadiense No. JH139505

El cesionario

Art Jen Complexus, Inc.

(firmado)

Arthur Barat

Director Ejecutivo Jefe

Certificado Notarial (Sociedad)

Escrito en inglés y español por un Notario Público del Condado de Macomb, Estado de Michigan, quien certifica que el firmante del documento, Arthur Barat, lo hace en representación de ART JEN COMPLEXUS, INC., sobre la existencia, objeto y domicilio de la sociedad, y sobre los documentos vistos para emitir tal certificación. Fechado el 4 de diciembre, 2004.

Deborah A. Lombardi

Condado de Macomb actuando en Wayne

Mi comisión vence 4-7-2006

APOSTILLE**(Convención de La Haya del 5 de octubre 1961)**

1. País: Estados Unidos de América
- El presente documento publico
2. ha sido suscrito por Deborah A. Lombardi
3. actuando en su calidad de Notario Público de Michigan
4. llevando el sello/timbre de Deborah A. Lombardi
- Condado de Macomb, Michigan

CERTIFICADO

5. en Lansing, Michigan
6. El 19 de enero, 2005
7. por el Secretario de Estado, Estado de Michigan
8. No. 02549F-05
9. Sello/impresión
10. Firma
- (Sello)
- (Firmado)
- Terry Lynn Land

Certificado Notarial

Escrito en inglés y español por un Notario Público del Condado de Wayne, Estado de Michigan, quien certifica que el firmante del documento, Joseph D. Artiss, lo hace en nombre propio, y sobre los documentos vistos para emitir tal certificación. Fechado el 20 de diciembre, 2004.

Brenda Sue Batts**Notario Público, Condado de Wayne****Mi comisión vence marzo 7, 2006**

APOSTILLE**(Convención de La Haya del 5 de octubre 1961)**

2. País: Estados Unidos de América
El presente documento publico
2. ha sido suscrito por Brenda S. Batts
3. actuando en su calidad de Notario Público de Michigan
4. llevando el sello/timbre de Brenda S. Batts
- Condado de Wayne, Michigan
- CERTIFICADO
5. en Lansing, Michigan 6. El 26 de enero, 2005
7. por el Secretario de Estado, Estado de Michigan
8. No. 03799W-05
- | | |
|-------------------------------|---|
| 9. Sello/impresión
(Sello) | 10. Firma
(Firmado)
Terry Lynn Land |
|-------------------------------|---|

Certificado Notarial

Escrito en inglés y español por un Notario Público del Condado de Wayne, Estado de Michigan, quien certifica que el firmante del documento, Catherine Jen, lo hace en nombre propio, y sobre los documentos vistos para emitir tal certificación. Fechado el 20 de diciembre, 2004.

Brenda Sue Batts
Notario Público, Condado de Wayne
Mi comisión vence marzo 7, 2006

APOSTILLE

(Convención de La Haya del 5 de octubre 1961)

3. País: Estados Unidos de América
El presente documento publico
2. ha sido suscrito por Brenda S. Batts

- 3. actuando en su calidad de Notario Público de Michigan
- 4. llevando el sello/timbre de Brenda S. Batts

Condado de Wayne, Michigan

CERTIFICADO

- 5. en Lansing, Michigan
- 6. El 26 de enero, 2005
- 7. por el Secretario de Estado, Estado de Michigan
- 8. No. 03800W-05
- 9. Sello/impresión (Sello)
- 10. Firma (Firmado)
Terry Lynn Land

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference
(if desired) (22 characters maximum) AJC 201.1PCT

Box No. I TITLE OF INVENTION	
COMPOSITIONS COMPRISING DIETARY FAT COMPLEXER AND METHODS FOR THEIR USE	
Box No. II APPLICANT ☐ This person is also inventor	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)	Telephone No. (248) 701-4722 Facsimile No. (248) 737-6480 Teleprinter No. Applicant's registration No. with the Office
ARTGEN COMPLEXUS, INC. 510 Westcourt Place 251 Goyeau Street Windsor, Ontario N9A 6V2 CANADA	
State (that is, country) of nationality: CA	State (that is, country) of residence: CA
This person is applicant for the purposes of: ☐ all designated States ☒ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box	
Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)	This person is: ☐ applicant only ☒ applicant and inventor ☐ inventor only (If this check-box is marked, do not fill in below.) Applicant's registration No. with the Office
JEN, Catherine 5159 Provincial Drive Bloomfield Hills Michigan 48302 UNITED STATES OF AMERICA	
State (that is, country) of nationality: US	State (that is, country) of residence: US
This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box	
☒ Further applicants and/or (further) inventors are indicated on a continuation sheet.	
Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE	
The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: ☒ agent ☐ common representative	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)	Telephone No. 202 662 0200 Facsimile No. 202 662 4643 Teleprinter No. Agent's registration No. with the Office 36,669
SCHOFIELD, Mary Anne FULBRIGHT & JAWORSKI, LLP. Market Square 801 Pennsylvania Avenue, N.W. Washington, D. C. 20004-2623 United States of America	
☐ Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.	

Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S) <i>If none of the following sub-boxes is used, this sheet should not be included in the request.</i>	
Name and address: <i>(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)</i> ARTISS, Joseph D. 3117 Curry Avenue Windsor, Ontario N9E 2T2 CANADA	This person is: ☐ applicant only ☒ applicant and inventor ☐ inventor only <i>(If this check-box is marked, do not fill in below.)</i> Applicant's registration No. with the Office
State (that is, country) of nationality: CA	State (that is, country) of residence: CA
This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box	
Name and address: <i>(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)</i> 	This person is: ☐ applicant only ☐ applicant and inventor ☐ inventor only <i>(If this check-box is marked, do not fill in below.)</i> Applicant's registration No. with the Office
State (that is, country) of nationality:	State (that is, country) of residence:
This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box	
Name and address: <i>(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)</i> 	This person is: ☐ applicant only ☐ applicant and inventor ☐ inventor only <i>(If this check-box is marked, do not fill in below.)</i> Applicant's registration No. with the Office
State (that is, country) of nationality:	State (that is, country) of residence:
This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box	
Name and address: <i>(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)</i> 	This person is: ☐ applicant only ☐ applicant and inventor ☐ inventor only <i>(If this check-box is marked, do not fill in below.)</i> Applicant's registration No. with the Office
State (that is, country) of nationality:	State (that is, country) of residence:
This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box	
☐ Further applicants and/or (further) inventors are indicated on another continuation sheet.	

Box No. V DESIGNATION OF STATES

Mark the applicable check-boxes below; at least one must be marked.

The following designations are hereby made under Rule 4.9(a):

Regional Patent

- ☐ **AP** ARIPO Patent: GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, MZ Mozambique, SD Sudan, SL Sierra Leone, SZ Swaziland, TZ United Republic of Tanzania, UG Uganda, ZM Zambia, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT (if other kind of protection or treatment desired, specify on dotted line)
- ☐ **EA** Eurasian Patent: AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- ☐ **EP** European Patent: AT Austria, BE Belgium, BG Bulgaria, CH & LI Switzerland and Liechtenstein, CY Cyprus, CZ Czech Republic, DE Germany, DK Denmark, EE Estonia, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, HU Hungary, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, RO Romania, SE Sweden, SI Slovenia, SK Slovakia, TR Turkey, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- ☐ **OA** OAPI Patent: BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GQ Equatorial Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on dotted line)

National Patent (if other kind of protection or treatment desired, specify on dotted line):

- | | | |
|--|---|--|
| ☐ AE United Arab Emirates | ☐ HR Croatia | ☐ OM Oman |
| ☐ AG Antigua and Barbuda | ☐ HU Hungary | ☐ PG Papua New Guinea |
| ☐ AL Albania | ☐ ID Indonesia | ☐ PH Philippines |
| ☐ AM Armenia | ☐ IL Israel | ☐ PL Poland |
| ☐ AT Austria | ☐ IN India | ☐ PT Portugal |
| ☐ AU Australia | ☐ IS Iceland | ☐ RO Romania |
| ☐ AZ Azerbaijan | ☐ JP Japan | ☐ RU Russian Federation |
| ☐ BA Bosnia and Herzegovina | ☐ KE Kenya | |
| ☐ BB Barbados | ☐ KG Kyrgyzstan | ☐ SC Seychelles |
| ☐ BG Bulgaria | ☐ KP Democratic People's Republic of Korea | ☐ SD Sudan |
| ☐ BR Brazil | ☐ KR Republic of Korea | ☐ SE Sweden |
| ☐ BY Belarus | ☐ KZ Kazakhstan | ☐ SG Singapore |
| ☐ BZ Belize | ☐ LC Saint Lucia | ☐ SK Slovakia |
| ☐ CA Canada | ☐ LK Sri Lanka | ☐ SL Sierra Leone |
| ☐ CH & LI Switzerland and Liechtenstein | ☐ LR Liberia | ☐ SY Syrian Arab Republic |
| ☐ CN China | ☐ LS Lesotho | ☐ TJ Tajikistan |
| ☐ CO Colombia | ☐ LT Lithuania | ☐ TM Turkmenistan |
| ☐ CR Costa Rica | ☐ LU Luxembourg | ☐ TN Tunisia |
| ☐ CU Cuba | ☐ LV Latvia | ☐ TR Turkey |
| ☐ CZ Czech Republic | ☐ MA Morocco | ☐ TT Trinidad and Tobago |
| ☐ DE Germany | ☐ MD Republic of Moldova | |
| ☐ DK Denmark | ☐ MG Madagascar | ☐ TZ United Republic of Tanzania |
| ☐ DM Dominica | ☐ MK The former Yugoslav Republic of Macedonia | ☐ UA Ukraine |
| ☐ DZ Algeria | ☐ MN Mongolia | ☐ UG Uganda |
| ☐ EC Ecuador | ☐ MW Malawi | ☐ US United States of America |
| ☐ EE Estonia | ☐ MX Mexico | |
| ☐ ES Spain | ☐ MZ Mozambique | ☐ UZ Uzbekistan |
| ☐ FI Finland | ☐ NI Nicaragua | ☐ VC Saint Vincent and the Grenadines |
| ☐ GB United Kingdom | ☐ NO Norway | ☐ VN Viet Nam |
| ☐ GD Grenada | ☐ NZ New Zealand | ☐ YU Serbia and Montenegro |
| ☐ GE Georgia | | ☐ ZA South Africa |
| ☐ GH Ghana | | ☐ ZM Zambia |
| ☐ GM Gambia | | ☐ ZW Zimbabwe |

Check-boxes below reserved for designating States which have become party to the PCT after issuance of this sheet:

- ☐ ☐ ☐

Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation (including fees) must reach the receiving Office within the 15-month time limit.)

Box No. VI PRIORITY CLAIM				
The priority of the following earlier application(s) is hereby claimed:				
Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is:		
		national application: country or Member of WTO	regional application: regional Office	international application: receiving Office
item (1) 19 August 2002 (19.08.2002)	60/404,366	US		
item (2) 11 April 2003	60/461,847	US		
item (3) 14 July 2003 (14.07.2003)	60/486,440	US		
item (4)				
item (5)				

☐ Further priority claims are indicated in the Supplemental Box.

The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) (only if the earlier application was filed with the Office which for the purposes of this international application is the receiving Office) identified above as:

☒ all items ☐ item (1) ☐ item (2) ☐ item (3) ☐ item (4) ☐ item (5) ☐ other, see Supplemental Box

* Where the earlier application is an ARIPO application, indicate at least one country party to the Paris Convention for the Protection of Industrial Property or one Member of the World Trade Organization for which that earlier application was filed (Rule 4.10(b)(II)):

Box No. VII INTERNATIONAL SEARCHING AUTHORITY	
Choice of International Searching Authority (ISA) (if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):	
ISA / US	
Request to use results of earlier search; reference to that search (if an earlier search has been carried out by or requested from the International Searching Authority):	
Date (day/month/year)	Number Country (or regional Office)

Box No. VIII DECLARATIONS		
The following declarations are contained in Boxes Nos. VIII (i) to (v) (mark the applicable check-boxes below and indicate in the right column the number of each type of declaration):		Number of declarations
☐ Box No. VIII (i)	Declaration as to the identity of the inventor	:
☐ Box No. VIII (ii)	Declaration as to the applicant's entitlement, as at the international filing date, to apply for and be granted a patent	:
☐ Box No. VIII (iii)	Declaration as to the applicant's entitlement, as at the international filing date, to claim the priority of the earlier application	:
☐ Box No. VIII (iv)	Declaration of inventorship (only for the purposes of the designation of the United States of America)	:
☐ Box No. VIII (v)	Declaration as to non-prejudicial disclosures or exceptions to lack of novelty	:

Box No. IX CHECK LIST; LANGUAGE OF FILING		
This international application contains: (a) In paper form, the following number of sheets: request (including declaration sheets) : 5 description (excluding sequence listings and/or tables related thereto) : 45 claims : 8 abstract : 1 drawings : 8 Sub-total number of sheets : 65 sequence listings : tables related thereto : <i>(for both, actual number of sheets if filed in paper form, whether or not also filed in computer readable form; see (c) below)</i> Total number of sheets : 65 (b) ☐ only in computer readable form (Section 801(a)(i)) (i) ☐ sequence listings (ii) ☐ tables related thereto (c) ☐ also in computer readable form (Section 801(a)(ii)) (i) ☐ sequence listings (ii) ☐ tables related thereto Type and number of carriers (diskette, CD-ROM, CD-R or other) on which are contained the ☐ sequence listings : ☐ tables related thereto : <i>(additional copies to be indicated under items 9(ii) and/or 10(ii), in right column)</i>		This international application is accompanied by the following item(s) (mark the applicable check-boxes below and indicate in right column the number of each item): 1. ☒ fee calculation sheet : 1 2. ☒ original separate power of attorney : 3 3. ☐ original general power of attorney : 4. ☐ copy of general power of attorney; reference number, if any: : 5. ☐ statement explaining lack of signature : 6. ☐ priority document(s) identified in Box No. VI as item(s): : 7. ☐ translation of international application into (language): : 8. ☐ separate indications concerning deposited microorganism or other biological material : 9. ☐ sequence listings in computer readable form (indicate type and number of carriers) (i) ☐ copy submitted for the purposes of international search under Rule 13ter only (and not as part of the international application) : (ii) ☐ (only where check-box (b)(i) or (c)(i) is marked in left column) additional copies including, where applicable, the copy for the purposes of international search under Rule 13ter : (iii) ☐ together with relevant statement as to the identity of the copy or copies with the sequence listings mentioned in left column : 10. ☐ tables in computer readable form related to sequence listings (indicate type and number of carriers) (i) ☐ copy submitted for the purposes of international search under Section 802(b-quater) only (and not as part of the international application) : (ii) ☐ (only where check-box (b)(ii) or (c)(ii) is marked in left column) additional copies including, where applicable, the copy for the purposes of international search under Section 802(b-quater) : (iii) ☐ together with relevant statement as to the identity of the copy or copies with the tables mentioned in left column : 11. ☐ other (specify): :
Figure of the drawings which should accompany the abstract: 3	Language of filing of the international application: English	

Box No. X SIGNATURE OF APPLICANT, AGENT OR COMMON REPRESENTATIVE
Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).

Mary Anne Schofield July 29, 2003
 Mary Anne Schofield, Esq. Date

For receiving Office use only	
1. Date of actual receipt of the purported international application:	2. Drawings: ☐ received: ☐ not received:
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:	
4. Date of timely receipt of the required corrections under PCT Article 11(2):	
5. International Searching Authority (if two or more are competent): ISA /	6. ☐ Transmittal of search copy delayed until search fee is paid

For International Bureau use only
Date of receipt of the record copy by the International Bureau:

28

This sheet is not part of and does not count as a sheet of the international application.

PCT

FEE CALCULATION SHEET Annex to the Request

For receiving Office use only

International Application No.

Date stamp of the receiving Office

Applicant's or agent's
file reference

AJC 201.1PCT

Applicant

ARTGEN COMPLEXUS, INC.

CALCULATION OF PRESCRIBED FEES

1. TRANSMITTAL FEE 240.00 **T**

2. SEARCH FEE 450.00 **S**

International search to be carried out by US
(If two or more International Searching Authorities are competent to carry out the international search, indicate the name of the Authority which is chosen to carry out the international search.)

3. INTERNATIONAL FEE

Basic Fee

Where items (b) and/or (c) of Box No. IX apply, enter Sub-total number of sheets } 67
Where items (b) and (c) of Box No. IX do not apply, enter Total number of sheets }

b1 first 30 sheets 476.00 **b1**

b2 37 x 12.00 = 444.00 **b2**
number of sheets in excess of 30 fee per sheet

b3 additional component (only if sequence listings and/or tables related thereto are filed in computer readable form under Section 801(a)(i), or both in that form and on paper, under Section 801(a)(ii)):

400 x = **b3**
fee per sheet

Add amounts entered at b1, b2 and b3 and enter total at B 920.00 **B**

Designation Fees

The international application contains 811 designations.

5 x 104.00 = 520.00 **D**
number of designation fees payable (maximum 5) amount of designation fee

Add amounts entered at B and D and enter total at I 1,440.00 **I**

(Applicants from certain States are entitled to a reduction of 75% of the international fee. Where the applicant is (or all applicants are) so entitled, the total to be entered at I is 25% of the sum of the amounts entered at B and D.)

4. FEE FOR PRIORITY DOCUMENT (if applicable) 60.00 **P**

5. TOTAL FEES PAYABLE 2,190.00

Add amounts entered at T, S, I and P, and enter total in the TOTAL box

TOTAL

☐ The designation fees are not paid at this time.

MODE OF PAYMENT

☐ authorization to charge deposit account (see below) ☐ postal money order ☐ cash ☐ coupons
☒ cheque ☐ bank draft ☐ revenue stamps ☐ other (specify):

AUTHORIZATION TO CHARGE (OR CREDIT) DEPOSIT ACCOUNT (This mode of payment may not be available at all receiving Offices)

☐ Authorization to charge the total fees indicated above.
☒ (This check-box may be marked only if the conditions for deposit accounts of the receiving Office so permit) Authorization to charge any deficiency or credit any overpayment in the total fees indicated above.
☐ Authorization to charge the fee for priority document.

Receiving Office: RO/ US

Deposit Account No.: 06-2375

Date: July 29, 2003

Name: Mary Anne Schofield

Signature: Mary Anne Schofield

COMPOSITIONS COMPRISING DIETARY FAT COMPLEXER AND METHODS FOR THEIR USE

This application claims priority to U.S. provisional patent applications Serial No. 60/486,440 filed July 14, 2003, Serial No. 60/461,847 filed April 11, 2003, and Serial No. 60/404,366 filed August 19, 2002, all incorporated herein in their entirety by reference.

FIELD OF THE INVENTION

This invention relates to consumable products, particularly fat-containing consumable products, comprising α -cyclodextrin and methods of their use. The invention also relates to methods of reducing the bioavailability of fats in fat containing consumable products and to methods for enhancing organoleptic properties of fat containing consumable products.

BACKGROUND OF THE INVENTION

Efforts to control body weight through diet, exercise and drugs have met with only limited success. Obesity continues to be of epidemic proportions in the USA. It was estimated that in 2000, more than 64.5% of the US adult population were overweight or obese and across the US, 30.5% of the population were obese (Flegal et al., *JAMA* 288: 1723-1727 (2002)). There also appears to be a US epidemic in diabetes with 7.3% of the US population being diabetic (Mokdad et al., *JAMA* 286: 1195-1200 (2001)). While physicians advise their patients battling with weight gain, obesity and diabetes to exercise and manage the quantity as well as the quality of food eaten, the evidence suggests that a major portion of the population are unable or unwilling to make the major changes in lifestyle that may be necessary to decrease their body mass.

The strategies recommended by health care providers to reduce and/or maintain weight often involve changes in life style and in some cases the additional use of drugs or dietary supplements. Those individuals that are able to maintain weight loss (defined as >10% below the initial body weight after one year) generally adopt all or at least some combination of these strategies (McGuire et al., "Behavioral strategies of individual who have maintained long-term weight losses" *Obes Res* 7:334-341 (1999)). Nonetheless, despite all of the efforts made by obese individuals and governments, the success rate for keeping weight off is disappointingly low. A meta-analysis has shown that the success rate of "self-cure" ranged from 9% to 43% after a one-year follow-up (Bartlett et al., "Is the prevalence of successful weight loss and maintenance higher in the general community than the research

clinic?" *Obes Res* 7:407-413 (1999)). The National Weight Control Registry has reported that 47%-49% of the obese patients maintained at least 10% weight loss after one year and 25% - 27% have maintained this amount of weight loss over 5 years (McGuire et al., "The prevalence of weight loss maintenance among American adults" *Int J Obes Metab Disord* 23:1314-1319 (1999)). However, after 5-15 years, only 5% of the obese patients were able to maintain the weight loss (Drenick and Johnson, "Weight reduction by fasting and semistarvation in morbid obesity: long term follow-up". *Int. J. Obes.* 2:25-34 (1978) and Sarlio-Lahteenkorva and Rissanen "A descriptive study of weight loss maintenance: 6 and 15 years follow-up of initially overweight adults" *Int J Obes* 24:116-125 (2000)).

Pharmaceutical treatments for obesity have been developed but their use has limitations. Currently there are only two Food and Drug Administration (FDA) approved antiobesity drugs, Orlistat and Sibutramine. Orlistat inhibits pancreatic lipase activity in the small intestine. Pancreatic lipase breaks down triglycerides into fatty acids and monoglycerides which are subsequently absorbed into the body. Thus inhibition of lipase activity effectively reduces fat absorption. However, if the patient fails to follow a reduced fat diet, which is recommended while on this medication, the fat is metabolized by the intestinal bacteria and causes osmotic shifts and gas production resulting in diarrhea and flatulence, rather unpleasant side effects of this medication. Thus, while this drug can induce modest weight loss and better weight maintenance than diet alone, in the absence of major dietary changes the adverse effects of gastrointestinal discomfort, diarrhea and flatulence have limited its use (Heck et al., "Orlistat, a new lipase inhibitor for the management of obesity". *Pharmacotherapy* 20:270-279(2000)).

Sibutramine is a serotonin and norepinephrine reuptake inhibitor and reduces body weight by suppressing appetite (Bray G., "Drug treatment of obesity". *Rev Endocr Metab Disord* 2:403-418(2001)). FDA has approved it for the treatment of obesity for up to 2 years. However, Sibutramine inhibits the reuptake of norepinephrine and thus may increase blood pressure. Therefore this drug is contraindicated for use in some obese patients (Bray 2001 *supra* and Sramek et al. "Efficacy and safety of sibutramine for weight loss in obese patients with hypertension well controlled by beta-adrenergic blocking agents: a placebo-controlled, double-blind, randomized trial" *J Hum Hypertens* 16:13-19 (2002)). Other side effects of Sibutramine include increased heart rate, insomnia, constipation, headache, abdominal pain etc. For normotensive obese patients, Sibutramine in combination of diet and behavioral

modifications has shown beneficial effects (Astrup and Toubro "When, for whom and how to use sibutramine?" *Int J Obes Relat Metab Disord* 25 (suppl 4):S2-S7 (2001)) but to date there have been no human studies that used Sibutramine alone, that is without any life-style modifications. In addition, in one animal study, the appetite suppressing effects of Sibutramine gradually attenuated over several days of administration (Strack et al. "Regulation of body weight and carcass composition by sibutramine in rats" *Obes Res* 10:173-181 (2002)).

Dietary supplements have also been used to reduce weight gain, to maintain weight and to treat some of the metabolic abnormalities associated with obesity. For example, omega 3-fatty acids and linolenic acid have been shown to reduce weight gain and affect triglyceride levels and/or insulin resistance. Omega 3 fatty acids are known to reduce blood lipid levels in normal, hyperlipidemic and diabetic humans and have been reported to decrease body weight. Diabetic patients without hyperlipidemia fed a diet comprising fish oil, which is known to be high in omega 3 fatty acid, did not display reduced blood lipid levels, although their blood pressures were reduced. However, diabetic patients having hyperlipidemia had significantly reduced blood triglyceride levels and reduced blood pressure after the omega 3 fatty acid fish oil feeding (Kasmin et al. *J. Clin Endocrinol Metab* 67:1-5 (1988)). The effect of diets comprising fish oil fed to genetically obese Zucker rats and their lean counterparts demonstrated that both the obese and normal rats had a reduction in body weight and blood lipid levels as compared to controls (Jen et al., *Nutrition Research* 9:1217-1228 (1989)). A high fat diet made with fish oil induced the least amount of weight gain and insulin resistance compared to a high fat diet made with other types of oil (Pellizzon et al., *Obesity Res.* 10:947-955 (2002)). Omega 3 fatty acids also appear to beneficially affect insulin resistance. Rats fed high fat diets comprising fish oil had less insulin resistance than rats fed diets comprising other oils, e.g., lard, corn oil or medium chain triglycerides (Hill et al. *Int. J. Obesity*, 17:223-236 (1993)).

Linolenic acid added to diets has also been shown to reduce body fat content and to facilitate fatty acid β -oxidation in the liver (Takada et al., *J. Nutr.* 124:469-474 (1994)). Aged rats were fed diets made with various fatty acids, i.e., α -linolenic acid (n-3 PUFA) or gamma linolenic acid (n-6 PUFA) (10% w/w) with added cholesterol for 15 weeks and it was found that both the α -and gamma linolenic diets inhibited the increase in blood total cholesterol, VLDL+IDL+LDL cholesterol levels in the rats when fed high cholesterol diets

(Fukushima et al. *Lipids* 36:261-266 (2001)). Similar results were found in obese Zucker rats which had reduced body weight gain and body fat when gavaged daily with gamma linolenic acid (Phinney et al. *Metabolism* 42:1127-1140 (1993)). In humans, a mixture of n-3 PUFA and gamma linolenic acid also favorably altered blood lipids and fatty acid profiles in women
5 after administration for about 28 days (Laidlaw and Holub, *Am J. Clin. Nutr.* 77:37-42 (2003)).

Life style changes to promote weight loss and other beneficial health effects include e.g. an increase in physical activity; a reduced caloric intake and a reduced dietary fat intake. The United States has seen a gradual reduction in the percentage of dietary fat intake from
10 43.7% in 1965 to 33.1 % in 1995 (Kennedy et al., "Dietary-fat intake in the US population" *J Am Coll Nutr* 18:207-212 (1999)), however, the average number of calories eaten has increased more than the increase in fat consumption. Therefore even though the percentage of dietary fat intake has decreased, the total fat intake has increased since 1995 to 100.6 g (males). Due to the relative ease with which dietary fat is converted to adipose tissue, a diet
15 high in fat leads to an elevated weight gain as compared to a lower fat diet even though the calorie intake is comparable. This phenomenon has been reported to occur in both humans and rats (Astrup et al., "Obesity as an adaptation to a high-fat diet: evidence from a cross-sectional study" *Am J Clin Nutr*;59:350-355 (1994)); (Jen "Effects of diet composition on food intake and carcass composition in rats" *Physiol Behav* 42:551-556 (1988) and; Jen et al.,
20 "Long-term weight cycling reduces body weight and fat free mass, but not fat mass in female Wistar rats" *Int J Obesity* 19:699-708 (1995)).

Various low fat and/or low calorie foods have been developed in an effort to promote weight loss or inhibit weight gain. Many "low fat" foods are prepared by reducing the percentage of fat but the percentage of carbohydrates in the foods is increased to make the
25 foods more palatable by compensating for the loss of the taste and texture provided by the fat. Increasing the amount of carbohydrates, e.g., sugars, in the food often make the foods "low fat" but the caloric content may not be reduced and in many instances is actually increased. Many low calorie food are prepared by simply replacing the caloric components of the food with a non-caloric filler, e.g., a dietary fiber. However, replacing significant portions of
30 carbohydrates with fiber fillers often alters the taste and texture of the food making the food less palatable for some consumers. In addition, consumption of large amounts of dietary fiber often have unwanted side effects such as e.g., flatulence, and a diet comprising more

than about 60g fiber may result in deficiencies in calcium, iron, zinc and increased risk of bowel obstruction. While high fiber diets, comprising about 25-35g/d are recognized as having beneficial effects, e.g., reducing blood triglycerides and cholesterol levels, many persons should not take high levels of fiber, e.g., the elderly, growing children and those suffering from particular medical conditions e.g., acute or subacute diverticulitis, and the acute phases of certain inflammatory conditions of the bowel, e.g., ulcerative colitis or Crohn's disease. After some types of intestinal surgery, e.g., a colostomy or ileostomy, a low fiber, low residue diet is used as a transition to a regular diet is preferred. Thus it is desirable to develop a food product that has the taste and texture desired by consumers but also reduces weight gain, blood triglycerides and cholesterol levels and is not necessarily high fiber.

Cyclodextrins are a family of cyclic polymers of glucose produced by enzymatic digestion of cornstarch with a cyclodextrin glyceryltransferase. α -, β - and γ -cyclodextrins contain 6, 7 and 8 glucose molecules and take on a toroid or truncated cone conformation in aqueous solution. The molecules have a hydrophobic interior and hydrophilic exterior forming an internal pore. The different polymer lengths yield different pore sizes.

The unique properties of β and γ -cyclodextrins have been exploited in a variety of fields. For example, they have been used to stabilize and solubilize drugs and also to enhance food flavors. While the β and γ -cyclodextrins have found considerable use in the pharmaceutical and food industries, α -cyclodextrin has found relatively little use in these industries because of its small pore size as well as the fact that it does not appear to be metabolized by pancreatic amylase or intestinal flora (Suzuki and Sato, "Nutritional significance of cyclodextrins: indigestibility and hypolipemic effect of α -cyclodextrin" *J Nutr Sci Vitaminol* (Tokyo) 1985; 31:209-223), although this latter aspect has been disputed by one of the manufacturers of the material (Antisperger G SG. "Toxicological comparison of cyclodextrins" presented in the 8th International Cyclodextrin Symposium in Budapest 1996:1-7). α -cyclodextrin efficiently complexes free fatty acids (FFA) in solution (McGowan et al. "A peroxidase-coupled method for the colorimetric determination of serum triglycerides" *Clin. Chem.* 29(3):538-542 (1983)) and has been used to eliminate the turbidity caused by FFA in a number of clinical diagnostic reagents (Morgan, Artiss and Zak "A study of turbidity in hypertriglyceridemic specimens" *Microchem. J.* 64:147-154(2000)). α -cyclodextrin has also been used for the specific and selective removal of free fatty acids from used cooking oil (US Patent No. 5,560,950).

Previous studies disclose that α -cyclodextrin is essentially indigestible and may exert an effect on weight gain only if it exceeds about 20% of the total dietary intake, as determined in a rat model. Japanese patent application JP 05-298849 (Publ. No. 07115934) assays the effects of linolenic acid and α -cyclodextrin on weight gain in rats. This application reports that rats fed diets comprising either 16% α -cyclodextrin or 1% linolenic acid gain weight approximately the same as rats fed a control diet. In contrast, this Japanese application discloses that rats fed diets comprising a combination of 14% α -cyclodextrin and 2% linolenic acid incur significant weight loss. Japanese patent application S60-149752 also analyzes the effect of linolenic acid in combination with α -cyclodextrin on weight gain in rats. This application reports that a diet comprising 14% w/w α -cyclodextrin has little effect on weight gain in rats while the combination of 14% w/w α -cyclodextrin and 0.5%w/w linolenic acid produces significant weight loss. Japanese patent application H5-298850 analyzes the effects of diets comprising linolenic acid (1.5-2%w/w) and α -cyclodextrin (14%w/w) and a barley green element. This application reports that the diets comprising 14%w/w α -cyclodextrin in combination with 1.5-2% w/w linolenic acid produce only a small decrease in body weight while the addition of a barley green element to the linolenic acid and cyclodextrin results in significant reduction in weight gain. This application does not report the effects of diets comprising only α -cyclodextrin as the additional component. None of these applications discloses the fat content of the diets and they teach the importance of additional ingredients and/or the ineffectiveness of α -cyclodextrin alone.

Japanese patent application H4-333575 supplemented the diet of rats with particular total amounts of linolenic acid and/or α -cyclodextrin and/or a peptide hydrollysate by gavaging rats with wheat starch compositions comprising either 0.9%w/w linolenic acid alone, 9% w/w α -cyclodextrin alone, or 100%w/w of a compositions of small molecular weight hydrolytes of a larger molecular weight protein, or with compositions comprising combinations of the three components. The fat content of the diets was not described. Only the diets containing a combination of linolenic acid, α -cyclodextrin and the peptide hydrollysate displayed a significant change in the rate of weight gain over time.

Japanese applications JP05-113603 (Publ. No. 08187060) and JP05-164024 (Publ. No. 06343419) assay the effect of a mixture of about 15% α -cyclodextrin and 1.5% linolenic acid on weight gain in humans. The applications disclose that subjects ingesting the α -cyclodextrin/linolenic acid compositions in an amount based on their body weight, such that

the daily dose of the composition was about 0.015g/kg body weight three times a day, which is 1.37g/91kg (200lb) individual three times per day, which corresponds to 4.11 g of total composition per day or 0.62 g α -cyclodextrin per day (0.21g/meal) and 0.068 g linolenic acid per day (0.023 g/meal), display a significant increase in weight loss as compared to subjects who did not ingest the combination. However, these applications did not assay the effect of α -cyclodextrin alone or linolenic acid alone nor did they disclose the fat content of the diets. Linolenic acid is well known to reduce weight and fat gain in both animal and human studies (Jen et al., *Nutri. Res* 9:1217-1228 (1989) and Takada et al., *J. Nutri.* 124:469-474 (1994) and Couet et al. *Int. J. Obes.* 21:637-643 (1997)) and is likely to be the component that actually promoted the observed weight loss reported in these applications.

U.S. Patent 4,880,573 discloses a process for eliminating cholesterol from fatty substances of animal origin, e.g. lard, suet or butter. The process combines β -cyclodextrin with the liquified fatty substance under a non-oxidizing atmosphere and then removes the complexes of cholesterol and cyclodextrin leaving a fatty substance free of cyclodextrin and with a reduced cholesterol content.

U.S. Patent 5,189,149 discloses the use of complexes of cyclodextrins and long chain fatty acids, their salts and esters, inclusive of fish and vegetable oil glycerides, to deliver long chain fatty acids to a subject and avoid the unctuous characteristics associated with the fish and vegetable oil glycerides and their unpleasant taste and odor.

U.S. Patent 5,232,725 relates to a process for reducing the cholesterol and free fatty acids in a fat containing material, e.g., fresh cream, by combining water, the fat containing material and cyclodextrin under conditions suitable for forming an oil-in-water type "fine" emulsion, which facilitates the formation of complexes of cyclodextrin and cholesterol or free fatty acids. The complexes are then mechanically separated to produce a fat-containing material with reduced levels of cholesterol and free fatty acids. U.S. 5,232,725 does not describe a food product comprising complexes of triglyceride and α -cyclodextrin, wherein the bioavailability of the fat in the food product is reduced, as described herein.

U.S. Patent 5,560,950 relates to a process for reducing the free fatty acid content of a used oil by mixing the used oil with cyclodextrin, preferably with an absorbent, e.g., silica, under conditions that form agglomerates of cyclodextrin/absorbent and fatty acids and then

removing the cyclodextrin agglomerates from the oil. The process produces a oil that is cyclodextrin free and has a reduced level of free fatty acids.

U.S. Patent 5,571,554 relates to a process for reducing triglycerides in an egg yolk by preparing a mixture of egg yolk with water, or a salt solution, and combining the mixture with a cyclodextrin and then removing the cyclodextrin and the added water or salt solution. The process produces a cyclodextrin free egg yolk product with reduced levels of triglycerides.

U.S. Patent 5,738,898 relates to a process for reducing cholesterol in egg yolk by preparing a mixture of egg yolk, water and cyclodextrin at a pH between 7.5 and 12. The cyclodextrin cholesterol complexes are removed and the pH adjusted to pH 6-7. The process produces a cyclodextrin free egg yolk product with reduced cholesterol.

Many consumers, including obese individuals, appear to have a preference for foods that have a high fat content (Mela and Sacchetti, "Sensory preferences for fats: relationships with diet and body composition" *Am J Clin Nutr* 1991;53:908-915). Thus, it is very difficult for many individuals, particularly obese individuals, to reduce their fat intake in order to reduce their body weight and the adverse health effects associated with increased weight gain. Therefore, a substance that reduces the absorption of dietary fat without the unpleasant side effects of the current medications is extremely desirable. Such a substance would have significant health benefits in reducing obesity and its related disorders, such as Type II diabetes (NIDDM). It would be desirable to develop a food product that promotes weight loss, reduces lipid levels and reduces the symptoms of other disorders associated with weight gain/obesity and yet has desirable organoleptic properties. Described herein are fat containing consumable products having the organoleptic properties such as taste, texture and moistness that consumers desire and yet promote weight loss and other health benefits.

SUMMARY OF THE INVENTION

This invention relates to a fat containing consumable food product that comprises α -cyclodextrin and fat wherein the ratio of α -cyclodextrin to fat is about 1:20 w/w - 1:3 w/w. Preferably the ratio of α -cyclodextrin to fat is about 1:13 w/w - 1:5 w/w, and most preferably the ratio of α -cyclodextrin to fat is about 1:9 w/w. The total cyclodextrin in the foods of this invention is less than about 9-10% w/w, preferably less than about 6%, and more preferably

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below 3%w/w, and particularly in the case of fat containing consumable farinaceous food products of this invention the amount of total cyclodextrin is below about 3% w/w. Preferably the fat containing food products of this invention comprise, by caloric content, about 7% to about 80% fat, preferably about 20% to about 70% fat, more preferably about 5 40% to about 70% fat, or by weight, 5% to about 50% w/w fat, preferably about 5-30% w/w fat, and more preferably about 7-25% w/w fat. "Fats" as defined herein are triglycerides. Cyclodextrins are often sold as mixtures of α , β -, γ -cyclodextrin and n-dextrin. Preferably the α -cyclodextrin composition that may be used in the products and methods of this invention, is a substantially pure α -cyclodextrin comprising at least about 95% α -cyclodextrin, preferably 10 at least 98% α -cyclodextrin. The α -cyclodextrin in the foods herein may provide a source of fiber in addition to its other beneficial effects. The consumable products may be a farinaceous food product or a non-farinaceous food product, e.g., a dairy food product, a prepared vegetable product, or a prepared meat product, e.g. a prepared beef, lamb, pork, poultry or seafood food product. The consumable food products of this invention are suitable 15 for consumption by mammals, e.g., mice, rats, cats, dogs and humans but preferably humans.

Cyclodextrins have been used previously in methods to reduce the levels of free fatty acids, cholesterol or triglycerides in food products but in contrast to the food products of this invention, those methods produced products that are essentially cyclodextrin free and have reduced levels of free fatty acids, cholesterol and triglycerides as compared to a like food 20 product that has not been treated. If assayed by bomb calorimetry, the products produced by those methods will have a lower caloric content due to the reduced levels of cholesterol and triglycerides. The consumable food products of this invention comprise α -cyclodextrin and do not have reduced levels of fatty acids, cholesterol or triglycerides as compared to a like food product without the added α -cyclodextrin. As such, the consumable products of this 25 invention do not have a substantially reduced caloric content, as assayed by bomb calorimetry, as compared to a like product that does not contain α -cyclodextrin, and yet the food products of this invention inhibit the rate of weight gain, promote weight loss and provide other health benefits. Thus the consumable food product of this invention is a diet food that inhibits the rate of weight gain, promotes weight loss and provides other health 30 benefits.

Shimada et al. (Shimada et al. "Structure of inclusion complexes of cyclodextrins with triglyceride at vegetable oil/water interface" *J. Food Sci.* 1992; 57(3):655-656) reported that

two molecules of α -cyclodextrin complex with one fatty acid group (FFA), while Szejtli (Szejtli J. "Utilization of cyclodextrins in industrial products and processes" *J. Mater. Chem.* 1997;7:575-587) suggests that this phenomenon is dependent upon the chain length of the fatty acids and that it is possible for 3-4 molecules of α -cyclodextrin to complex with each of the three fatty acids of a triglyceride molecule, which suggests 9-12 molecules of α -cyclodextrin would be required to completely complex one molecule of triglyceride. If this were the case it would be difficult to imagine being able to feed enough α -cyclodextrin to an animal to complex sufficient amounts of triglycerides to make a significant difference in body weight.

Suzuki et al. *infra* and Kaewprasert et al. *infra* both report that a cyclodextrin composition alone mixed into a food does not promote significant weight loss, even at concentrations of 20% w/w of total dietary intake. In particular, Suzuki et al., *Denpun Kagaku* 30(2):240-246 (1983) analyzed the effect of a diet comprising 20% cyclodextrin on the weight gain of rats and reported that there were no differences in the weight gain of rats fed a 20% cyclodextrin diet and those fed a 20% starch diet. Likewise, Kaewprasert et al., *J. Nutri. Sci. Vitaminol.* 47:335-339 (2001) reported that the body weight gain in rats fed a 5% α -cyclodextrin diet was not significantly different from rats fed control diets. Kaewprasert discloses a diet comprising cyclodextrin and fat at a ratio of about 1:1.4. Suzuki did not discuss the fat content of the experimental diets or disclose the ratio of cyclodextrin to fat in the diet. This effect of relatively large amounts of cyclodextrin was also noted in Japanese application S60-094912. S60-094912 suggests that cyclodextrins may inhibit the rate of weight gain and decrease neutral fat (triacylglycerides) in liver and plasma, but only if cyclodextrin is administered at levels of 20% w/w and more. If the α -cyclodextrin is less than 20% of the total dietary intake, S60-094912 reports there is no significant difference in weight loss as compared to a control diet. Likewise Suzuki and Sato, *J. Nutri. Sci. Vitaminol.* 31:209-223 (1985) report that rats fed diets comprising a mixture of α -dextrin and α -, β - and γ - cyclodextrins (50:30:15:5% w/w) displayed a weight loss substantially different from the control group only when at least 58.5% w/w of the diet consisted of the cyclodextrin mixture. In contrast, we have found that significant weight loss can be obtained in subjects with much lower levels of α -cyclodextrin if the subjects are consuming fat containing diets and the ratio of ingested α -cyclodextrin to ingested fat in the diet is sufficient to form complexes of fat and cyclodextrin. The body naturally forms a fine emulsion of fat in water, which is necessary for lipase to catalyze the hydrolysis of fat. Without wishing to be bound by theory, the

invention described herein disrupts this process by forming large complexes of α -cyclodextrin and fat so that the lipase cannot act on the fat. Thus the fat in the fat containing food products of this invention is not bioavailable because it is in the form of α -cyclodextrin/fat complexes that are resistant to lipase activity.

5 The levels of cyclodextrin in the foods of this invention are well below the levels that S60-94912 and Suzuki and Sato (*J Nutri Sci Vitaminol* 1985 *supra*) indicate are necessary for weight loss. The total cyclodextrin in the foods of this invention is less than about 9% w/w, preferably less than about 6% w/w, and more preferably below 3%w/w, particularly in the case of the consumable farinaceous food products of this invention. Subjects fed a diet
10 comprising the α -cyclodextrin-containing foods of this invention, preferably those which comprise the amounts of α -cyclodextrin disclosed herein and wherein the α -cyclodextrin to fat ratio is within the ratios disclosed herein, display *inter alia* weight loss, increase in HDL levels and a reduction in blood triglycerides.

Without wishing to be bound by theory, the results presented herein suggest that the
15 α -cyclodextrin is particularly suitable for complexing fat in a food composition thereby reducing the fat's bioavailability. By ingesting α -cyclodextrin in an appropriate amount with a fat-containing meal, or shortly before or after ingesting a fat-containing meal, a subject may complex the ingested fat and inhibit its absorption by the body. The amount of α -cyclodextrin should be sufficient to form complexes with the fat thereby reducing the fat
20 bioavailability, preferably the amount of α -cyclodextrin is sufficient to obtain a ratio of α -cyclodextrin to fat of 1:20 to 1:3, preferably 1:13 to 1:5 and more preferably about 1:9 such that complexes of fat and cyclodextrin are formed. Without wishing to be bound by theory, it is the reduction in the bioavailability of the ingested fat (the amount of ingested fat that is absorbed and thus available to the body for use) that results in, e.g., the observed weight loss,
25 increase in HDL cholesterol, decreased leptin levels and reduction in serum triglycerides.

This invention also relates to methods for complexing fat contained in an ingested food product, particularly a high fat food product, thus reducing the bioavailability of the ingested fat. The method comprises ingesting an amount of an α -cyclodextrin with a food product such that the ratio of α -cyclodextrin to fat of about 1:20 to about 1:3 w/w preferably
30 about 1:13 to about 1:5 w/w most preferably about 1:9 w/w. The α -cyclodextrin may be ingested prior to, concurrently with or subsequent to ingestion of the food product. At such ratios the fat is complexed with the α -cyclodextrin and the bioavailability of the ingested fat

is reduced. Alternatively the α -cyclodextrin may be combined with the food product prior to consumption in an amount such the ratio of α -cyclodextrin to fat in the ingested food product is about 1:20 to about 1:3 w/w preferably about 1:13 to about 1:5 w/w most preferably about 1:9 w/w and the food product comprising the α -cyclodextrin and fat is ingested.

5 This invention also relates to methods for producing a fat containing food product having fat with reduced bioavailability by forming complexes of α -cyclodextrin and fat within the food product, particularly a high fat food product. The method comprises combining α -cyclodextrin with a food product under conditions that favor the formation of
10 complexes of fat and α -cyclodextrin, wherein the conditions avoid the formation of a fine emulsion of fat within the food product. The amount of an α -cyclodextrin is such that the food product comprises a ratio of α -cyclodextrin to fat of about 1:20 to about 1:3 w/w preferably about 1:13 to about 1:5 w/w most preferably about 1:9 w/w. At such ratios and under such conditions, the fat is complexed with the α -cyclodextrin the bioavailability of the ingested fat is reduced. The food product may be a farinaceous food product e.g., snack bars,
15 breakfast cereals, pancakes, waffles, muffins, fruit filled pastries, tortillas, corn chips, tortilla chips, snack crackers, breads, cakes, cookies, or pies, or non-farinaceous food product, e.g., a vegetable, dairy, or meat food product e.g. french fries, tempura, veggie burgers, refried beans, hummus, tahini, margarine and nut butters, (e.g., peanut, cashew, almond, hazelnut), marzipan, potato chips; milk, cream, pudding, butter, ice cream, and cheese and processed
20 cheese products, prepared beef, lamb, pork, poultry or seafood products, e.g., frankfurters, deli slices, sausages, fish sticks, chicken fingers, and ground meats, e.g., meatloaf, meatballs and hamburgers, yogurt and yogurt products, and egg products.

 Thus this invention also relates to a method for promoting weight loss or inhibiting weight gain in a subject comprising administering to a subject in need thereof α -cyclodextrin
25 in an amount and for a time sufficient to produce a weight loss or inhibit weight gain. Preferably the α -cyclodextrin is administered to a subject consuming an average fat diet (about 100g fat/day, about 33 g fat/meal) wherein the amount administered to the subject is such that the ratio of α -cyclodextrin to fat ingested per meal, or daily, by the subject is about 1:20 to about 1:3 w/w, preferably the ratio is about 1:13 to about 1:5 w/w and more
30 preferably about 1:9 w/w. Once the desired weight is lost, the α -cyclodextrin may be included in the diet in an amount to inhibit or preferably prevent weight gain. For a loss of about 1-1.5lbs per week for a subject whose dietary intake is 100g fat/day (about 33 g

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fat/meal), the amount of α -cyclodextrin administered is preferably about 2g/meal, thus reducing the bioavailability of approximately 54g of fat per day.

Serum cholesterol is found in combination with proteins in the blood. Of particular interest are high density (HDL the good cholesterol) and low density lipoprotein (LDLs the bad cholesterol). This invention relates to a method for increasing the level of high density lipoprotein (HDL) in a subject comprising administering α -cyclodextrin to a subject in need thereof in an amount and for a time sufficient to increase HDL levels. Preferably the amount α -cyclodextrin administered to the subject is about four to about eleven grams per day. Preferably, the α -cyclodextrin is administered in an amount such that the ratio of α -cyclodextrin to fat ingested per meal, or daily, is about 1:20 to 1:3 w/w more preferably 1:13-1:5 w/w or most preferably about 1:9w/w. The α -cyclodextrin may be administered in a variety of forms, e.g., a tablet, capsule, pill, elixir, wafer, beverage, or in a food product, e.g., bread products, e.g., buns, rolls, biscuits, and breakfast cereals, e.g., oatmeal, cream of wheat, raisin bran, corn flakes, or other ready to eat cereals, meat products and dairy products, and particularly the consumable food products of this invention. Preferably the tablet, pill, capsule, elixir, wafer, beverage, or the consumable food products comprises a cyclodextrin that is predominantly α -cyclodextrin, e.g., the cyclodextrin is at least about 90-98% α -cyclodextrin.

It is possible that the total levels of cholesterol in the blood will remain constant even though the levels of HDL are elevated if there is a reduction in the levels of LDL. Preferably the total cholesterol levels are substantially reduced or are unchanged by the methods of this invention. Thus, this invention also relates to a method for reducing the cholesterol/HDL ratio in a subject comprising administering to a subject in need thereof α -cyclodextrin in an amount and for a time sufficient to reduce the cholesterol/HDL ratio. The α -cyclodextrin may be administered in a variety of forms, e.g., a tablet, pill, capsule, elixir, wafer, beverage, or in food products, e.g., bread products, e.g., buns, rolls, biscuits, and breakfast cereal, e.g., oatmeal, cream of wheat, raisin bran, corn flakes, or other ready to eat cereal, and particularly the consumable food products of this invention. The tablet, pill, capsule, elixir, wafer, beverage, or food products may contain α -cyclodextrin in combination with other cyclodextrins, e.g. β and/or γ cyclodextrins or with n-dextrin. Preferably the cyclodextrin in the tablet, pill, capsule, elixir, wafer, beverage, or the food products is predominantly α -cyclodextrin, e.g., the cyclodextrin is at least about 90-98% α -cyclodextrin.

This invention also relates to a method of reducing triglyceride levels in a subject comprising administering to a subject in need thereof an amount of α -cyclodextrin sufficient to reduce triglyceride levels. The amount of α -cyclodextrin administered to the subject is such that the ratio of α -cyclodextrin to fat ingested per meal, or daily, by the subject is about 1:20 to about 1:3 w/w, preferably the ratio is about 1:13 to about 1:5 w/w and more preferably the ratio is about 1:9 w/w. The α -cyclodextrin may be administered in a variety of forms, e.g., a tablet, capsule, pill, elixir, wafer, beverage, or in food products, e.g., bread products, e.g., buns, rolls, biscuits, and breakfast cereal, e.g., oatmeal, cream of wheat, raisin bran, corn flakes, or other ready to eat cereals, and, particularly the consumable food products of this invention. The tablet, pill, capsule, elixir, wafer, beverage, or food products may contain α -cyclodextrin in combination with other cyclodextrins, e.g. β and/or γ cyclodextrins or with n-dextrin, but preferably the cyclodextrin in the tablet, pill, capsule, elixir, wafer, beverage or the food products is predominantly α -cyclodextrin, e.g., the cyclodextrin is at least about 90-98% α -cyclodextrin.

This invention further relates to a method for reducing leptin levels in a subject comprising administering α -cyclodextrin to a subject in need thereof in an amount and for a time sufficient to reduce leptin levels in the subject. The α -cyclodextrin may be administered in a variety of forms, e.g., a tablet, capsule, pill, elixir, wafer, beverage or in food products, e.g., bread products, buns, rolls, biscuits and breakfast cereal, e.g., oatmeal, cream of wheat, raisin bran, corn flakes, or other ready to eat cereals, and particularly the consumable food products of this invention. The tablet, pill, capsule, elixir, wafer, beverage or food products may contain α -cyclodextrin in combination with other cyclodextrins, e.g. β and/or γ cyclodextrins or with n-dextrin, but preferably the cyclodextrin in the tablet, pill, capsule, elixir, wafer, beverage or the food products is predominantly α -cyclodextrin, e.g., the cyclodextrin is at least about 90-98% α -cyclodextrin.

This invention also relates to a method for suppressing appetite by administering α -cyclodextrin to a subject in need thereof in an amount and for a time sufficient to suppress the subject's appetite. The amount of α -cyclodextrin administered to the subject is such that the ratio of α -cyclodextrin to fat ingested per meal, or daily, by the subject is about 1:20 to about 1:3 w/w, preferably the ratio is about 1:13 to about 1:5 w/w and more preferably the ratio is about 1:9 w/w. The α -cyclodextrin may be administered in a variety of forms, e.g., a tablet, capsule, pill, elixir, wafer, beverage or in food products, e.g., bread products, buns, rolls,

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biscuits, and breakfast cereal, e.g., oatmeal, cream of wheat, raisin bran, corn flakes, or other ready to eat cereals, and particularly the consumable food products of this invention. The tablet, pill, capsule, elixir, wafer, beverage or food products may contain α -cyclodextrin in combination with other cyclodextrins, e.g. β and/or γ cyclodextrins or with n-dextrin, preferably the cyclodextrin in the tablet, pill, capsule, elixir, wafer, beverage or the food products is predominantly α -cyclodextrin, e.g., the cyclodextrin is at least about 90-98% α -cyclodextrin.

This invention further relates to a method for reducing insulin levels and insulin resistance in a subject comprising administering α -cyclodextrin to a subject in need thereof in an amount and for a time sufficient to reduce insulin levels and insulin resistance in the subject. Preferably the amount of α -cyclodextrin administered to the subject is such that the ratio of α -cyclodextrin to fat ingested per meal or daily by the subject is in a ratio of about 1:20 to about 1:3 w/w, preferably the ratio is about 1:13 to about 1:5 w/w and more preferably the ratio is about 1:9 w/w. The α -cyclodextrin may be administered in a variety of forms, e.g., a tablet, capsule, pill, elixir, wafer, beverage or in food products, e.g., bread products, buns, rolls, biscuits, and breakfast cereal, e.g., oatmeal, cream of wheat, raisin bran, corn flakes, or other ready to eat cereal, and particularly the consumable food products of this invention. Preferably the cyclodextrin in the tablet, pill, capsule, elixir, wafer, beverage or food products is predominantly α -cyclodextrin, e.g., the cyclodextrin is at least about 90-98% α -cyclodextrin.

This invention also relates to a method for reducing diarrhea in a subject in need thereof comprising administering to a subject in need thereof α -cyclodextrin in an amount and for a time sufficient to reduce diarrhea in the subject. Preferably the amount of α -cyclodextrin administered to the subject is such that the ratio of α -cyclodextrin to fat ingested per meal or daily by the subject is in a ratio of about 1:20 to about 1:3 w/w, preferably the ratio is about 1:13 to about 1:5 w/w and more preferably the ratio is about 1:9 w/w. The α -cyclodextrin may be administered in a variety of forms, e.g., a tablet, capsule, pill, elixir, wafer, beverage or in food products, e.g., bread products, buns, rolls, biscuits, and breakfast cereal, e.g., oatmeal, cream of wheat, raisin bran, corn flakes, or other ready to eat cereals, and particularly the consumable food products of this invention. Preferably the cyclodextrin in the tablet, pill, capsule, elixir, wafer, beverage or the food products is predominantly α -cyclodextrin, e.g., the cyclodextrin is at least about 90-98% α -cyclodextrin.

This invention also relates to methods for enhancing organoleptic properties of a fat containing food product without reducing the percentage of fat in the food product or the caloric content due to the fat, as assayed by bomb calorimetry. The method comprises adding α -cyclodextrin to the fat containing food product such that it is present during processing and in the final ingested food product. The amount of α -cyclodextrin that is added to the food product may be based on the amount of fat in the finished consumable product.

BRIEF DESCRIPTION OF THE FIGURES

Figure 1 depicts the cumulative total mass of food consumed by the four groups of rats and demonstrates that there was no significant difference in the mass of food consumed by the different groups.

Figure 2 depicts the cumulative caloric intake of the four groups of rats and indicates that there was no significant difference in the calories of food that the two pairs of rats (low fat and high fat) consumed.

Figure 3 illustrates the change in body weight of the four groups of adult rats during the entire study period.

Figure 4 depicts the fecal fat content of four groups of rats. Groups sharing a common superscript are not significantly different.

Figure 5 depicts the blood plasma parameters of four groups of rats at sacrifice. The plasma glucose, cholesterol and triglyceride concentrations were measured on all of the animals.

Figure 6 compares the plasma leptin values obtained from the four groups of rats.

Figure 7 depicts the serum triglyceride levels of volunteers fed a high fat breakfast following an overnight fast.

Figure 8 depicts the change in body weight of a human volunteer over a period of approximately 6 months.

Figure 9A-9C depicts the results of an *in vitro* study of vegetable oil (4g), water (6g) (with added food coloring for contrast) and varying amounts of (A) α -cyclodextrin (100-2,000mg; right to left), (B) β -cyclodextrin or (C) γ -cyclodextrin. A band of "wax-like" material layered between the oil and aqueous phases is apparent in the tubes. The size of this band

increases with increasing amounts of α -cyclodextrin to a maximum in the tube labeled 10% (400mg α -cyclodextrin/4g oil). Note the increasing size (right to left) of a white layer of un-reacted α -cyclodextrin in the bottom of the tubes. This material is displaced from solution by either the oil or the α -cyclodextrin-oil complex. These tubes were centrifuged in order to improve the definition of the layers. The "wax-like" complex is of such a consistency that all of the tubes except for the furthest two to the right can be inverted without leakage of the aqueous phase around the complex.

DESCRIPTION OF THE INVENTION

This invention relates to a fat containing consumable food product containing α -cyclodextrin and to methods for its use. The consumable food products are suitable for consumption by mammals, e.g., a mouse, rat, a cat, a dog, a cow, a horse, a monkey, an ape or a human, and thus include e.g., a pet food product for a e.g. cat, dog or horse or a human consumable food product. The consumable food products of this invention comprise α -cyclodextrin and fat, preferably the ratio of the amount of α -cyclodextrin to fat is about 1:20-1:3 w/w, more preferably the ratio of α -cyclodextrin to fat of about 1:13-1:5 w/w, and most preferably the ratio of α -cyclodextrin to fat of about 1:9 w/w. Preferably the total cyclodextrin in the consumable food products is less than about 9% w/w, more preferably the total cyclodextrin in the consumable food products is less than about 6% w/w and most preferably the total cyclodextrin in the food products is less than about 3%. Preferably complexes of cyclodextrin and fat are distributed evenly throughout the food product. Preferably the consumable food products of this invention are high fat containing food products comprise by caloric content about 7% to about 80% fat, preferably about 20% to about 70% fat, more preferably about 40% to about 70% fat, or by weight about 5% w/w fat to about 50% w/w fat preferably about 5-30% w/w fat and more preferably about 7% w/w fat to about 25% fat. Methods for determining or calculating the amount of fat in a food product are well known in the art. See for example the software program "Food Processor" by ESHA Research, Salem, OR, incorporated herein by reference. Preferably the food products of this invention are made with less than 2% linolenic acid, more preferably less than 0.2% linolenic acid. More preferably the food products of this invention are made without detectable levels of linolenic acid. Linolenic acid has been shown to promote weight loss but at the levels necessary to promote weight loss, about 2%, the shelf life of products containing the linolenic acid are reduced due to its tendency to become rancid. In addition, high purity linolenic acid

is very expensive. Thus linolenic acid is preferably not added to the food products of this invention before, during or after their preparation.

Various forms of cyclodextrins are commercially available. For example, Wacker-Chemie GmbH produces a variety of natural and modified cyclodextrins. Cyclodextrins are often sold as mixtures of α -, β - and γ -cyclodextrins and can be produced by a variety of methods. Generally cyclodextrins are produced by treating a starch, e.g. potato or corn, with a cyclodextrin transferase, which is produced by a variety of organisms, e.g., *Bacillus macerans*. The cyclodextrins may be isolated from the treated starch using a variety of methods that combine concentration, fractionation, filtration, spray drying, granulation etc. For a more complete discussion of methods for the production and isolation of cyclodextrins see e.g. Schmid "Preparation and industrial production of cyclodextrins", Comprehensive Supramolecular Chemistry (1996), 3: 41-56. Eds Szejtli, Jozsef; Osa, Tetsuo. Elsevier, Oxford, UK incorporated herein by reference.

The fat containing consumable food products of this invention may be a farinaceous food product, e.g., snack bars, breakfast cereals, pancakes, waffles, muffins, fruit filled pastries, tortillas, corn chips, tortilla chips, snack crackers, breads, cakes, cookies, or pies, or a non-farinaceous food product, e.g. a prepared vegetable product (vegetables as described herein include vegetables, fruits and nuts), particularly those made with a fat ingredient, e.g. french fries, tempura, veggie burgers, refried beans, hummus, tahini, margarine and nut butters, (e.g., peanut, cashew, almond, hazelnut), marzipan, potato chips; a dairy food product e.g., milk, cream, pudding, butter, ice cream, and cheese and processed cheese products; yogurt and yogurt products, egg products and meat products, e.g., prepared beef, lamb, pork, poultry or seafood products, e.g., frankfurters, deli slices, sausages, fish sticks, chicken fingers, and ground meats, e.g., meatloaf, meatballs and hamburgers. Preferably the dairy product is one wherein α -cyclodextrin/fat complexes are distributed throughout the product, preferably a solid or semi-solid dairy product e.g., pudding, butter, ice cream, and cheese and processed cheese products and yogurt and preferably the organoleptic properties of the product are not adversely affected. The food products of this invention may also include among others, e.g., a pre-packaged farinaceous food product, e.g., a pre-packaged prepared pasta dish such as, e.g., lasagna, manicotti, spaghetti with sauce, ravioli, tortellini, or macaroni and cheese, or a packaged dairy product, a packaged prepared vegetable product, or a pre-packaged prepared meat product, wherein the food product comprises α -cyclodextrin

and fat in ratios as set forth herein. Preferably, a serving of the pre-packaged product provides about 160 mg to 11g α -cyclodextrin/serving, preferably about 1g to about 7g/serving and more preferably about 2-4g per serving, and most preferably at about 2-3g/serving. A pre-packaged food product may be enclosed in plastic, paper, cardboard or metal, e.g., tin or flexifoil. The pre-packaged food product may be packaged in bulk, multiserving packages or packaged as single servings.

This invention also relates to confectionery products e.g., hard candies such as lollipops and breath mints or after dinner mints, and condiments, e.g., gravies, sauces, salad dressings, mayonnaise etc., comprising α -cyclodextrin. Preferably, the confectionery product is a fat containing product such as, e.g., chocolates.

The α -cyclodextrin may be added to a consumable food product that is cooked, e.g., baked, roasted or fried, or to an uncooked consumable food product, e.g., milk, cream, whipped cream, non-dairy whipped toppings or fillings, yogurt or a beverage, e.g. a milkshake, eggnog, or a smoothie (fruit and yogurt drink). The α -cyclodextrin may be added to the food product at any stage of its preparation, e.g., the α -cyclodextrin may be mixed with the ingredients so that it is distributed throughout the food product and the product may then be cooked. However, in some instances the α -cyclodextrin may be applied to the surface of the food product, e.g., as a glaze or coating, to achieve the desired levels of α -cyclodextrin to fat.

This invention also relates to a method for promoting weight loss or reducing body weight gain in a subject comprising administering to a subject in need thereof an amount of α -cyclodextrin sufficient to reduce body weight gain or promote weight loss. A preferred method comprising ingesting sufficient amounts of α -cyclodextrin to complex a desired amount of fat in a fat containing meal, or desired amount of fat per day, to promote weight loss, reduce weight gain or to maintain weight. Preferably the weight loss for a human that is about 1-1.5lbs/week. An aspect of this invention is a method comprising ingesting sufficient amount of α -cyclodextrin to complex the fat in excess of a desired amount of fat per meal or day that a subject wishes to absorb. The method comprises determining the amount of fat that a subject desires to absorb per meal or per day, determining the amount of ingested fat that in excess of the amount that the subject desires to absorb, and then ingesting sufficient amounts of α -cyclodextrin to complex the excess fat such that only the desired amount of fat

is absorbed. For example, based on the disclosure herein that about 1g of α -cyclodextrin can complex about 9g of fat, the amount sufficient to promote a weight loss of 1-1.5 lbs/week in a subject consuming a daily diet of 2500g/day, such diet comprising about 100g fat/day, the preferred amount of ingested α -cyclodextrin is about 2g/meal three meals a day. Preferably the total α -cyclodextrin ingested daily is about 500mg to about 33 g per day, more preferably about 5g to about 20g per day, most preferably about 6-11g/day. Preferably the α -cyclodextrin is administered with a meal such that the ratio of α -cyclodextrin to the ingested fat that one wishes to prevent from being absorbed by the body is about 1:20 w/w to about 1:3 w/w, preferably the ratio is about 1:13 w/w to about 1:5 w/w, more preferably the ratio is about 1:9 w/w. A subject in need thereof is one who is in need of or who wishes to lose weight or inhibit weight gain, e.g., one who is prone to weight gain or one who is already overweight or obese. The subject may also be one who consumes a daily diet comprising about 30% or more fat by calorie. The α -cyclodextrin may be administered to the subject in the form of a powder, a tablet, a capsule, a drink or another delivery medium suitable for consumption, preferably one that does not comprise linolenic acid. The α -cyclodextrin may be administered prior to, concurrently with or subsequent to, ingestion of a fat containing meal. Preferably the α -cyclodextrin is administered just prior to or concurrently with the ingestion of a fat containing meal. More preferably the α -cyclodextrin is administered to a human subject while consuming a fat containing meal. The α -cyclodextrin may be administered in the form of a food product, e.g., bread products, e.g., buns, rolls, or biscuits, or a breakfast cereal, e.g., oatmeal, cream of wheat, raisin bran, corn flakes, or other ready to eat cereal, or preferably in the form of the food products of this invention. The subject may be a mammal, e.g., mouse, rat, cat, dog, cow, horse, monkey, ape or human but preferably human and it is within the skill of the art to adjust the total amounts of α -cyclodextrin administered to the mammal to complex sufficient fat to achieve the desired amount of weight loss. For example, 2g of α -cyclodextrin per meal reduces the bioavailability of about 18 g of fat per meal or about 54g of fat per day. This equates to 1-1.5lbs of body weight per week. This amount of fat represents approximately one-half of the normal daily fat consumption for average North Americans.

This invention also relates to methods for reducing the bioavailability of fat in a fat containing food product comprising combining an amount of an α -cyclodextrin with a food product such that the food product comprises a ratio of α -cyclodextrin to fat of about 1:20 to

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about 1:3w/w, preferably about 1:13 to about 1:5 w/w most preferably about 1:9 w/w. Preferably the total cyclodextrin in the food products of this invention is less than about 9% w/w, more preferably less than about 6% w/w and most preferably less than about 3% w/w. This method may be applied to a variety of fat containing food products, e.g., a farinaceous food product, a prepared vegetable product, a dairy product, a prepared meat or seafood product, gravies, sauces and salad dressings. For example, the farinaceous food product may be a e.g. snack bar, breakfast cereal, pancakes, waffles, muffins, tortillas, corn chips, tortilla chips, snack crackers, breads, cakes, cookies, doughnuts, zeppolies and pies. A dairy product of this invention may be e.g., milk, cream, evaporated or condensed milk, pudding, butter, ice cream, milkshakes, yogurt and drinks prepared with yogurt, e.g., a fruit and yogurt "smoothie", and cheese or processed cheese products or egg products, e.g. an omelet or egg noodles. The vegetable product may be one which is made with fat as one of the ingredients, cream based vegetable soup, soups with meat based stocks, or a vegetable burger, or the vegetable product may be one which is fried in a fat containing material, e.g., french fries, potato chips or falafel, wherein the amount of α -cyclodextrin in the product is based on the estimate of the amount of fat containing material that will be absorbed in the final product. The meat product may be a prepared beef, lamb, pork, poultry or seafood product, e.g., frankfurters, deli slices, sausages, fish sticks, chicken fingers and ground meats to be made into, e.g., hamburgers or meatloaf. The method is also applicable to battered or coated products, e.g., french fries, fish sticks, chicken fingers or tempura, that are fried and to batters that are used to coat products that are fried in a fat containing material. The amount of cyclodextrin in the batter of a batter coated product is based on the estimate of the amount of fat containing material that will be absorbed by the batter coated product. The method is also applicable to candies and condiments, e.g., chocolates, sauces, mayonnaise and salad dressings.

The α -cyclodextrin may be added to the consumable food product at any stage in its production and may be added under conditions that favor formation of complexes of α -cyclodextrin and fat such that the complexes are distributed throughout the consumable food product. Alternatively, the α -cyclodextrin may be combined with a fat containing food product as it is consumed by determining the approximate amount of fat in the food product and then ingesting α -cyclodextrin in amount sufficient to obtain a ratio of ingested α -cyclodextrin to ingested fat of 1:20 to about 1:3, preferably 1:13 to about 1:5 and more preferably about 1:9 w/w. Preferably, the consumable fat containing food product comprises

by caloric content 7-80% fat, more preferably 20-70% fat and most preferably 40-70% fat or by weight 5-50% fat, preferably 7-25% fat.

This invention also relates to methods for reducing a pathologic condition often associated with obesity and excess weight, e.g., high cholesterol/HDL ratio, high triglyceride levels, high leptin levels, high insulin levels, and insulin resistance, by administering α -cyclodextrin to a subject in need thereof in sufficient amounts and for sufficient time to reduce the pathologic condition associated with obesity and excess weight.

Serum cholesterol is found in combination with proteins in the blood. Of particular interest are high density (HDL) and low density lipoproteins (LDL). This invention also relates to a method for increasing the level of high density lipoprotein cholesterol(HDL) in a subject comprising administering α -cyclodextrin to a subject in need thereof in an amount sufficient, and for a time sufficient, to increase HDL levels. Preferably the amount of α -cyclodextrin administered to the subject is about 500mg to about 33 grams per day, preferably about 3-21g per day and more preferably about 6-11g per day. The α -cyclodextrin may be administered prior to, concurrently with or subsequent to ingestion of a fat containing meal. The subject may be one who consumes about 100g fat/day. Preferably the α -cyclodextrin is administered to the subject with a fat containing meal. A sufficient amount of α -cyclodextrin is about 165mg – 11g/meal, preferably about 1-7g/meal or more preferably about 2-3.3g meal. The α -cyclodextrin may be administered in any suitable form, e.g., a tablet, pill, capsules liquid or other delivery medium suitable for human consumption, or in the form of food products, e.g., bread products, buns, rolls, biscuits, and breakfast cereal, e.g., oatmeal, cream of wheat, raisin bran, corn flakes, or other ready to eat cereal, and particularly the food products of this invention. Preferably a serving size of the food product for use in this method contains about 165mg – 11g/meal, preferably about 1-7g/meal or more preferably about 2-4g α -cyclodextrin. Preferably, the α -cyclodextrin is administered to the subject in an amount such that the ratio of α -cyclodextrin to fat of about 1:20 to about 1:3 w/w, preferably about 1:13 to about 1:5 w/w, most preferably about 1:9 w/w per meal, or daily.

It is possible that the total levels of cholesterol in the blood will remain constant even though the levels of HDL are elevated if there is a reduction in levels of LDL. Thus another aspect of this invention is method for increasing HDL levels and reducing LDL levels, reducing the cholesterol/HDL ratio, and or reducing cholesterol levels in a subject in need

thereof by administering α -cyclodextrin in an amount and for a time sufficient to increase the HDL levels and/or reduce the LDL levels, decrease the total cholesterol/HDL ratio and/or reduce cholesterol. The reduction in LDL and increase in HDL reduces the total ratio of cholesterol to HDL. Preferably the total cholesterol levels are not substantially reduced or increased.

The α -cyclodextrin may be administered to the subject in the form of a powder, tablet, a capsule, a drink or another delivery medium suitable for consumption, preferably one that does not comprise linolenic acid. A sufficient amount of α -cyclodextrin is about 165mg – 11g/meal, preferably about 1-7g/meal or more preferably about 2-3.3g/meal. Preferably the total α -cyclodextrin ingested daily is about 500mg to about 33 g per day, more preferably about 5g to about 20g per day, most preferably about 6-11g/day. Preferably the α -cyclodextrin is administered with a meal such that the ratio of α -cyclodextrin to fat is about 1:20 w/w to about 1:3 w/w, preferably the ratio is about 1:13 w/w to about 1:5 w/w, more preferably the ratio is about 1:9 w/w per meal.

A subject in need of increasing the level of HDL and/or reducing LDL Levels, reducing the cholesterol/HDL ratio or reducing cholesterol levels is one who has, or has a predisposition for, a high ratio of total cholesterol to HDL levels. Methods for determining blood cholesterol, HDL and LDL levels are well known in the art and need not be elaborated on herein. However, for a discussion of cholesterol levels and methods for determining cholesterol, HDL and LDL levels (see e.g., Expert Program on detection, evaluation, and treatment of high blood cholesterol in adults. Executive Summary of the Third Report of the National Cholesterol Education Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III), *JAMA* 285(19): 2486-97:2001, and; Handbook of Lipoprotein Testing, Rifai N, Warnick GR and Dominiczak MH, eds. Chapters 9, 11 and 12. AACC Press, Washington DC, 2000 both incorporated herein by reference.)

This invention also relates to a method of reducing triglycerides in a subject comprising administering to a subject in need thereof an amount of α -cyclodextrin sufficient to reduce triglyceride levels. A subject in need thereof is one who has high triglyceride levels, has a predisposition for high triglyceride levels or has a family history of high triglyceride levels. High triglyceride levels are implicated in a variety of pathological conditions. Thus, this invention also relates to treating a pathological condition, e.g., cardiovascular disease, acute pancreatitis, insulin resistance and uncontrolled diabetes and

various dislipidemias associated with high triglyceride levels by administering α -cyclodextrin to a subject in need thereof in an amount sufficient to reduce the levels of triglycerides in the subject. Those of skill in the art are well versed in methods for determining the triglyceride levels in a subject. For a review of methods for determining blood triglyceride levels see e.g.,

5 Handbook of Lipoprotein Testing, Rifai N, Warnick GR and Dominiczak MH, eds. Chapter 10. AACC Press, Washington, DC 2000 incorporated herein by reference. The α -cyclodextrin may be administered prior to, concurrently with or subsequent to ingestion of the fat containing meal. More preferably the α -cyclodextrin is administered to the subject with a fat containing meal. A sufficient amount of α -cyclodextrin is about 165mg-11g/meal,

10 preferably about 1-7g/meal or more preferably about 2-4g meal. Preferably the total α -cyclodextrin ingested daily is about 500mg to about 33 g per day, more preferably about 5 g to about 20g per day most preferably about 6-11g/day. Preferably the α -cyclodextrin: fat ratio ingested per meal or daily is about 1:20 to about 1:3 w/w, preferably the ratio is about 1:13 to about 1:5 w/w and more preferably the ratio is about 1:9 w/w. The α -cyclodextrin

15 may be administered to the subject in the form of a powder, tablet, a capsule, a drink or another delivery medium suitable for consumption, preferably one that does not comprise linolenic acid. The α -cyclodextrin may be administered to the subject in the form of a food product, particularly a food product of this invention.

This invention further relates to a method for reducing leptin levels in a subject

20 comprising administering α -cyclodextrin to a subject in need thereof in an amount sufficient to reduce leptin levels in the subject. The α -cyclodextrin may be administered prior to, concurrently with or subsequent to ingestion of the fat containing meal. Preferably the α -cyclodextrin is administered just prior to or concurrently with the ingestion of the fat containing meal. More preferably the α -cyclodextrin is administered to the subject with a fat

25 containing meal. The amount of α -cyclodextrin ingested per meal is preferably about 165mg-11g/meal, more preferably 1-7g/meal and most preferably 2-3.3g/meal. Preferably the total α -cyclodextrin ingested daily is about 500mg to about 33 g per day, more preferably about 5g to about 20g per day most preferably about 6-11g/day. Preferably the amount of α -cyclodextrin administered daily to the subject and fat ingested daily by the subject is in a ratio

30 of about 1:20 to about 1:3 w/w, preferably the ratio is about 1:13 to about 1:5 w/w and more preferably the ratio is about 1:9 w/w. A subject in need of reducing leptin is one who has high leptin levels, has a predisposition for leptin resistance. Leptin levels can be determined using

any method known in the art for determining leptin levels. For a review of various assays for determining leptin resistance see e.g., Maffei et al., *Nature Med* 1:1155-1161 (1995) incorporated herein by reference. The α -cyclodextrin may be administered to the subject in the form of a powder, tablet, capsule, drink, confection or other delivery medium suitable for human consumption, preferably one that comprises less than 2% linolenic acid, more preferably one that comprises less than 0.2% linolenic acid and most preferably one that does not comprise linolenic acid. The α -cyclodextrin may be administered to the subject in the form of a food product, preferably a food product of this invention.

This invention further relates to a method for reducing blood insulin levels and insulin resistance in a subject comprising administering α -cyclodextrin to a subject in need thereof in an amount sufficient to reduce blood insulin levels in the subject. Insulin resistance is typically the cause of Type II diabetes. Insulin resistance can be estimated by triglyceride/HDL-cholesterol ratios and glucose/insulin ratios. A subject in need thereof is one who displays high insulin levels, has Type II diabetes or who has a predisposition for developing Type II diabetes or who has a family history of high insulin levels or Type II diabetes. Any method used routinely for determining insulin levels can be used herein to assay and monitor insulin levels and resistance. See for example Berson et al. (Eds) Methods in Investigative and Diagnostic Endocrinology, ch 3, Part III, Vol. 28. American Elsevier Publishing Co., New York, 1973, incorporated herein by reference, for a description of assays for determining insulin levels. The α -cyclodextrin may be administered prior to, concurrently with or subsequent to ingestion of the fat containing meal. Preferably the α -cyclodextrin is administered just prior to or concurrently with the ingestion of the fat containing meal. More preferably the α -cyclodextrin is administered to the subject with a fat containing meal. The amount of α -cyclodextrin ingested per meal is preferably about 165mg-11g/meal, more preferably about 1-7g/meal and most preferably about 2-3.3g/meal. The total α -cyclodextrin ingested daily is about 500mg to about 33 g per day, preferably about 5g to about 20g per day and more preferably about 6-11g/day. Preferably the amount of α -cyclodextrin administered daily to the subject is based on the fat ingested daily by the subject and is in a ratio of about 1:20 - 1:3 w/w, preferably the ratio is about 1:13 - 1:5 w/w and more preferably the ratio is about 1:9 w/w. The α -cyclodextrin may be administered to the subject in the form of a powder, tablet, a gel, capsule, a liquid or another delivery medium suitable for human consumption, preferably one that does not comprise linolenic acid. The α -

cyclodextrin may be administered to the subject in the form of a food product, preferably a food product of this invention.

This invention also relates to a method for reducing diarrhea in a subject in need thereof comprising administering to a subject in need thereof α -cyclodextrin in an amount and for a time sufficient to reduce diarrhea in the subject. The subject may be a mammal, e.g., mouse, rat, cat, dog, cow, horse, monkey, ape or human. Such a subject may be one who is prone to diarrhea, or is currently suffering from diarrhea, e.g., the subject may be a cholecystectomy patient prone to or having diarrhea, a patient suffering from fat aggravated diarrhea, or a patient having acute or subacute diverticulitis, the acute phases of certain inflammatory conditions of the bowel, e.g., ulcerative colitis or Crohn's disease and after some types of intestinal surgery, e.g., a colostomy or ileostomy. The α -cyclodextrin may be administered in the form of a food product, preferably a food product of this invention for example a farinaceous or non-farinaceous food product of this invention. The α -cyclodextrin may also be administered to the subject in the form of a powder, tablet, a capsule, a gel, a liquid or another delivery medium suitable for consumption. The α -cyclodextrin may be administered with a meal at about e.g. 165mg-11g/meal, preferably about 1-7g/meal and more preferably about 2-3.3g/meal. Preferably the total α -cyclodextrin ingested daily is about 500mg to about 33 g per day, more preferably about 5g to about 20g per day, most preferably 6-11g/day. The ratio of ingested α -cyclodextrin to ingested fat per meal, or daily, preferably per meal, is about 1:20 - 1:3 w/w, preferably the ratio is about 1:13-1:5 w/w, more preferably the ratio is about 1:9 w/w. The α -cyclodextrin may be administered prior to, concurrently with or subsequent to ingestion of the fat containing meal. Preferably the α -cyclodextrin is administered just prior to or concurrently with the ingestion of the fat containing meal.

The addition of α -cyclodextrin to a pet food product maintains or promotes good feces quality of a pet and/or improves feces quality of a pet. Good quality pet feces is a very desirable trait as perceived by the pet owner in that it is not only generally more aesthetically pleasing but is also an indicator of good pet health. As such, this invention is also related to a pet food product which comprises α -cyclodextrin in an amount sufficient to maintain or promote good feces quality of a pet and/or improve the feces quality of a pet. Feces having good quality are firm and well formed maintaining their shape. A feces with a moisture content such that the shape is not maintained (loose stools or diarrhea) or a moisture content such that the feces are hard and dry, are not good quality feces. The pet food is preferably a

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packaged pet food. The packaging may be plastic, paper, cardboard or metal, e.g. tin or flexifoil. The pet food may be a moist pet food, such as those packaged in cans or flexifoil or a dry pet food such as those packaged in paper or cardboard, e.g., kibble or biscuits. Preferably the pet food is a food developed for a cat, dog, cow or horse. This invention also relates to a method for maintaining or promoting good feces quality of a pet and/or improving feces quality of a pet by administering α -cyclodextrin to a pet, preferably a pet in need thereof, in an amount and for a time sufficient to maintain or promote good feces quality of the pet and/or to improve feces quality of a pet. The α -cyclodextrin may be administered with a meal at about e.g. 165mg-11g/meal, preferably about 1-7g/meal and more preferably about 2-3.3g/meal. Preferably the total α -cyclodextrin ingested daily is about 500mg to about 33 g per day, more preferably about 5g to about 20g per day, most preferably 6-11g/day. The ratio of ingested α -cyclodextrin to ingested fat per meal, or daily, preferably per meal, is about 1:20 - 1:3 w/w, preferably the ratio is about 1:13-1:5 w/w, more preferably the ratio is about 1:9 w/w. The α -cyclodextrin may be administered prior to, concurrently with or subsequent to ingestion of the fat containing meal. Preferably the α -cyclodextrin is administered just prior to or concurrently with the ingestion of the fat containing meal. The α -cyclodextrin may be administered to the pet in the form of a pill, wafer, tablet capsule etc or in the form of a pet food product, particularly a pet food product of this invention, including moist pet foods such as that packaged in a can or flexifoil or a dry pet food such as those packaged in a paper or cardboard container e.g. a kibble or biscuit. A pet in need thereof is one having poorly formed feces or having a predisposition to have poorly formed feces, e.g. a pet with diarrhea or having a predisposition to diarrhea.

In the methods of this invention, the α -cyclodextrin may be administered in the form of a single dosage unit consisting essentially of α -cyclodextrin. The single dosage unit may be in the form of a powder, tablet, capsule, gel, pellet, liquid, etc., the α -cyclodextrin may be incorporated into a powder, tablet, capsule, gel, pellet, liquid, etc by any means that is routinely used in the art. The α -cyclodextrin may be incorporated into the powder, tablet, gel, capsule, pellet, liquid, etc. with other commonly used additives, e.g. colorants, anti-oxidants, fillers, starches, sugars, anti-bacterial or anti-fungal agents, preservatives, stabilizers or emulsifiers. The α -cyclodextrin may be combined with any pharmaceutical carrier acceptable for oral administration, e.g. it may be enclosed in a hard or soft shell gelatin capsule, compressed into tablets, or incorporated directly into the individual's diet.

Specifically, α -cyclodextrin may be incorporated with excipients and used in the form of digestible tablets, capsules, elixirs, suspensions, syrups, wafers, and the like. The α -cyclodextrin may be mixed with other food forms and pharmaceutically acceptable flavor enhancers. Suitable pharmaceutical carriers and formulations are described, for example, in
5 Remington's Pharmaceutical Sciences (19th ed.) (Genarro, ed. (1995) Mack Publishing Co., Easton, Pa.), incorporated herein by reference. Preferably the formulation is such that the α -cyclodextrin is released in the stomach to mix with the ingested food so that complexes of α -cyclodextrin and fat are formed such that the α -cyclodextrin: fat complexes are already formed when the chyme is pushed into the jejunum and is mixed with bicarbonate and lipase.

10 Because only a relatively small amount of total cyclodextrin (e.g. less than about 9% w/w preferably less than about 6% w/w, more preferable less than about 3% w/w) is added to food products to achieve the desired α -cyclodextrin to fat ratio, the α -cyclodextrin may be added to a food composition rather than using α -cyclodextrin as a filler to replace an equal amount of the dry ingredients in the food product. Thus the caloric content of the food
15 products of this invention as determined by bomb calorimetry is not substantially altered by the addition of total cyclodextrin. Even if dry ingredients are removed from the food product to compensate for the relatively small amount of cyclodextrin added to the food product (less than about 9% preferably less than about 6%w/w, more preferably less than about 3%w/w) the caloric content of the food would not be substantially reduced.

20 This invention also relates to methods for enhancing organoleptic properties of a fat containing consumable food product without reducing the caloric content (as assayed by bomb calorimetry) or substantially reducing the percentage of fat in the food product. The method comprises adding α -cyclodextrin to the fat containing food product during the preparation of the product. The amount of α -cyclodextrin added to the foods is based on the
25 amount of fat in the finished product. The food products of this invention typically have a ratio of α -cyclodextrin to fat of about 1:20-1:3 w/w, preferably about 1:13-1:5 w/w, and more preferably about 1:9 w/w. The total amount of cyclodextrins added to the product is typically less than 9% w/w, preferably less than 6% w/w and more preferably less than 3% w/w. Products made with as low as 0.7% w/w α -cyclodextrin have enhanced organoleptic
30 properties, e.g. a sweeter taste and a smoother texture. The consumable fat containing food product may comprise by calorie content 7-80% fat, preferably 20-70% or more preferably 40-70% fat or by weight 5-50% w/w fat or preferably 7-25% w/w fat. This method may be

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applied to a variety of fat containing food products, e.g., a farinaceous food product, a prepared vegetable product, a dairy product, a prepared meat poultry or seafood product, soups and condiments e.g., gravies, sauces, mayonnaise, salad dressing etc. For example, the farinaceous food product may be e.g., a snack bar, breakfast cereal, pancake, waffle, muffin, tortilla, corn chips, tortilla chips, snack cracker, bread, cake, cookie, doughnut zeppoli and pie or other fruit or nut filled baker product. A dairy product of this invention may be e.g., milk, cream, evaporated or condensed milk, pudding, butter, ice cream milkshakes, and cream based sauces or soups, yogurt and drinks prepared with yogurt, e.g., a fruit and yogurt "smoothie", and cheese or processed cheese products, or egg products, e.g., an omelet or egg noodles. The vegetable product may be one which is made with fat as one of the ingredients, e.g., hummus, tahini, margarine and nut butters, or may be one which is fried in a fat containing material, e.g., french fries, vegetable tempura, or falafel, wherein the amount of a α -cyclodextrin in the fried product is based on the amount of fat containing material that is estimated to be contained in the fried food product after frying. The meat product may be a prepared beef, lamb, pork, poultry or seafood product, e.g., frankfurters, deli slices, sausages, fish sticks, chicken fingers and ground meats to be made into, e.g., hamburgers, meatballs or meatloaf. The method is also applicable to batters that are used to coat products, e.g., french fries or tempura, for frying in a fat containing material, e.g., lard or oil. In addition the method is applicable to soups, and condiments, e.g., gravies, sauces and salad dressing, wherein the α -cyclodextrin to fat ratio described *supra* may enhance the texture and/or flavor of the product. The products of this invention often taste comparable to a like product made without α -cyclodextrin and/or they have a smoother texture and a sweeter taste. In addition, the inclusion of α -cyclodextrin in evaporated or condensed milk produces a whiter product as compared to a like product without the α -cyclodextrin.

This invention also relates to a method for reducing the amount of time required to prepare whipped cream comprising adding α -cyclodextrin to cream prior to or during whipping. The α -cyclodextrin is added in an amount sufficient to reduce the amount of time required to form whipped cream. Preferably the amount of α -cyclodextrin is sufficient to attain a ratio of α -cyclodextrin to fat in the cream of about 1:20 – 1:3 w/w, preferably about 1:13-1:5 w/w and more preferably about 1:9 w/w. Reducing the amount of time required for whipped cream to form reduces the amount of power needed to run a mixer, which when calculated on a commercial scale results in a large monetary savings in both electricity and

manpower. The whipped cream remains soft and scoopable and the whey does not separate from the rest of the components.

5 It is envisioned herein that the α -cyclodextrin-containing whipped cream may be used as a topping on another fat containing material that may or may not contain α -cyclodextrin and the amount of α -cyclodextrin in the whipped cream would be sufficient to complex the fat in the other fat containing material when consumed thus reducing its bioavailability as well.

EXAMPLES

EXAMPLE 1

Figures 9A-9C depict the results of an *in vitro* study of vegetable oil (4g), water (6g) (with added food coloring for contrast) and varying amounts of (A) α -cyclodextrin (100-
5 2,000mg, right to left), (B) β -cyclodextrin or (C) γ -cyclodextrin. A band of "wax-like" material layered between the oil and aqueous phases is apparent in the tubes. The size of this band increases with increasing amounts of α -cyclodextrin to a maximum in the tube labeled 10% (400mg α -cyclodextrin/4g oil). Note the increasing size (right to left) of a white layer of un-reacted α -cyclodextrin in the bottom of the tubes. This material is displaced from solution
10 by either the oil or the α -cyclodextrin-oil complex. These tubes were centrifuged in order to improve the definition of the layers. The "wax-like" complex is of such a consistency that all of the tubes in 9A except for the furthest two to the right can be inverted without leakage of the aqueous phase around the complex.

The pore size of α -cyclodextrin is significantly smaller than the pore size of β -
15 cyclodextrin and γ -cyclodextrin. Thus one would not have expected α -cyclodextrin to complex triglyceride molecules because the molecules would not fit within the pore of the α -cyclodextrin. However, the amount of complexed fat in the tubes containing the oil/ β -cyclodextrin (Figure 9B) and oil/ γ -cyclodextrin mixture (Figure 9C) is significantly less than seen in the tubes containing the oil/ α -cyclodextrin mixture (Figure 9A). This difference is
20 even more dramatic in Figure 9C wherein a band of wax-like material is barely noticeable. The white substance in the bottom of the tubes is precipitated cyclodextrin.

EXAMPLE 2 ANIMAL STUDIES

To examine the effect of α -cyclodextrin on body weight gain and plasma lipid levels in animals fed high fat and low fat diets, we conducted a short-term feeding study using
25 Wistar rats. Forty-two male Wistar rats, 10 weeks old, were obtained from Harlan-Sprague Dawley. Following a one-week adaptation while being fed the control low fat diet (LF), they were divided equally into two groups, one low-fat (LF) diet and the other high-fat (HF) diet. These two groups were further divided into two subgroups. Two groups were fed the LF or HF diet and served as controls for the other two test groups which were fed the LF or HF diet
30 containing α -cyclodextrin, wherein the amount of α -cyclodextrin was such that the ratio of α -cyclodextrin to fat in the food was 1:10 w/w. The LF diet was formulated according to AIN-93M diet and contains 4% (w/w) soybean oil as the fat source. The HF diet was a

modification of the LF diet with 40% soybean oil. Therefore, the LF group receiving α -cyclodextrin (LF-cyclodextrin) ingested 0.4g of α -cyclodextrin/100g of food and the HF group receiving α -cyclodextrin (HF-cyclodextrin) ate 4g α -cyclodextrin/100g of food. The caloric density of the 4 diets were: LF: 3.96 kcal/g; LF-cyclodextrin: 3.66 kcal/g; HF: 5.70 kcal/g; HF-cyclodextrin: 5.59 kcal/g.

The rats were housed as pairs for five weeks prior to being placed in individual metabolic cages for the sixth week of the study. All of the rats' feces were collected during the final three days of the study. At the end of the sixth week of the study period the rats were sacrificed by decapitation after a brief exposure to carbon dioxide gas. Trunk blood and the livers were collected from each animal. The rest of the body was eviscerated and all visible fat from the internal cavity was collected and weighed. The carcass was frozen for body composition analysis at a later date.

Food and energy intake:

The amount of food ingested by the animals was monitored for the first five weeks of the study and from these data the caloric intake was calculated. These data are presented in Table 1 and Figures 1 and 2 as an average for each group $\pm$ SD.

Table 1: Total food and caloric intake of 4 groups of rats during the first 5 weeks of the study (mean $\pm$ SD).

<u>Group</u>	<u>Total Food Ingested (g)</u>	<u>Caloric Intake (Kcal)</u>
LF	779 $\pm$ 40	2,970 $\pm$ 154
LF-cyclodextrin	786 $\pm$ 87	2,978 $\pm$ 332
HF	753 $\pm$ 70	4,072 $\pm$ 921
HF-cyclodextrin	769 $\pm$ 107	3,986 $\pm$ 560

There was no statistical difference amongst any of the groups with regards to the amount (g) of food ingested. Due to the higher caloric content of the HF diet, rats in the 2 HF groups consumed significantly more calories compared to that of the 2 LF fed groups. It should be noted that caloric intake between the two HF groups or the two LF groups was not affected by the ingestion of α -cyclodextrin. These data demonstrate that (1) all of the rats were satiated by the amount of the food ingested, and (2) that if the α -cyclodextrin was complexing a portion of the fat and thus preventing the fat from being digested by the rats,

the rats were not consuming more food to compensate for it. There is no statistical difference amongst the groups as it pertains to water consumption.

Body weight change:

Figure 1 illustrates the change in body weight of the four groups of growing rats during the entire study period. As we have previously demonstrated (Jen *Physiol Behav* 42:551-556 (1988) and Jen et al. *Int J Obesity* 19:699-708 (1995) incorporated herein by reference) those animals receiving the HF diet gained more weight than did those receiving the LF diet. Interestingly Figure 3 demonstrates that those animals receiving diet comprising α -cyclodextrin and fat at a ratio of 1:10 w/w gained weight at a slower rate relative to their respective control groups. Although the control group on the HF diet appears to still be gaining weight at a significant rate, the rate of weight gain of the other three groups appear to have reached a plateau. In this example the animals fed the α -cyclodextrin/high fat diet appear to have gained weight at nearly an identical rate as the animals receiving the low fat diet (4% w/w fat) without α -cyclodextrin. Thus by adding α -cyclodextrin to the diet the animals wherein the amount of α -cyclodextrin is based on the amount of fat in the diet, in this example 4% w/w α -cyclodextrin and 40% w/w fat, the rate of weight gain is significantly inhibited. This is in sharp contrast to previous studies wherein a cyclodextrin composition was added to rat diets did not exert an effect on the rate of weight gain until the percentage of the cyclodextrin composition in the food was at least 58.5% w/w.

Body composition:

Body composition analysis reveals that adding α -cyclodextrin to the LF diet did not affect body fat content. However, when α -cyclodextrin was added to the HF diet, it significantly reduced body fat mass (LF: 48.3 ± 2.4 g; LF-cyclodextrin: 51 ± 6.5 g; HF: 71.3 ± 5.8 g; HF-cyclodextrin: 55.6 ± 2.4 g, mean $\pm$ SE). This implies that α -cyclodextrin is most effective at reducing body fat when the dietary fat is high.

Stoichiometry:

Shimada et al. (Shimada et al. "Structure of inclusion complexes of cyclodextrins with triglyceride at vegetable oil/water interface" *J. Food Sci.* 1992; 57(3):655-656) have reported that two molecules of α -cyclodextrin complex with one free fatty acid (FFA) while Szejtli (Szejtli J. "Utilization of cyclodextrins in industrial products and processes" *J. Mater. Chem.* 1997;7:575-587) suggests that this phenomenon is dependent upon the chain length of the

fatty acids and that it is possible for 3-4 molecules of α -cyclodextrin to complex with each of the three fatty acids of a triglyceride molecule. These results suggest 9-12 molecules of α -cyclodextrin would be required to completely complex one molecule of triglyceride. If this were the case it would be difficult to imagine being able to feed enough of the α -cyclodextrin to an animal in order to complex sufficient triglycerides to make a significant difference in body weight as triglycerides and α -cyclodextrin have similar molecular weights. However, from the data disclosed herein wherein e.g., a diet comprising 4% α -cyclodextrin and 40% fat inhibits weight gain and reduces body fat mass, as the molecular weights are very similar, we have calculated that one α -cyclodextrin molecule can complex approximately nine molecules of triglyceride, the equivalent of 27 free fatty acids. Thus we can convert this directly to 1 gram of α -cyclodextrin complexes approximately 9 grams of triglyceride. Without wishing to be bound by theory, the difference in the ratio of α -cyclodextrin molecules needed to complex a triglyceride based on the disclosure of Shimada or Szejtli and the ratio of α -cyclodextrin to fat disclosed herein as forming complexes with fat suggest that the α -cyclodextrin catalyzes the formation of large particles of triglyceride coated with α -cyclodextrin in the form of a very stable micelle, thus reducing the bioavailability of the fats in those particles. We have been able to demonstrate that when purified olive oil is premixed with α -cyclodextrin the lipolytic activity of porcine pancreatic lipase is significantly reduced. As these particles are formed in the midst of chyme, a very complex "soup", the particles may be analogous to lipoprotein particles of the blood stream. This would also explain why the bacterial flora do not appear to be able to metabolize the α -cyclodextrin fat complexes coming from the small intestine.

Fecal fat content:

Total lipid determinations were performed on the collected feces using standard techniques Folch et al. *J Biol. Chem* 226: 497-509 (1957) incorporated by reference. The results (Figure 4) indicate a significant increase in fecal fat in HF-cyclodextrin ($p < 0.05$) but not in LF-cyclodextrin fed rats. On average this increase was approximately 25%. These data indicate that the α -cyclodextrin reduced the bioavailability of the fat by preventing the fat from being absorbed when fat intake is high, and, furthermore, prevented it from being metabolized by the intestinal flora of the animals' large bowel. The latter observation was confirmed by visual inspection of the feces. All of the collected material appeared to be of normal shape and consistency; there was no indication of diarrhea.

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Plasma glucose, cholesterol and triglyceride levels:

The plasma glucose, cholesterol and triglyceride concentrations were measured on all of the sacrificed animals using standard clinical laboratory techniques as may be found in Tietz Textbook of Clinical Chemistry, second edition. Burtis CA and Ashwood ER eds., W.B. Saunders Company A Division of Harcourt Brace & Company, 1994, Philadelphia incorporated herein by reference. (Figure 5). On average the α -cyclodextrin appeared to have decreased the plasma total cholesterol levels by about 10%. This decrease was not statistically significant over this short study period; we expect that with longer feeding period, cholesterol levels will continue to decline. The HDL cholesterol was also decreased but by a lesser extent, approximately 6-8%. LDL cholesterol levels on all of the animals were too low to measure reliably since in rats the majority of the cholesterol is carried in the HDL-cholesterol fraction, and very little is carried in the LDL-cholesterol fraction. The triglyceride levels were significantly reduced ($p < 0.05$) by about 30% in the animals that received the α -cyclodextrin. Glucose levels were not affected significantly by HF or α -cyclodextrin feeding in contrast to the results reported in Japanese Patent application S60-94912 wherein the high levels of cyclodextrins (19.5%, 39%, 58.5% or 78% w/w CD:total food) reduced blood glucose significantly.

Insulin Resistance:

Increased insulin resistance, elevated blood triglycerides and reduced HDL cholesterol levels are all the risk factors of Syndrome X. Insulin/glucose ratios as well as triglyceride/HDL ratios were calculated to provide indications about insulin resistance and risk of Syndrome X. (Szejtli J. Mater. Chem. 1997;7:575-587 incorporated herein by reference). Although, due to the short period of the study, HF feeding did not significantly induce insulin resistance there did appear to be a trend in that direction. Similarly, the HF-cyclodextrin animals showed a trend towards reduced insulin resistance. We expect based on the human data presented below that when the feeding period is lengthened insulin resistance will become significant and that α -cyclodextrin may significantly reduce the insulin resistance seen in HF fed rats. The reduction in triglyceride/HDL cholesterol ratios by α -cyclodextrin indicated a significant decrease in the risk for Syndrome X.

Leptin:

Leptin is a protein hormone with important effects in regulating body weight, metabolism and reproductive function. Leptin is secreted predominantly by adipocytes, supporting the idea that body weight is sensed as the total mass of fat in the body. Thus we
5 analyzed the plasma leptin levels in the animals fed the LF and HF diets $\pm$ α -cyclodextrin using standard techniques.

Figure 6 compares the plasma leptin values obtained from the four groups of rats wherein leptin levels were determined by using an RIA rat leptin kit (Linco Research, St. Charles, MO) following manufacturers instructions, incorporated here in by reference. The
10 amount of leptin present in the plasma of the HF rats ($18.1 \pm 3.2 \text{ ng/mL}$) is statistically higher ($p < 0.001$) than that of the LF rats ($7.5 \pm 1.9 \text{ ng/mL}$). The plasma leptin concentration of the HF-cyclodextrin rats ($9.6 \pm 1.8 \text{ ng/mL}$) is not statistically different from the LF rats. As adipose is the source tissue for leptin the data suggests that there is more body fat in the HF rats relative to the other three groups. Since leptin reduces food intake and body weight, the
15 higher levels of leptin indicate a state of leptin resistance in these HF fed rats. However, when α -cyclodextrin was added to the HF diet, rats consuming this diet had significantly lower leptin levels. This demonstrates that body fat mass was reduced in HF-cyclodextrin rats, and suggests leptin resistance in these rats is reduced. These results suggest that these rats are more sensitive to the effects of leptin and therefore future weight regain may be more
20 difficult. When leptin per gram of adipose tissue was calculated, it was revealed that both diet fat and α -cyclodextrin had independent effects on blood leptin levels (LF: $0.11 \pm 0.02 \text{ ng/mL/g}$ of adipose tissue; LF-CD: 0.075 ± 0.01 ; HF: 0.24 ± 0.03 ; HF-CD: 0.17 ± 0.03 ; diet effect $p < 0.001$; CD effect $p < 0.001$). In rats fed the HF diet with added α -cyclodextrin, the reduction in blood leptin level was more than that which can be accounted for by the
25 reduction of body fat mass. Therefore, α -cyclodextrin reduces blood leptin levels and reduces leptin resistance in addition to that induced by reduced body weight/fat. Similar results were obtained in human studies (see Example 4).

EXAMPLE 3: INITIAL CLINICAL DATA**Effect of α -cyclodextrin on serum triglyceride levels**

30 To determine the effect of α -cyclodextrin on triglyceride levels, eight volunteers were fed on two consecutive days a two-egg cheese (54g) omelet and a milkshake containing a

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total of 47g of fat after an overnight fast. On the first day the meal also contained approximately 5g of α -cyclodextrin. Blood samples (10ml) from each volunteer taken via an in-dwelling venous catheter immediately prior the meal (zero-time) and at 1, 2 and 3 hours after the meal was consumed and were assayed for serum triglyceride levels. The zero-time sample were used as the baseline to calculate the percentage change in blood serum triglyceride levels of the human volunteers at one, two and three hours. Figure 7 illustrates the data collected from the volunteers. It is of note that the expected increase in serum triglyceride levels is less when the α -cyclodextrin was mixed with the food than when it is not present, although the difference failed to reach significance ($p < 0.08$) due to large variation among the individuals and the small number of individuals included in this study.

Figure 7 also contains data from three of the volunteers who had partaken in an earlier two-hour study with a smaller meal (denoted "*"). The earlier two hour study also demonstrates that the change in triglyceride levels is less when α -cyclodextrin is included in the meal.

15 Weight loss effects

To determine if α -cyclodextrin added to a high fat diet resulted in weight loss, α -cyclodextrin was added to the high fat diet of a test subject, i.e., a 50 year old male human volunteer, five feet seven inches tall with an initial weight of 267 pounds. The α -cyclodextrin was added to the subject's diet in a proportion of one gram of α -cyclodextrin for every nine grams of fat that were estimated to be consumed by the subject. Figure 8 demonstrates the change in the body weight of the subject over a period of 200 days, approximately 6 months. By 6 months the subject's body weight was reduced by 32 pounds. In addition to the weight loss, within the first two weeks of the study, the subject's elevated blood pressure fell to the point where he was forced to reduce his prescribed beta-blocker by one-third. His blood triglycerides were also assayed during this time and his blood serum triglyceride levels were decreased by 23% within the first month and 46% by the end of six months. The effects of the α -cyclodextrin on various parameters are set forth in Table 2.

TABLE 2

Parameter	Baseline	1 month	6 months
Cholesterol (mmol/L)	4.76	4.76	4.0
HDL cholesterol (mmol/L)	0.97	1.00	1.11
Cholesterol/LDL	4.91	4.76	4.41
Triglycerides (mmol/L)	2.76	2.13	1.50
Insulin Resistance	2.85	2.13	1.35
Body Mass Index		39.17	37.27
Body Fat (%)		33.5	30.0
Waist (cm)		124	117
Hip (cm)		127	117
Dietary Energy Kcal/d		1,656	1,795
Total Fat (g/d)		112	103
Proportion fat (%)		60.9	51.7
Total Carbohydrate (g/d)		56	84
Proportion Carbohydrates (%)		13.5	18.7
Total Protein (g/d)		106	133
Proportion Protein (%)		25.6	29.6

α -cyclodextrin was also added to the diet of two additional volunteers. The α -cyclodextrin was added in a proportion such that each meal comprised about 2g of α -cyclodextrin. Table 3 sets forth the effects of the α -cyclodextrin on reducing the levels of cholesterol, LDL, cholesterol/HDL ratio and serum triglycerides. It is of note that both of these volunteers, as well as the initial volunteer, had been and still were taking one of the statin pharmaceuticals for lowering their blood serum cholesterol. All three volunteers were taking different statins. In addition volunteer "FK" was taking 3g/d niacin which he reduced by 50% in the first two weeks of the study because of the unpleasant side effects of this medication.

46

TABLE 3

Volunteer	Period Months	Cholesterol	Cholesterol/HDL	LDL	TG
FK	2.5	-18.5%	-16.1%	-25.6%	-22.2%
JA	6	-10.2	-8.8	-15.0	-37.5%

EXAMPLE 4: INSULIN AND LEPTIN LEVELS

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Blood samples were taken from the two additional subjects in Example 3 at various timepoints and assayed for insulin levels and leptin levels by the method of Linco Research (St. Charles, MO) using human insulin and leptin radioimmune assays.

10 The results of this analysis, presented in Table 4, demonstrate that the reduction in levels of insulin and leptin is more than that which can be accounted for by the reduced body weight.

Table 4.	Days on diet	Body weight (lb/kg)	Insulin (uU/ml)	Leptin (ng/ml)
Subject 1	0	196/89.09	14	3.6
	55	188/85.45	13	2.9
	112	180/81.82	8	1.6
	% decrease	5.0%	42.9%	55.6%
Subject 2	0	232/105.45	26	6.1
	28	230/104.55	28	6.0
	62	220.5/100.23	16	3.9
	% decrease	5.0%	38.5%	36%

EXAMPLE 5

15 An eighteen month old, neutered male dog of unknown parentage having chronic diarrhea was de-wormed twice and placed on hypoallergenic food in an effort to control the diarrhea. However, the chronic diarrhea was not alleviated and the dog stopped eating for a day or two on two or three separate occasions.

20 The dog was then treated with α -cyclodextrin as follows: The dog was placed on a diet comprising a teaspoon (2.5g) of α -cyclodextrin mixed with two cups dry food twice a day for two and one-half weeks. Based on the fat content in the food, the ratio of α -cyclodextrin to fat was about 1:9. The dog's chronic diarrhea was eliminated during this

period except for an acute episode of loose stools after a day of swimming in a river but the stool has been formed ever since.

The dog was then fed an identical diet that did not comprise α -cyclodextrin for 4 days. The dog very quickly lost his appetite, self restricted his food intake by about one-half and began eating grass, grass helps to bind his stool. The diarrhea returned.

α -cyclodextrin (5g) was then re-introduced into the dogs food and the diarrhea was once again eliminated.

EXAMPLE 6: FOOD PRODUCTS

The amount of α -cyclodextrin incorporated into the foods of this invention is based on the amount of fat contained in the food product. The following describes a variety of conventional fat containing foods products wherein α -cyclodextrin has been added in accordance with this invention. Table 5 sets forth the total weight of the food products and the amounts of α -cyclodextrin, fat and carbohydrates in the products described in this example compared to products described in other references.

A. Chocolate Chocolate Chip Espresso Cookies

- 260g pastry flour
- 75g cocoa powder
- 3.8g baking powder
- 2.8g salt
- 226g margarine
- 150g sugar
- 180ml (165g) molasses or brown sugar
- 28g α -cyclodextrin
- 5g vanilla extract
- 22g espresso (room temperature)
- 2 eggs
- 115g chocolate chips

The flour, cocoa, baking powder and salt were mixed together and then the margarine, sugar, molasses (or brown sugar), α -cyclodextrin, vanilla and espresso were added to the mixture. Lightly beaten eggs were stirred into the batter and the chocolate chips were folded in. Large teaspoon-size dollops of the batter were placed on a lightly greased cookie sheet

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and then baked for about 15 minutes in a conventional oven or 10-12 minutes in a convection oven preheated at 375°F. The cooked cookies were cooled on a wire rack.

Most blinded tasters found that the baked cookies were indistinguishable from those prepared from the same recipe without the addition of the α -cyclodextrin. Those who detected a difference preferred those that included the α -cyclodextrin as they were described to be; richer, smoother, tastier and moister with a more pleasing texture in the mouth than the cookies without the α -cyclodextrin.

B. Honey Oatmeal Cookies

10 42g butter
110g brown sugar
85g honey
1 egg
15g water
15 58g flour
2.5g salt
0.75g baking soda
81g rolled oats
4g α -cyclodextrin
20

In a mixer, preferably with a paddle attachment, the wet ingredients, butter, brown sugar, honey, egg and water, were mixed together. The remaining dry ingredients except for the rolled oats, were sifted together into a bowl. The rolled oats were then added to the dry ingredients. The wet and the dry ingredients were then mixed together and aliquots of the batter were deposited onto a greased cookie sheet and baked for 12-15 minutes in a conventional oven preheated to 350°F or 8-10 minutes in a convection oven. The cooked cookies were cooled on a wire rack.

Most blinded tasters found that the baked cookies were indistinguishable from those prepared from the same recipe without the addition of the α -cyclodextrin. Those who detected a difference preferred those that included the α -cyclodextrin as they were described to be; richer, smoother, tastier and moister with a more pleasing texture in the mouth than the cookies without the α -cyclodextrin.

C. Five Layer Bars

69g corn flake crumbs
100g sugar
113g butter or margarine
5 115g chocolate chips
115g butterscotch chips
124g flaked coconut
63g chopped nuts
1can (14oz, 400g) sweetened condensed milk
10 36g α -cyclodextrin

Corn flake crumbs, sugar, melted butter and 18g α -cyclodextrin were mixed together in a 13 x 9 x 2-inch baking pan, stir together. The mixture was pressed evenly and firmly in
15 bottom of pan to form a crust.

The chocolate chips, butterscotch chips, coconut, and chopped nuts were spread evenly in layers over the crust and 14 oz (400g) of sweetened condensed milk mixed with 18g of α -cyclodextrin were poured evenly over the 5 layers and then baked at 350° F for 23 minutes or until lightly browned around edges. The product was cooled completely and cut
20 into 24 pieces.

Most blinded tasters found that the baked bars were indistinguishable from those prepared from the same recipe without the addition of the α -cyclodextrin. Those who detected a difference preferred those that included the α -cyclodextrin as they were described to be; richer, smoother, tastier, sweeter and moister with a more pleasing texture in the mouth
25 than the bars without the α -cyclodextrin. It is of note that sweetened condensed milk undergoes a significant change upon mixing with α -cyclodextrin. Typically sweetened condensed milk is very thick making it difficult to pour and is an unappealing off-white color. Upon mixing with the α -cyclodextrin it becomes much smoother and more fluid in nature as well as changing in appearance to a very bright white color.

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CA
48**D. Macaroni with Cheese**

	98g	butter
	29g	flour
	484g	half and half cream
5	4g	salt
	0.53g	ground white pepper
	6g	chili sauce
	106g	grated parmesan cheese
	57g	grated cheddar cheese
10	50g	grated fontina cheese
	50g	grated gruyere cheese
	450g	macaroni
	3g	minced garlic
	25g	fresh bread crumbs
15	3g	seasoning
	33g	α -cyclodextrin
	1/2 tsp	seasoning
	33g	α -cyclodextrin

20 29g of flour and 33g of α -cyclodextrin were added to 56g of butter, melted and cooked for 3 minutes. The half and half was added slowly to the melted butter and flour mixture and then cooked with frequent stirring until thickened, about 4 to 5 minutes. The mixture was removed from the heat and the salt, pepper, hot sauce and half of the grated parmesan were added to the mixture and stirred until the cheese melted.

25 The macaroni was cooked in boiling water and the cooked macaroni was combined with butter and the minced garlic. The cheese mixture was added to the macaroni. The remaining cheeses were mixed and added to the macaroni mixture, the bread crumbs were layered over the macaroni and cheese and baked for 40 to 45 minutes.

30 Blinded tasters found that the food prepared with the α -cyclodextrin was creamier and moister than the same food prepared without the α -cyclodextrin.

Table 5	Total weight, g	Total CHO, g	Total fat, g	Added α-CD, g	α-CD as % total wt	α-CD as % of CHO	α-CD as % of fat	Kcal fat (%)	fat wt /total wt (%)	Kcal CHO (%)	CHO wt /total wt (%)
Cheese omelet	162	5	30	3.5	2.2%	70%	11.7%	68%	18.5%	5%	3.1%
Peanut butter	34 (2 tsp)	8	16	2.0	5.9%	25%	12.5%	70%	47%	15%	23.5%
Meatloaf	1659	146	317	36	2.2%	24.7%	11.4%	69%	19.1%	14%	8.8%
Macaroni w/ 4 cheeses	1586	395	293	33	2.1%	8.4%	11.3%	51%	18.5%	31%	24.9%
Five layer bars	1241	702	292	35	2.8%	5.0%	12%	46%	23.5%	49%	56.6%
French-apple bread pudding ¹	1365	295	112	10.5	0.8%	3.6%	9.4%	42.4%	8.2%	49.6%	21.6%
Honey oatmeal cookies	492	308	48	3.5	0.7%	1.1%	7.3%	24%	9.8%	69%	62.6%
Chocolate chocolate chip espresso cookies	1020	556	231	28	2.8%	5.0%	12.2%	46%	22.7%	49%	54.5%
Biscotti	1323	870	108	12	0.9%	1.4%	11.1%	20%	8.2%	71%	65.8%
Butter cake Japanese application S60-94912	470	170	141	50 (CD comp) ²	10.6% (CD comp) ² 3.2% α-CD	29.4% (CD comp) ² 8.8% α-CD	35.5% (CD comp) ² 10.6% α-CD	64%	30%	31%	36.2%
Chinese noodles Japanese application S60-94912	1336	535	22.15	300 (CD comp) ²	22.5% (comp) ² , 7.5% α-CD	56.1% (CD comp) ² , 18.7% α-CD	1364% (CD comp) ² 454% α-CD	7%	1.7% (18.8% frying)	72%	74.9%
Biscuit Japanese application S60-94912	2015	1400	400	500 (CD comp) ²	24.8% (CD comp) ² 7.4% α-CD	35.7% (CD comp) ² 10.7% α-CD	125% (CD comp) ² 37.5% α-CD	45%	19.9%	49%	69.5%

CD comp. = a mixture of cyclodextrins ²From Best Recipes This Side of Heaven Holy Trinity Anglican Church Cookbook Committee, Yorkton, Saskatchewan p. 172, Perksen Printers Ltd. Steinbach, Manitoba ROA 2A0 CA

A clear relationship exists between weight gain, obesity and a variety of pathologic disorders, e.g., diabetes, insulin resistance, cardiovascular disease, elevated blood lipid levels, sleep apnea, arthritis, certain types of cancer and elevated mortality rates (Solomon and
5 Manson, "Obesity and mortality: a review of the epidemiological data". *Am J Clin Nutr* 1997;66:1044S-1050S). The total health care and lost productivity costs for obesity-related disorders reached \$117 billion in 2000 (Overweight and obesity: At a glance. Office of the Surgeon General, 2001). Changes in body mass index (BMI) are reported to precede onset of
10 diabetes (Resnick et al., "Relation of weight gain and weight loss on subsequent diabetes risk in overweight adults" *J Epidemiol Community Health* 2000;54:596-602), and for every one kg increase in body weight the prevalence of diabetes increases by 9% (Mokdad et al. "Diabetes trends in the U.S.: 1990-1998". *Diabetes Care* 2000;23:1278-1283). Although type II diabetes is associated with excess body weight, other metabolic abnormalities observed in
15 obesity may contribute to the onset of Type II diabetes. Obese individuals tend to be hyperlipidemic, hyperinsulinemic and insulin resistant, all of which have been shown to increase the risk of developing Type II diabetes (Kissebah et al. Health risks of obesity. *Med Clin North Am* 1989;73:111-138; Kreisberg et al., Insulin secretion in obesity. *N Engl J Med* 1967;276:314-319, and; Olefsky J. Insulin resistance and insulin action: an in vitro and in vivo perspective. *Diabetes* 1981;30:148-162). Therefore, a reduction in the severity of any of
20 these abnormalities will also reduce the risk of developing Type II diabetes. The products of this invention have organoleptic properties desired by consumers and also promote weight loss and other health benefits.

WE CLAIM

1. A consumable farinaceous food product comprising α -cyclodextrin and fat, wherein said food product has a ratio of α -cyclodextrin to fat of 1:20 w/w to about 1:3 w/w of said food product and wherein said food product comprises less than about 9% w/w total cyclodextrin.
2. The consumable farinaceous food product of claim 1, comprising at least about 7% to about 80% fat by caloric content.
3. The consumable farinaceous food product of claim 1 comprising less than about 6% w/w total cyclodextrin.
4. The consumable farinaceous food product of claim 1 wherein the food product is cooked.
5. A consumable non-farinaceous food product comprising complexes of α -cyclodextrin and fat, wherein said non-farinaceous food product has a ratio of α -cyclodextrin to fat of 1:20 w/w to about 1:3 w/w of said food product.
6. The consumable non-farinaceous food product of claim 5 wherein said non-farinaceous food product is a dairy, meat or vegetable food product.
7. The consumable non-farinaceous food product of claim 6 comprising less than about 9% w/w total cyclodextrin.
8. The consumable non-farinaceous food product of claim 5 comprising 5% to 50% fat w/w.
9. A method for enhancing organoleptic properties of a fat containing consumable food product comprising adding α -cyclodextrin to said fat containing food product such that the food product has a ratio of α -cyclodextrin to fat of about 1:20-1:3 w/w and wherein said food product comprises less than about 9% w/w total cyclodextrin.
10. The method of claim 9, wherein the α -cyclodextrin is a substantially pure α -cyclodextrin.

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11. The method of claim 9, wherein said consumable food product comprises about 7% to about 80% fat by caloric content.
12. The method of claim 9, wherein the fat containing consumable food product is a consumable farinaceous food product.
13. A method for reducing the bioavailability of a fat in a consumable fat containing food product comprising determining the amount of fat in a consumable fat containing food product and combining α -cyclodextrin with the consumable fat containing food product such that the consumable fat containing food product comprises a ratio of α -cyclodextrin to fat of about 1:20 to about 1:3 w/w wherein said α -cyclodextrin is not removed from said food product prior to consumption.
14. The method of claim 13, wherein the consumable food product is a consumable farinaceous food product.
15. The method of claim 13, wherein the consumable food product is a consumable dairy, meat or vegetable product.
16. The method of claim 13 wherein the consumable food product comprises about 7% to 80% fat w/w by caloric content.
17. The method of claim 13 wherein the α -cyclodextrin is administered in the form of a pill, tablet, powder, capsule, liquid or confection.
18. A method for increasing the level of high density lipoprotein (HDL) cholesterol in a subject in need thereof comprising administering α -cyclodextrin to a subject in need thereof in an amount sufficient to increase HDL levels.
19. The method of claims 18 wherein about 165mg to 11g of α -cyclodextrin is administered to said subject with a fat containing meal.
20. The method of claim 18, wherein said subject consumes about 100g fat per day.
21. The method of claim 18, wherein α -cyclodextrin is in an amount such that it is in a ratio of 1:20 to about 1:3 of fat ingested daily by the subject

22. The method of claim 18, wherein total cholesterol levels are not increased in said subject.
23. The method of claim 18, wherein the α -cyclodextrin is administered in a form selected from the group consisting of a tablet, powder, capsule, liquid and a confection.
24. The method of claim 18, wherein the α -cyclodextrin is administered to the subject in the form of the consumable farinaceous food product of claim 1.
25. The method of claim 21 wherein about 500mg to 33g of α -cyclodextrin is administered to the subject in need thereof daily to increase the level of high density lipoprotein (HDL)
26. A method for reducing the cholesterol/HDL ratio in a subject comprising administering to a subject in need thereof an amount of α -cyclodextrin wherein the amount of α -cyclodextrin administered to said subject and fat ingested daily by said subject is in a ratio of about 1:20 to about 1:3 w/w.
27. The method of claim 26, wherein the α -cyclodextrin is administered in a form selected from the group consisting of a tablet, powder, capsule, liquid and confection.
28. The method of claim 26, wherein the α -cyclodextrin is administered to the subject in the form of the food product of claim 1.
29. The method of claim 26 wherein about 500mg to 33g of α -cyclodextrin is administered to the subject in need thereof daily to reduce the cholesterol/HDL ratio.
30. A method for promoting weight loss in a subject in need thereof comprising administering to a subject in need thereof an amount of α -cyclodextrin wherein the amount of α -cyclodextrin administered to said subject and the amount of ingested fat said subject desires to prevent from being absorbed, are in a ratio of about 1:20 to about 1:3 w/w.
31. The method of claim 30 wherein said subject consumes a daily diet comprising at least 30% fat by caloric content.

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32. The method of claim 30, wherein the α -cyclodextrin is administered in the form of a tablet, powder, capsule, liquid or confection
33. The method of claim 30, wherein the α -cyclodextrin is administered to the subject in the form of the consumable farinaceous food product of claim 1.
34. The method of claim 30 wherein about 500mg to 33g of α -cyclodextrin is administered to the subject in need thereof daily to promote weight loss.
35. A method of reducing triglyceride levels in a subject comprising administering to a subject in need thereof an amount of α -cyclodextrin wherein the amount of α -cyclodextrin administered to said subject and fat ingested daily by said subject is in a ratio of about 1:20 to about 1:3 w/w.
36. The method of claim 35, wherein the α -cyclodextrin is administered in the form of a tablet, powder, capsule, liquid or confection.
37. The method of claim 35, wherein the α -cyclodextrin is administered to the subject in the form of the consumable farinaceous food product of claim 1.
38. The method of claim 35 wherein about 500mg to 33g of α -cyclodextrin is administered to the subject in need thereof daily.
39. A method for reducing leptin levels, insulin levels or insulin resistance in a subject comprising administering α -cyclodextrin to a subject in need thereof in an amount sufficient to reduce leptin levels, insulin levels or insulin resistance in said subject.
40. The method of claim 39, wherein the amount of α -cyclodextrin administered to said subject and fat ingested daily by said subject is in a ratio of about 1:20 to about 1:3 w/w.
41. The method of claim 39, wherein the α -cyclodextrin is administered in the form of a tablet, powder, capsule, liquid or confection.
42. The method of claim 39, wherein the α -cyclodextrin is administered to the subject in the form of the consumable farinaceous food product of claim 1.

43. The method of claim 39, wherein about 500mg to 33g of α -cyclodextrin is administered to the subject in need thereof daily.
44. A method for reducing diarrhea in a subject comprising administering to a subject in need thereof α -cyclodextrin in an amount sufficient to reduce diarrhea in said subject.
45. The method of claim 44 wherein said subject is a cholecystectomy subject or a patient suffering from fat aggravated diarrhea.
46. The method of claim 44, wherein the α -cyclodextrin is administered in the form of the consumable farinaceous food product of claim 1.
47. The method of claim 44 wherein the α -cyclodextrin is administered in the form of a pill, capsule, wafer, tablet, powder, liquid or confection.
48. The method of claim 44, wherein about 500mg to 33g of α -cyclodextrin is administered to the subject in need thereof daily.
49. The method of claim 44, wherein the amount of α -cyclodextrin administered to said subject and fat ingested daily by said subject is in a ratio of about 1:20 to about 1:3 w/w.
50. The method of claim 18, wherein the α -cyclodextrin is administered to the subject in the form of the consumable non-farinaceous food product of claim 5.
51. The method of claim 26 wherein the α -cyclodextrin is administered to the subject in the form of the consumably non-farinaceous food product of claim 5.
52. The method of claim 30, wherein the α -cyclodextrin is administered to the subject in the form of the consumable non-farinaceous food product of claim 5.
53. The method of claim 35, wherein the α -cyclodextrin is administered to the subject in the form of the consumable non-farinaceous food product of claim 5.
54. The method of claim 39, wherein the α -cyclodextrin is administered to the subject in the form of the consumable non-farinaceous food product claim 5.

55. The method of claim 44, wherein the α -cyclodextrin is administered in the form of the consumable non-farinaceous food product of claim 5.
56. The method of claim 44 wherein the consumable food product comprises about 20% to 70% fat w/w or calories.
57. The method of claim 54 wherein the consumable food product comprises about 40% to 70% fat w/w or calories.
58. The method of claim 44 wherein the subject is a mammal.
59. The method of claim 58 wherein the mammal is selected from the group consisting of human, horse, cow, dog, and cat.
60. The method of claim 59 wherein the α -cyclodextrin is administered in the form of a pet food.
61. A method for reducing the amount of time required to produce whipped cream comprising adding α -cyclodextrin to cream during or prior to whipping said cream wherein α -cyclodextrin is added in an amount sufficient to reduce the amount of time required to produce whipped cream.

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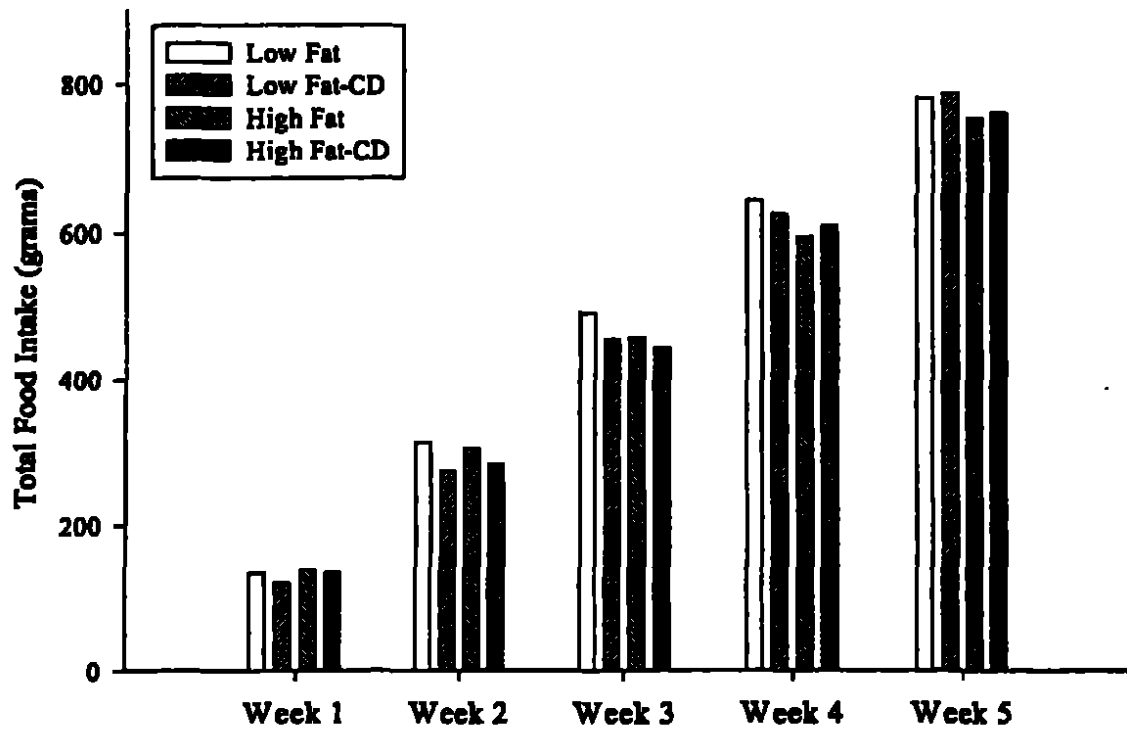


Figure 1

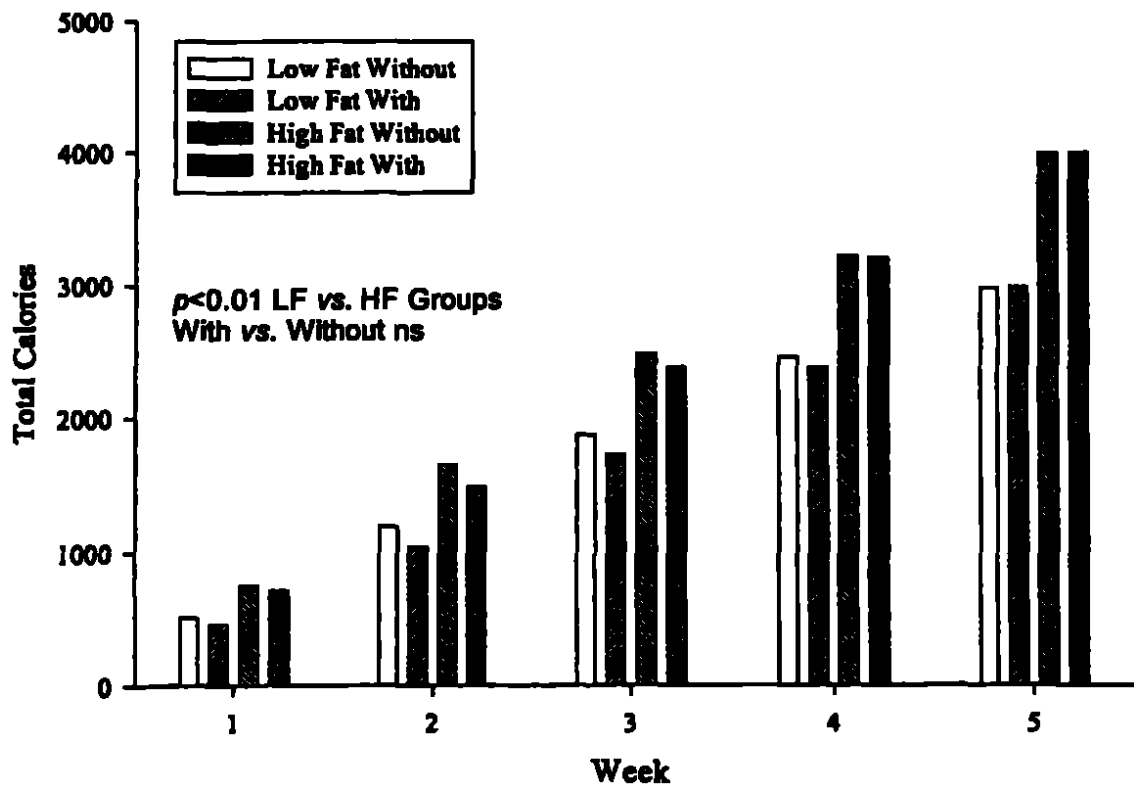


Figure 2

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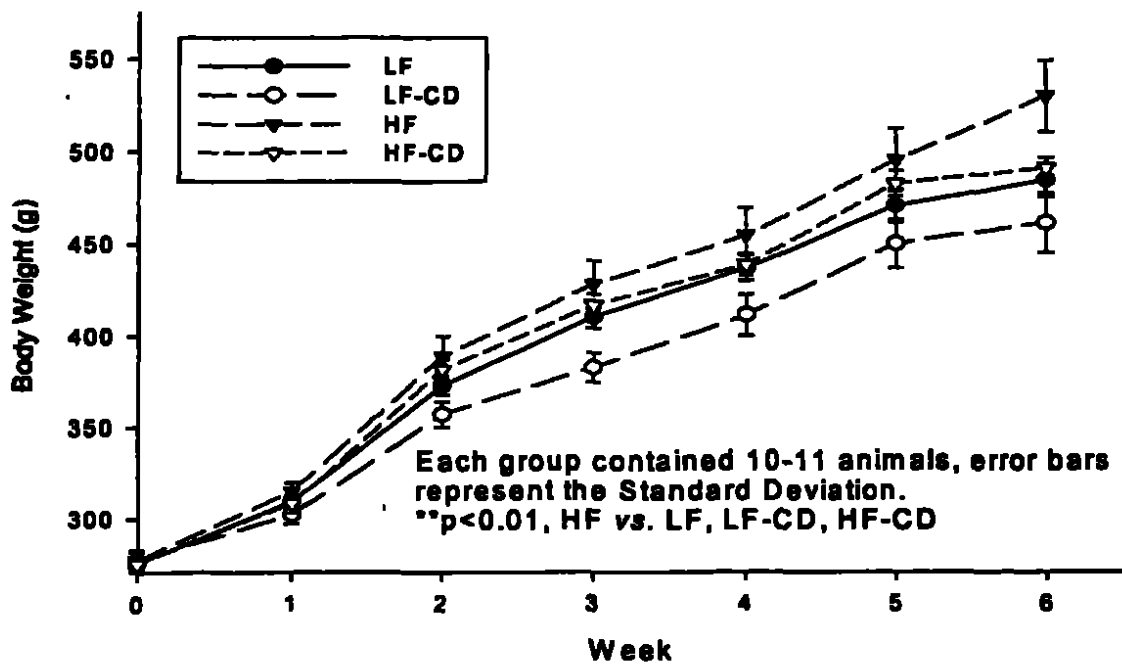
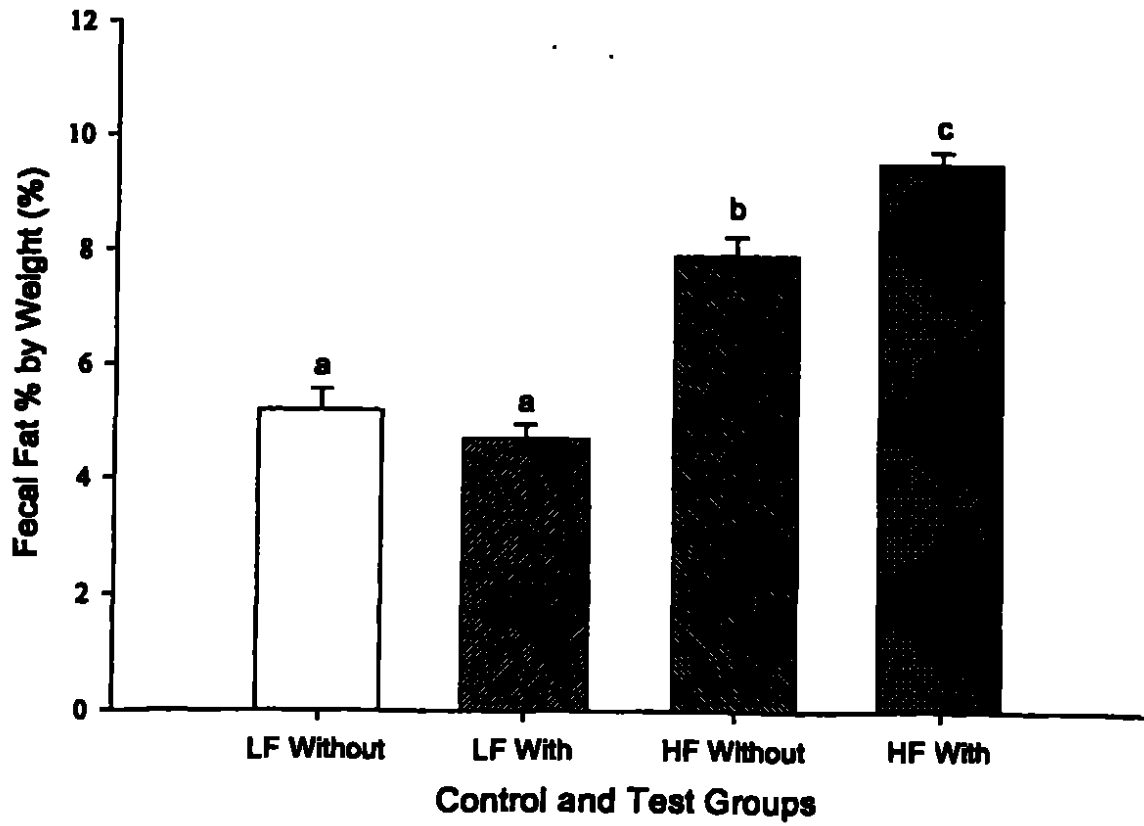


Figure 3



Groups sharing a common superscript are not significantly different

Figure 4

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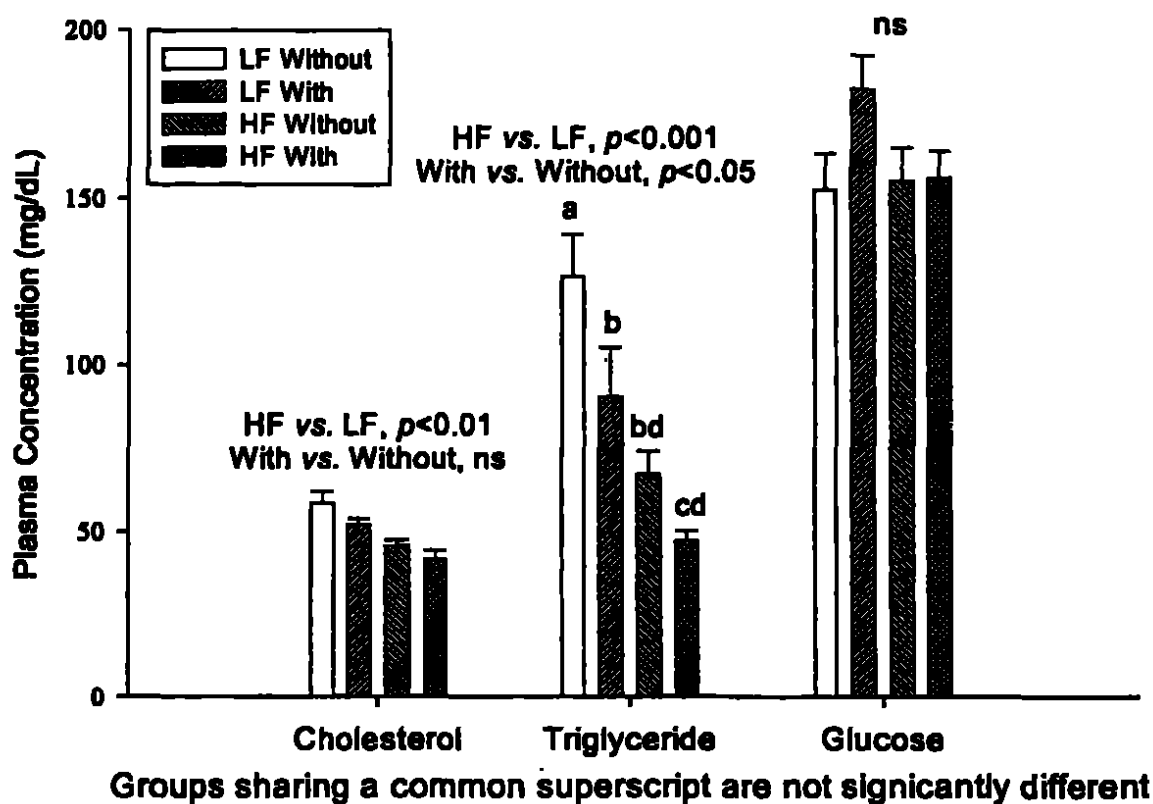
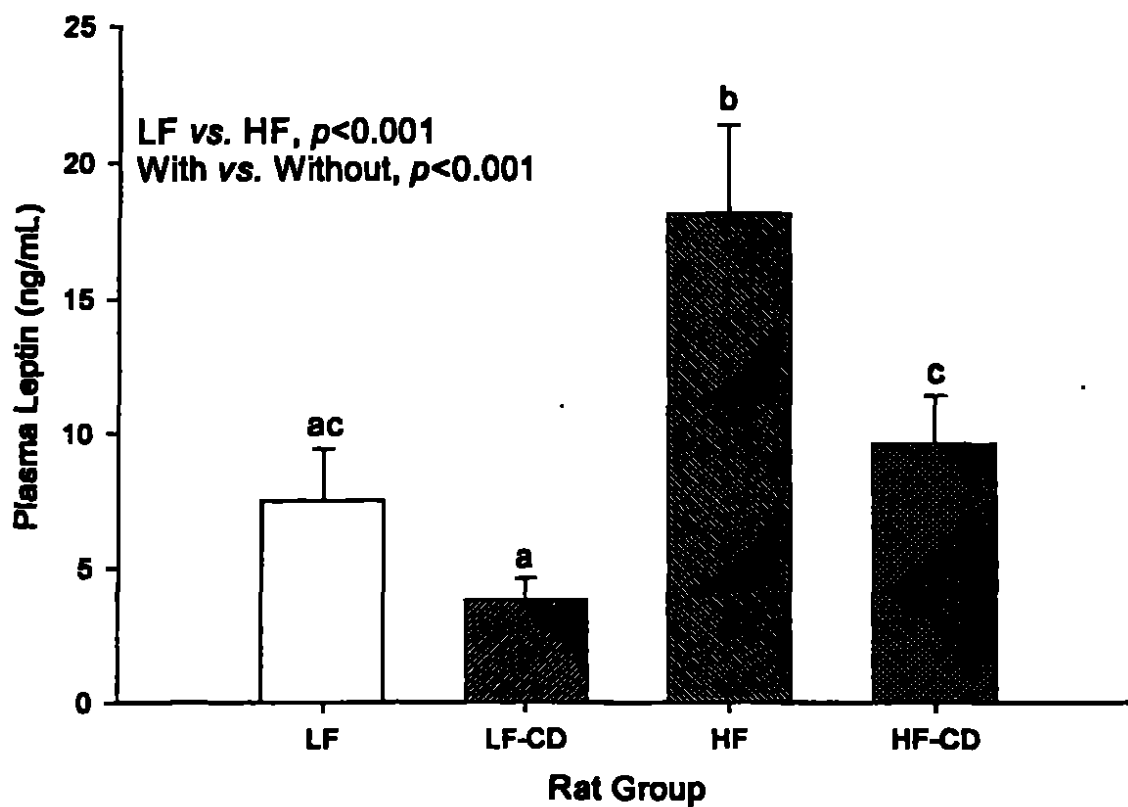


Figure 5

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**Figure 6**

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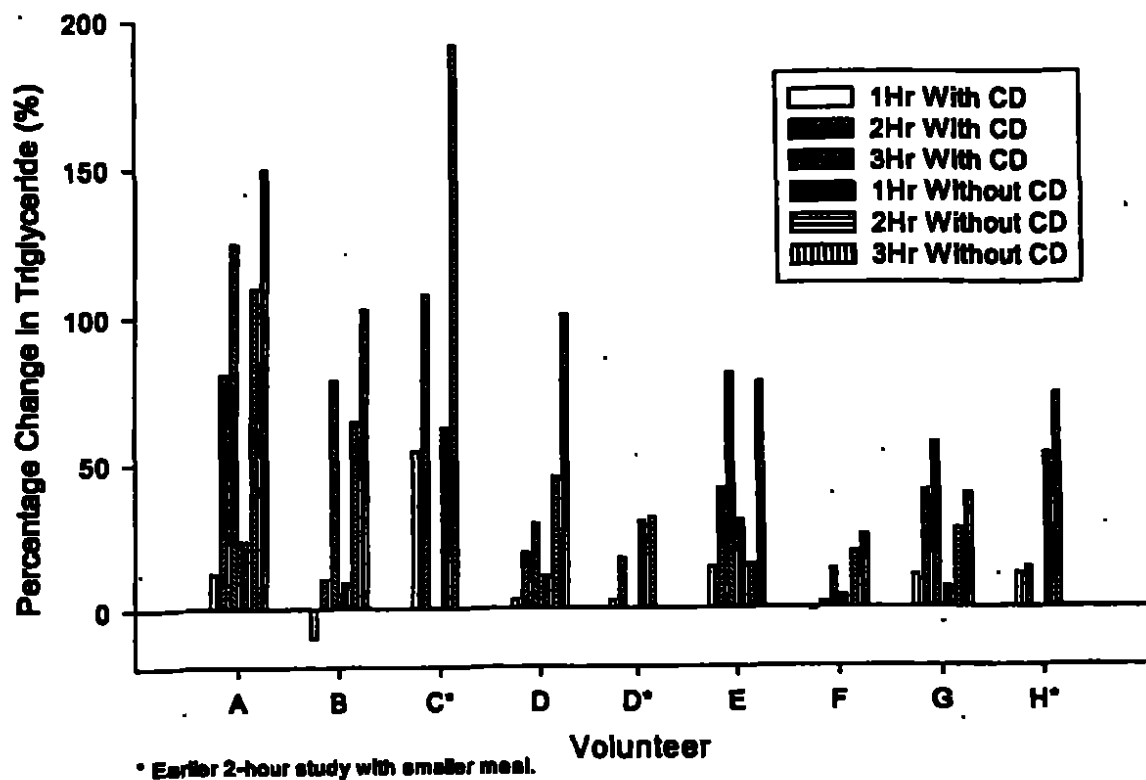


Figure 7

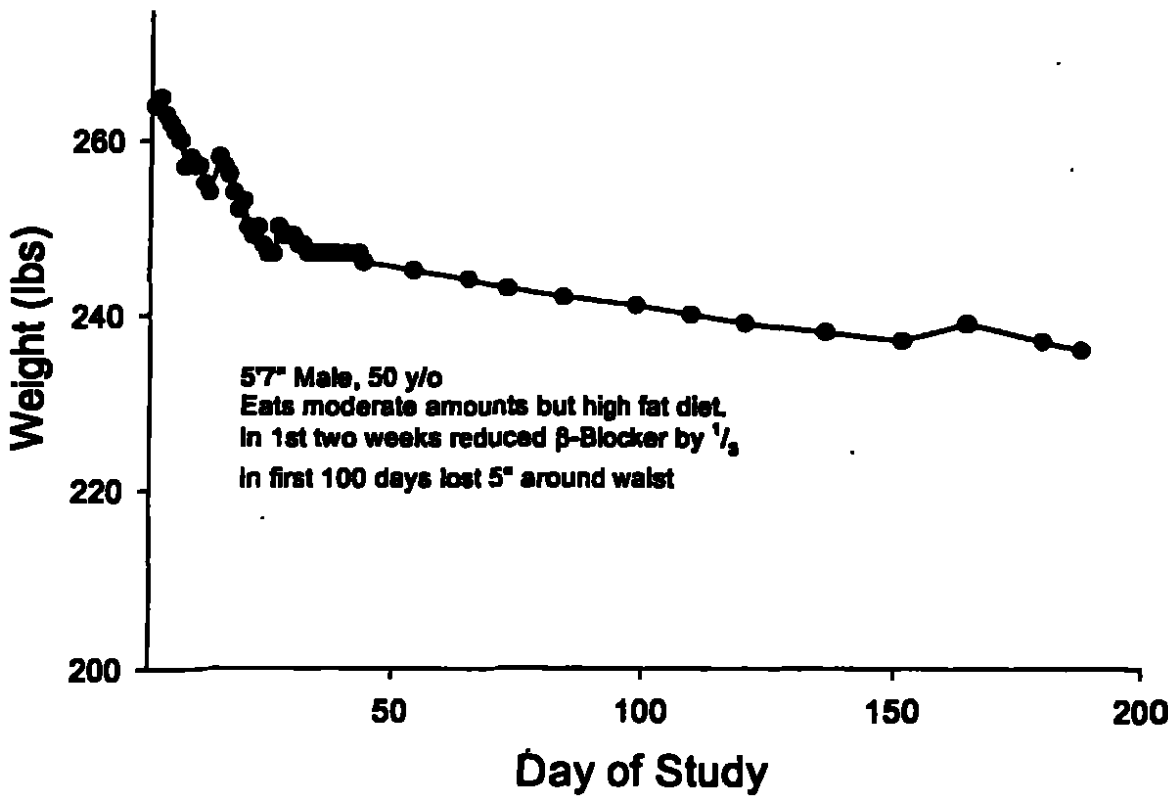


Figure 8

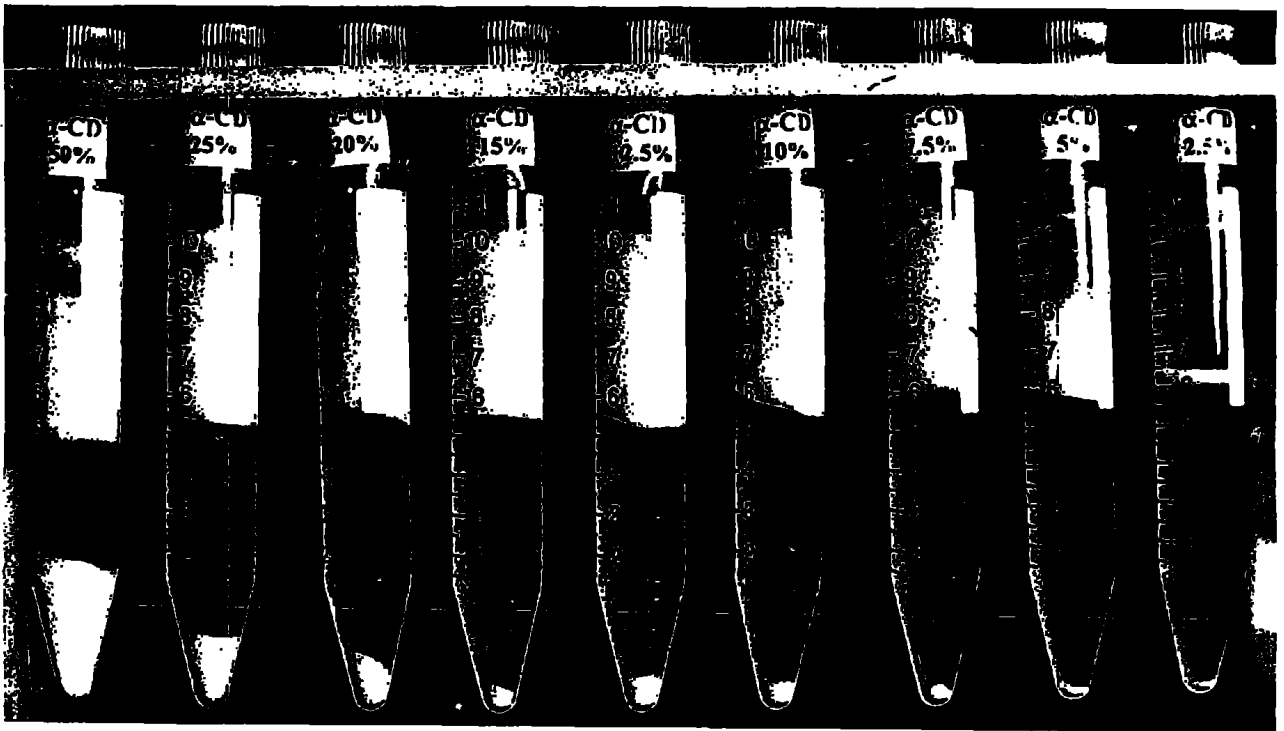


Figure 9A

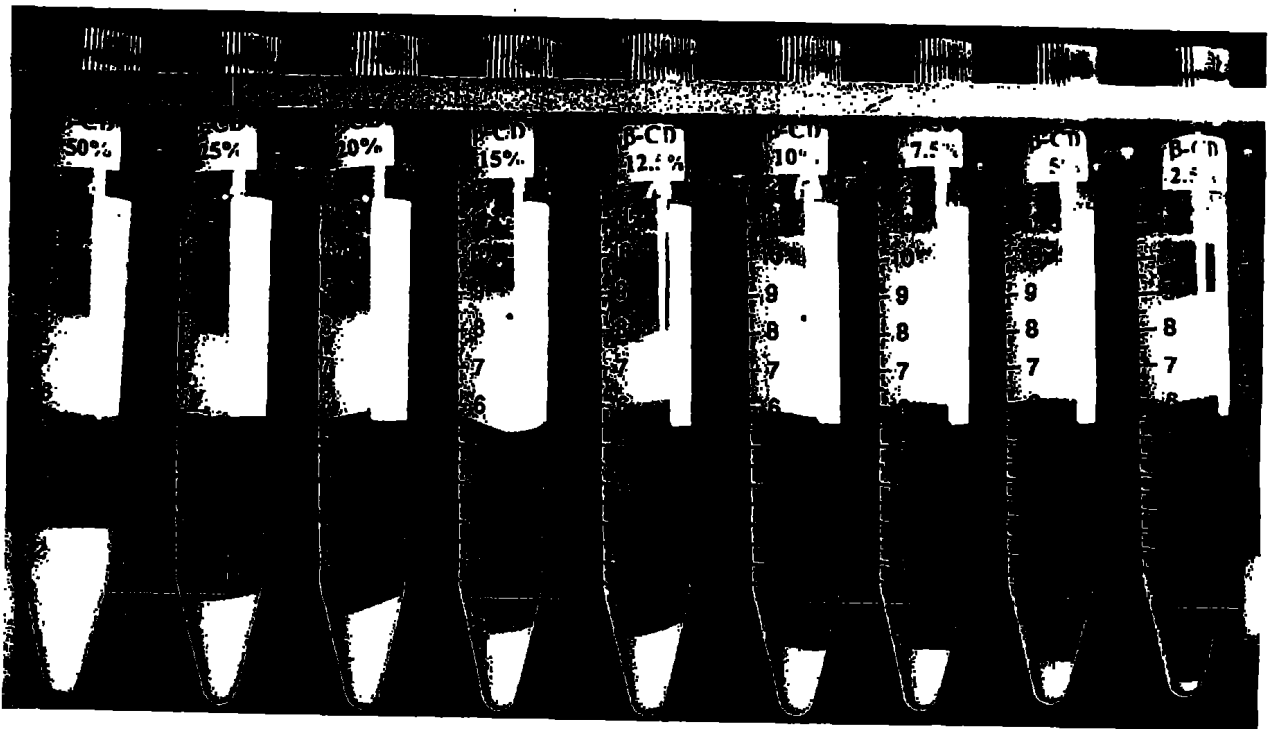


Figure 9B

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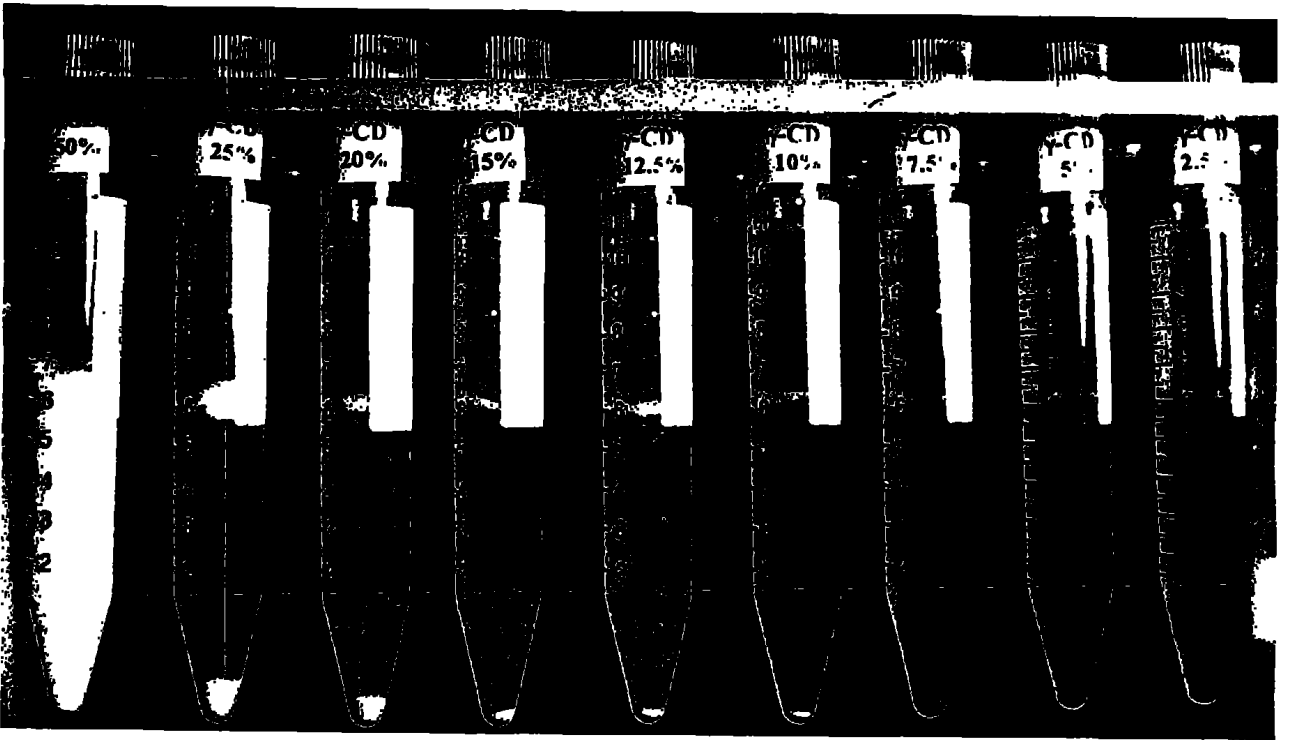


Figure 9C

COMPOSICIONES QUE COMPRENDEN UN UNIDOR DE GRASA DIETETICA Y METODOS PARA SU USO

Esta solicitud reivindica prioridad en la Solicitud Provisional de Patente de los E.U. Serie No. 60/486,440 presentada en Julio 14, 2003, la Serie No. 60/461,847 presentada en Abril 11, 2003, y la Serie No. 60/404,366 presentada en Agosto 19, 2002, todas incorporadas en su totalidad en este, por referencia.

CAMPO DEL INVENTO

El invento se relaciona con productos consumibles, específicamente productos consumibles que contienen grasa, comprendiendo α -ciclodextrina y los métodos para su uso. El invento también se relaciona con métodos para reducir la biodisponibilidad de grasas en productos consumibles que contienen grasa y con métodos para aumentar las propiedades organolépticas de productos consumibles que contienen grasa.

ANTECEDENTES DEL INVENTO

Los esfuerzos para controlar el peso del cuerpo a través de dietas, ejercicio y drogas han encontrado solamente un éxito limitado. La obesidad en los E.U.A. continúa siendo de proporciones epidémicas. Fue estimado que en el 2000, mas del 64.5% de la población adulta de los EUA tenia sobrepeso o era obesa y que a lo largo de los E.U.A. 30.5% de la población era obesa (Flegal et al., JAMA 288: 1723-1727 (2002)). También parece haber una epidemia de diabetes en los E.U.A. donde 7.3% de la población de los E.U.A. es diabética (Mokdad et al., JAMA 286: 1195-1200 (2001)). Mientras que los médicos aconsejan a sus pacientes que luchan contra el aumento de peso, la obesidad y la diabetes, que ejerciten y que administren la cantidad y calidad de la comida que comen, la evidencia sugiere que una gran proporción de la población no pueden o no quieren hacer los grandes cambios en su estilo de vida que pueden ser necesarios para disminuir su masa corporal.

Frecuentemente las estrategias recomendadas por los proveedores de cuidados de salud de reducir y/o mantener el peso envuelven cambios en el estilo de vida y, en algunos casos, el uso adicional de drogas o suplementos dietéticos. Los individuos que son capaces de mantener la pérdida de peso (definido como >10% por debajo del peso corporal inicial después de un año) generalmente adoptan todas o al menos una combinación de estas estrategias (McGuire et al., "Estrategias de comportamiento de individuos que han mantenido pérdida de peso a largo plazo" *Obes Res* 7:334-341 (1999)). Sin embargo, a pesar de todos los esfuerzos hechos por los individuos obesos y por los gobiernos, la tasa de éxito por mantener el peso bajo es frustrantemente pequeña. Un meta-análisis ha mostrado que la tasa de éxito de la "cura propia" esta entre 9% y 43% después de un año de seguimiento (Barlett et al., "Es la prevalencia de éxito y mantenimiento de la pérdida de peso alta en la comunidad en general que en una clinica de investigación?" *Obes Res* 7:407-413 (1999)). El Registro Nacional de Control de Peso ha reportado que 47% - 49% de los pacientes obesos mantuvieron por lo menos 10% de pérdida de peso después de un año y que 25% - 27% han mantenido dicha cantidad de pérdida de peso por 5 años (McGuire et al., "La prevalencia del mantenimiento de la pérdida de peso entre los adultos americanos" *Int J Obes Metab Disord* 23:1314-1319 (1999)). Sin embargo, después de 5 - 15 años, solamente el 5% de los pacientes obesos fueron capaces de mantener la pérdida de peso (Drenick and Johnson, "Reducción de peso mediante el ayuno y semi-inanición en la obesidad mórbida: seguimiento a largo plazo". *Int. J. Obes.* 2:25-34 (1978) y Sario-Lahteenkorva and Rissanen "Un estudio descriptivo del mantenimiento de la pérdida de peso: seguimiento a los 6 y 15 años de adultos inicialmente con sobrepeso" *Int J Obes* 24:116-125 (2000)).

Tratamientos farmacéuticos han sido desarrollados para la obesidad pero su uso tiene limitaciones. Actualmente solamente hay dos drogas antiobesidad aprobadas por la Administración de Alimentos y Drogas (FDA), Orlistat y Sibutramine. Orlistat inhibe la actividad lipasica pancreática en el intestino delgado. La lipasa pancreática rompe los triglicéridos en ácidos grasos y monoglicéridos, los que subsiguientemente son absorbidos por el cuerpo. Entonces la inhibición de la actividad lipasica efectivamente reduce la absorción de grasa. Sin embargo, si el paciente deja de seguir una dieta baja en grasas, la que es recomendada mientras este bajo este medicamento, la grasa es metabolizada por las bacterias intestinales y causa cambios osmóticos y producción de gases, lo que resulta en diarrea y flatulencia, efectos secundarios no placenteros de este medicamento. Entonces, aunque esta droga puede inducir a una pérdida modesta de peso y a un mejor mantenimiento del peso a la sola dieta, a falta de cambios mayores en la dieta los efectos adversos del malestar gastrointestinal, diarrea y flatulencia han limitado su uso (Heck et al., "Orlistat, un nuevo inhibidor de la lipasa para la administración de la obesidad". *Pharmacotherapy* 20:270-279 (2000)).

La Sibutramine es una serotonina y norepinefrina inhibidor retomador y reduce el peso corporal al suprimir el apetito (Bray G., "Tratamiento de la obesidad con medicamentos". *Rev. Endocr Metab Disord* 2:403-418(2001). El FDA la ha aprobado, hasta por dos años, para el tratamiento de la obesidad. Sin embargo, la Sibutramine inhibe el retomamiento de norepinefrina pudiendo entonces aumentar la presión sanguínea. Esta droga, entonces, es contraindicada para uso en pacientes obesos (Bray 2001 supra and Sramek et al. "Eficacia y seguridad de la Sibutramine para la pérdida de peso en pacientes obesos con hipertensión bien controlada por agentes de bloqueo beta-adrenergico: placebo-controlado, doblemente ciego, ensayo al azar" *J Hum Hypertens* 16:13-19 (2002)). Otros efectos secundarios de la Sibutramine incluyen un aumento en las pulsaciones del corazón, insomnio, constipación, dolor de cabeza, dolor abdominal etc. Para pacientes obesos normotensivos, la Sibutramine, en combinación con dieta y cambios de comportamiento, ha mostrado efectos benéficos (Astrup and Toubro "Cuando, para quien y como usar la Sibutramine?" *Int J Obes Relat Metab Disord* 25 (supp 4):S2-S7 (2001), pero a la fecha no ha habido estudios humanos que usaran solamente la Sibutramine, es decir, sin algún cambio en el estilo de vida. Además, en un estudio animal los efectos de la supresión del apetito de la Sibutramine gradualmente se atenuaron a lo largo de varios días de administración (Starck et al. "Regulación del peso corporal y composición de la carcasa de la sibutramine en ratas" *Obes Res* 10:713-181 (2002)).

Los suplementos dietéticos han sido también usados para reducir el aumento de peso, para mantener el peso, y para tratar algunas de las anormalidades metabólicas asociadas con la obesidad. Por ejemplo, se ha demostrado que el ácido graso 3 omega y el ácido linoléico reducen el aumento de peso y afectan los niveles de triglicéridos y/o la resistencia a la insulina. Es sabido que los ácidos grasos 3 omega reducen en humanos normales, hiperlipidémicos y diabéticos, los niveles de lípidos en la sangre y se ha reportado que reducen el peso corporal. Los pacientes diabéticos sin hiperlipidemia, alimentados con una dieta que comprenda aceite de pescado, que es conocida como alta en ácido graso 3 omega, no mostraron niveles reducidos de lípido en la sangre, a pesar de que disminuyó su presión sanguínea. Sin embargo, los pacientes diabéticos que tienen hiperlipidemia redujeron significativamente los niveles de triglicéridos en la sangre y redujeron la presión sanguínea después de ser alimentados con aceite de pescado ácido graso 3 omega (Kasmin et al. *J. Clin Endocrinol Metab* 67:1-5 (1988)). Los efectos de dietas dadas a ratas Zucker genéticamente obesas, y a sus contrapartes más delgadas, que comprende aceite de pescado, demostró que tanto las ratas obesas como las normales tuvieron una reducción en el peso corporal y en los niveles de lípidos en la sangre, según comparadas con los controles (Jen et al., *Nutrition Research* 9:1217-1228 (1989). Una dieta alta en grasa, con aceite de pescado, indujo a la menor cantidad de aumento de peso y resistencia a la insulina, en comparación con una dieta

alta en grasas hecha con otras clases de aceites (Pelizzon et al., *Obesity Res.* 10:947-955 (2002)). Los ácidos grasos 3 Omega también parecen afectar benéficamente la resistencia a la insulina. Las ratas alimentadas con dietas altas en grasa, comprendiendo aceite de pescado, tuvieron menos resistencia a la insulina que las ratas alimentadas con dietas que comprendían otros aceites, e.g. manteca, aceite de maíz o triglicéridos de la cadena media (Hill et al. *Int. J. Obesity*, 17:223-236 (1993)).

El ácido linolénico adicionado a las dietas también ha mostrado que reduce el contenido de grasa corporal y que facilita en el hígado el ácido graso β -oxidación (Takada et al., *J. Nutr.* 124:469-474 (1994)). En ratas de edad alimentadas con dietas hechas con varios ácidos grasos, i.e., ácido α -linolénico (n-3 PUFA) o ácido gamma linolénico (n-6 PUFA) (10% w/w) adicionado con colesterol, por 15 semanas, se encontró que tanto las dietas linolénicas α -y gamma inhibieron el aumento en el total de colesterol en la sangre, los niveles de colesterol VLDL+IDL+LDL de las ratas cuando fueron alimentadas con dietas altas en colesterol (Fukushima et al. *Lipids* 36:261-266 (2001)). Resultados similares fueron encontrados para ratas obesas Zucker, las que tuvieron una disminución en el aumento de peso y grasa corporal cuando diariamente rellenadas con ácido linolénico gamma (Phinney et al. *Metabolism* 42:1127-1140 (1993)). En humanos, la mezcla de n-3 PUFA y ácido gamma linolénico también altero favorablemente los lípidos sanguíneos y los perfiles de ácidos grasos en las mujeres, después de su administración por mas o menos 28 días (Laidlaw and Holub, *Am. J. Clin. Nutr.* 77:37-42 (2003)).

Los cambios en el estilo de vida para procurar la pérdida de peso y otros efectos benéficos a la salud incluyen e.g. un aumento en la actividad física; consumos con menos calorías y dietas con menos grasas. Los Estados Unidos han visto una gradual reducción del porcentaje de consumos de grasas dietéticas, de 43.7% en 1965 a 33.1% en 1995 (Kennedy et al., "Consumo de grasa en la dieta en la población de los E.U." *J. AM Coll Nutr* 18:207-212 (1999)), sin embargo, el promedio de calorías consumidas ha aumentado en forma superior al aumento en el consumo de grasa. Entonces, a pesar que el porcentaje de consumo de grasa dietética ha disminuido, el total de consumo de grasa ha aumentado desde 1995 a 100.6 g (hombres). Debido a la relativa facilidad con que la grasa dietética es convertida en tejido adiposo, una dieta alta en grasas conlleva a un aumento elevado de peso cuando al ser comparado con una dieta baja en grasas, a pesar de es comparable el consumo de calorías. Se ha reportado que este fenómeno ocurre tanto en humanos como en ratas (Astrup et al., "La obesidad como una adaptación a una dieta alta en grasa: evidencia de un estudio de secciones cruzadas" *Am J Clin Nutr*, 59:350-355 (1994)); (Jen "Efectos de la composición de la dieta en el consumo alimenticio y composición de la carcasa en ratas" *Physiol Behav* 42:551-556 (1988) and; Jen et al, "El ciclismo a largo plazo reduce el peso corporal y la masa libre de grasa, pero no la masa de grasa en las ratas Wistar hembras" *Int J Obesity* 19:699-708 (1995)).

Varios alimentos, bajos en grasa y/o bajos en calorías, han sido desarrollados en un esfuerzo para procurar la pérdida de peso o inhibir el aumento de peso. Muchos alimentos "bajos en grasa" son preparados mediante una disminución del porcentaje de grasa pero el porcentaje de carbohidratos de los alimentos es aumentado, para hacer que los alimentos sean mas agradables al paladar, compensando así la pérdida de sabor y textura ocasionada por la grasa. El aumentar la cantidad de carbohidratos, e.g., azúcares, en los alimentos frecuentemente hacen de los alimentos "bajos en grasa" pero el contenido calórico puede no reducirse y en muchas ocasiones es realmente aumentado. Muchos alimentos bajos en calorías son simplemente preparados reemplazando los componentes calóricos del alimento con un llenado no calórico, e.g., una fibra dietética. Sin embargo, el reemplazar partes significantes de carbohidratos con llenados de fibras frecuentemente altera el sabor y textura del alimento, haciendo del alimento, para algunos consumidores, menos sabroso al paladar. Además, el consumo de altas cantidades de fibra dietética frecuentemente tiene efectos laterales adversos

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como, e.g., flatulencia, y una dieta que comprende mas de mas o menos 60 g de fibra puede resultar en deficiencias de calcio, hierro, zinc y en un mayor riesgo de obstrucción intestinal. Mientras que las dietas altas en fibra, que comprenden aproximadamente 25-35 g/d, son reconocidas por tener efectos benéficos, e.g., reducción de los triglicéridos en la sangre y de los niveles de colesterol, muchas personas no deben consumir altos niveles de fibra, e.g., los ancianos, los niños en crecimiento y aquellos que sufren de condiciones medicas particulares, e.g., diverticulitis aguda o subaguda y las fases agudas de ciertas condiciones inflamatorias del intestino, e.g., colitis ulcerativa o enfermedad de Crohn. Después de que algunos tipos de cirugía intestinal, e.g., colostomía o ileostomía, una dieta baja en fibra, dieta de bajos residuos es usada como transición a una dieta regular y es preferida. Entonces es deseable desarrollar un producto alimenticio que tenga el sabor y la textura deseada por los consumidores, pero que también reduzca el aumento de peso, los triglicéridos de la sangre y los niveles de colesterol y que no sea necesariamente alta en fibra.

Las ciclodextrinas son una familia de polímeros cíclicos de glucosa producidos por digestión enzimática de almidón de maiz, con una ciclodextrina glicéridotransferase. La α -, β - y γ -ciclodextrina-y contienen 6, 7 y 8 moléculas de glucosa y toman una conformación de cono toroide o truncado en solución acuosa. Las moléculas tienen un interior hidrofóbico y un exterior hidrofílico, formando un poro interno. Los diferentes largos de polímeros dan diferentes tamaños de poros.

Las propiedades únicas de β y γ -ciclodextrinas-y han sido explotadas en una variedad de campos. Por ejemplo, han sido usadas para estabilizar y solubilizar medicamentos y también para aumentar los sabores de la comida. Mientras que el β y γ -ciclodextrinas-y han encontrado un uso considerable en las industrias farmacéutica y de alimentos, la α -ciclodextrina ha encontrado relativamente poco uso en estas industrias debido a su pequeño tamaño de poros así como al hecho de que no parece ser metabolizado por la amilasa pancreática o flora intestinal (Suzuki y Sato, "Significado nutricional de las ciclodextrinas: indigestibilidad y efecto hipolipémico de la α -ciclodextrina" J Nutr Sci Vitaminol (Tokyo) 1985;31:209-223), aunque este último aspecto ha sido disputado por uno de los productores del material (Antisperger G SG. "Comparación toxicológica de las ciclodextrinas" presentado en el 8 Simposio Internacional de Ciclodextrina en Budapest 1996:1-7). La α -ciclodextrina reúne eficientemente ácidos libres de grasa (FFA) en solución (McGowan et al. "Un método juntado con peroxidase para la determinación calorimétrica de los triglicéridos en el suero de la sangre" Clin. Chem. 29(3):538-542 (1983)), y ha sido usada para eliminar la turbiedad causada por el FFA en un número de re-agentes de diagnóstico clínico (Morgan, Artiss and Zak "Un estudio de turbiedad en especímenes de hipertriglicéridémicos" Microchem. J. 64:147-154 (2000)). La α -ciclodextrina también ha sido usada para la remoción específica y selectiva de ácidos grasos libres de aceite para cocinar usado (US patent No. 5,650,950).

Estudios previos muestran que la α -ciclodextrina es esencialmente indigerible y puede causar efecto en el aumento de peso solamente si excede mas o menos 20% del total de alimentos consumidos, según determinado en un modelo de rata. La solicitud japonesa de patente JP 05-298849 (Publ. No. 07115934) ensaya los efectos del ácido linoléico y la α -ciclodextrina en el aumento de peso en las ratas. Esta solicitud reporta que las ratas alimentadas con dietas que comprenden bien 16% de α -ciclodextrina o 1% de ácido linoléico aumentaron de peso aproximadamente lo mismo que las ratas alimentadas con una dieta controlada. En contraste, esta solicitud japonesa revela que las ratas alimentadas con dietas que comprenden una combinación de 14% de α -ciclodextrina y 2% de ácido linoléico tuvieron una disminución significativa de peso. La solicitud japonesa de patente S60-149752 también analiza el efecto del ácido linoléico en combinación con la α -ciclodextrina en el aumento de peso en ratas. Esta solicitud reporta que la dieta que comprende 14% w/w α -ciclodextrina tuvo poco efecto en el aumento de peso de las ratas mientras que la combinación de 14% w/w de α -ciclodextrina y de 0.5% w/w de ácido linoléico produjo una

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disminución significativa de peso. La solicitud japonesa de patente H5-298850 analiza los efectos de dietas que comprenden ácido linolenico (1.5 - 2% w/w) y α -ciclodextrina (14% w/w) y un elemento de cebada verde. Esta solicitud reporta que las dietas que comprenden 14% w/w de α -ciclodextrina en combinación con 1.5 - 2% de ácido linolenico tan solo producen una pequeña disminución en el peso corporal mientras que la adición de un elemento de cebada verde al ácido linolenico y de ciclodextrina resulta en una disminución significativa en el aumento de peso. Esta solicitud no reporta los efectos de las dietas que solo comprenden α -ciclodextrina como componente adicional. Ninguna de estas solicitudes muestra el contenido de grasa de las dietas y enseñan la importancia de los ingredientes adicionales y/o la ineffectividad de la sola α -ciclodextrina.

La solicitud japonesa de patente H4-333575 suplementa la dieta de las ratas con cantidades totales específicas de ácido linolenico y/o α -ciclodextrina y/o hidrolisato de peptona mediante la introducción a las ratas con composiciones de almidón de trigo que comprende bien 0.9% w/w de ácido linolenico solamente, 9% w/w de α -ciclodextrina solamente, o 10% w/w de una composición de hidrolitos de bajo peso molecular de una proteína de mayor peso molecular, o con composiciones que comprenden combinaciones de los tres componentes. El contenido de grasa de las dietas no fue descrito. Solamente las dietas que contenían una combinación de ácido linolenico, α -ciclodextrina y un hidrolisato de peptona mostraron un cambio significativo en el aumento de peso de las ratas, en el tiempo.

La solicitud japonesa JP05-113603 (Publ. No. 08187060 y JP05-164024 (Publ. No. 06343419) ensaya el efecto de una mezcla de mas o menos 15% de α -ciclodextrina y 1.5% de ácido linolenico en el aumento de peso en humanos. Estas solicitudes evidencian que los sujetos que ingieren las composiciones de α -ciclodextrina/ácido linolenico en una cantidad basada en su peso corporal, de tal manera que la dosis diaria de la composición mas o menos fuera de 0.015 g/kg peso corporal, tres veces al día, lo que es 1.37 g/91 kg (200lb) individuales, tres veces al día, que corresponde a 4.11 g de la composición total por día o 0.62 g de α -ciclodextrina por día (0.21 g/comida) y 0.068 g de ácido linolenico por día (0.023 g/comida), muestra un aumento significativo en la perdida de peso según comparado con sujetos que no ingirieron esa combinación. Sin embargo, estas solicitudes no ensayaron el efecto de la sola α -ciclodextrina o del solo ácido linolenico ni mostraron el contenido graso de las dietas. Es bien sabido que el ácido linolenico disminuye el peso y el aumento de grasa tanto por los estudios de animales como de humanos (Jen. Et al., Nutri. Res 9:1217-1228 (1989) y Takada et al., J. Nutri 124:469-474 (1994) y Couet et al. J. Obes. 21:637-643 (1997)) y es probable que sea el componente que realmente promovió la disminución de peso observada en estas solicitudes.

La Patente U.S. 4,880,573 revela un proceso para eliminar el colesterol de la sustancias grasas de origen animal, e.g. manteca de cerdo, sebo o mantequilla. El proceso combina β -ciclodextrina con la sustancia grasa licuificada bajo una atmósfera no oxidante para posteriormente remover los complejos de colesterol y de ciclodextrina, dejando una sustancia grasa libre de ciclodextrina y con un reducido contenido de colesterol.

La Patente U.S. 5,189,149 revela el uso de complejos de ciclodextrinas y de ácidos grasos de cadena larga, sus sales y éster, incluso de glicéridos de aceite de pescado y de vegetales, para entregar a un sujeto ácidos grasos de cadena larga y evitar las características untuosas asociadas con los glicéridos de aceite de pescado y de vegetales y su sabor y olor no placentero.

La Patente U.S. 5,232,725 relata el proceso para reducir el colesterol y los ácidos libres grasos en un material que contenga grasa, e.g., crema fresca, mediante la combinación de agua, material contentivo de grasa, y ciclodextrina, bajo condiciones adecuadas para formar una emulsión "fina", tipo aceite en agua, que facilita la formación de complejos de

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ciclodextrina y de colesterol o ácidos grasos libres. Los complejos son entonces separados mecánicamente para producir un material contentivo de grasa con reducidos niveles de colesterol y de ácidos grasos libres. La U.S. 5,232,725 no describe un producto alimenticio que comprenda complejos de triglicérido y de α -ciclodextrina, donde la biodisponibilidad de la grasa en el producto alimenticio sea disminuida, como aparece descrito en este.

La Patente U.S. 5,560,950 relata un proceso para reducir el contenido de ácido graso libre en un aceite usado mediante la mezcla del aceite usado con ciclodextrina, preferiblemente con un absorbente, e.g. sílice, bajo condiciones que formen aglomerados de ciclodextrina/absorbente ácidos grasos, y entonces remover los aglomerados de ciclodextrina del aceite. El proceso produce un aceite que es libre de ciclodextrina y que tiene niveles reducidos de ácidos grasos libres.

La Patente US 5,571,554 se relaciona con un proceso para reducir los triglicéridos en una clara de huevo mediante la preparación de una mezcla de yema de huevo con agua, o una solución salada, y combinar la mezcla con una ciclodextrina y después remover la ciclodextrina y el agua adicionada, o la solución salada. El proceso produce un producto de yema de huevo libre de ciclodextrina, con bajos niveles de triglicéridos.

La Patente US 5,738,898 se relaciona con un proceso para reducir el colesterol en la yema de huevo mediante la preparación de una mezcla de yema de huevo, agua y ciclodextrina, a un pH entre 7.5 y 12. Los complejos de ciclodextrina colesterol son removidos y el pH es ajustado a pH 6-7. El proceso produce un producto de yema de huevo libre de ciclodextrina, con un bajo colesterol.

Muchos consumidores, incluyendo individuos obesos, parecen tener preferencia por los alimentos que tienen un alto contenido de grasa (Mela and Sacchetti, "Preferencias sensoriales a las grasas: relación con la composición de la dieta y el cuerpo" Am J Clin Nutr 1991;53:908-915). Entonces, para muchos individuos es muy difícil, especialmente para individuos obesos, reducir su absorción de grasa para disminuir su peso corporal y los efectos adversos a la salud asociados con el aumento de peso. Entonces, es sumamente deseable una sustancia que reduzca la absorción de grasa dietética sin los efectos secundarios adversos de los actuales medicamentos. Tal sustancia tendría beneficios significativos para la salud al disminuir la obesidad y los desordenes relacionados con ella, tales como diabetes Tipo II (NIDDM). Sería deseable desarrollar un producto alimenticio que promueva la pérdida de peso, reduzca los niveles de lípidos, y reduzca los síntomas de los otros desordenes asociados con el aumento de peso/obesidad, y que sin embargo tenga propiedades organolépticas deseables. En este se describen productos consumibles contentivos de grasa que tienen las propiedades organolépticas, tales como sabor, textura y humedad, que los consumidores desean, y que también promueve la pérdida de peso y otros beneficios para la salud.

RESUMEN DEL INVENTO

Este invento se relaciona con un producto alimenticio consumible contentivo de grasa, que comprende α -ciclodextrina y grasa, donde la tasa de α -ciclodextrina a grasa es mas o menos de 1:20 w/w - 1:3 w/w. Preferiblemente la tasa de α -ciclodextrina a grasa es mas o menos de 1:13 w/w - 1:5 w/w, y mas preferiblemente la tasa de α -ciclodextrina a grasa es de mas o menos de 1:9 w/w. El total de ciclodextrina en los alimentos de este invento es menor que mas o menos 9-10% w/w, preferiblemente menor que mas o menos 6% y mas preferiblemente menor que 3% w/w, y particularmente, en el caso productos alimenticios harinosos consumibles contentivos de grasa de este invento la cantidad total de ciclodextrina es menor que mas o menos 3% w/w. Preferiblemente los productos alimenticios con contenido graso de este invento comprenden, por contenido calórico, mas o menos 7% hasta

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mas o menos 80% de grasa, preferiblemente mas o menos 20% a mas o menos 70% de grasa, mas preferiblemente mas o menos 40% a mas o menos 70% de grasa, o por peso, 5% a mas o menos 50% w/w de grasa, preferiblemente mas o menos 5-30% w/w de grasa, y mas preferiblemente mas o menos 7-25% w/w/ de grasa. "Grasa", según definido en este, son trigliceridos. Las ciclodextrinas frecuentemente son vendidas como mezclas de α , β -, γ -ciclodextrina y de n-dextrina. Preferiblemente la composición α -ciclodextrina que puede ser usada en los productos y métodos de este invento, es sustancialmente α -ciclodextrina pura, comprendiendo por lo menos 95% de α -ciclodextrina, preferiblemente por lo menos 98% de α -ciclodextrina. La α -ciclodextrina en los alimentos, en este, puede suministrar una fuente de fibra ademas de sus efectos benéficos adicionales. Los productos consumibles pueden ser un producto alimenticio harinoso o un producto alimenticio no harinoso, e.g. un producto de la leche, un producto vegetal preparado, o un producto de carne preparado, e.g. producto alimenticio preparado de res, cordero, cerdo, aves o mariscos. Los productos alimenticios consumibles de este invento son adecuados para el consumo por mamíferos, e.g., ratones, ratas, gatos, perros y humanos, pero preferiblemente por humanos.

La ciclodextrina ha sido anteriormente usada en métodos para reducir los niveles de ácidos grasos libres, colesterol o trigliceridos en productos alimenticios, pero en contraste con los productos alimenticios de este invento, esos métodos producen productos que son esencialmente libres de ciclodextrina y que tienen bajos niveles de ácidos grasos libres, colesterol y trigliceridos, según comparados con productos alimenticios similares que no han sido tratados. Si ensayados por bomba calorimetrica, los productos producidos con estos métodos tendrán un menor contenido calórico debido a los reducidos niveles de colesterol y de trigliceridos. Los productos alimenticios consumibles de este invento comprenden α -ciclodextrina y no tienen niveles bajos de ácidos grasos, colesterol o trigliceridos, según comparados con productos similares, sin adicionarles α -ciclodextrina. Como tales, los productos consumibles de este invento no tienen un nivel calórico sustancialmente reducido, como ensayado por bomba calorimétrica, según comparados con productos similares que no contienen α -ciclodextrina, y sin embargo los productos alimenticios de este invento inhiben la tasa de aumento de peso, promueven la perdida de peso, y suministran otros beneficios para la salud. Entonces el producto alimenticio consumible de este invento es un producto de dieta que inhibe la tasa de aumento de peso, que promueve la perdida de peso, y que suministra otros beneficios para la salud.

Shimada et al. (Shimada et al. "Estructura de la inclusión de uniones de ciclodextrinas con trigliceridos en la interfase con aceite/agua vegetal" J. Food Sci. 1992; 57(3):655-656) reporto dos moléculas de α -ciclodextrina reunidas con un grupo ácido graso (FFA), mientras que Szejtli (Szejtli J. "Utilización de ciclodextrinas en productos y procesos industriales" J. Mater. Chem. 1997; 7:575-587) sugiere que este fenómeno depende del largo de la cadena de los ácidos grasos, y que es posible que 3 - 4 moléculas de α -ciclodextrina se unan con cada uno de los tres ácidos grasos de una molécula triglicerida, lo que sugiere que 9-12 moléculas de α -ciclodextrina serán necesarias para completamente unir una molécula de triglicerido. Si este fuera el caso, seria difícil imaginarse el poder dar suficiente α -ciclodextrina a un animal para unir cantidades suficientes de trigliceridos que lleven a una significativa diferencia en el peso corporal.

Ambos Suzuki et al. Y Kaewprasert et al. infra reportan que una sola composición de ciclodextrina mezclada con un alimento no promueve una significativa perdida de peso, aun en concentraciones de 20% w/w del total de consumo dietético. Especialmente, Suzuki et al., Denpun Kagaku 30(2):240-246 (1983) analizo los efectos de una dieta, que comprenda 20% de ciclodextrina, en el aumento de peso de ratas, y reportó que no habia diferencias en el aumento de peso de ratas alimentadas en un 20% con una dieta de ciclodextrina y aquellas alimentadas con una dieta en un 20% de harinas. Similarmente, Kaewprasert et al., J Nutri. Sci. Vitaminol 47:335-339 (2001) reportó que el aumento de peso corporal en ratas

alimentadas con una dieta de 5% α -ciclodextrina no fue significativamente diferente al de ratas alimentadas con una dieta controlada. Kaewprasert revela una dieta que comprende ciclodextrina y grasa a una tasa de 1:1.4. Suzuki no discutió el contenido graso de las dietas experimentales o reveló la tasa de la ciclodextrina a la grasa en la dieta. Este efecto de cantidades relativamente grandes de ciclodextrina fue también anotado en la solicitud Japonesa 560-094912. La S60-094912 sugiere que la ciclodextrina puede inhibir la tasa de aumento de peso y disminuir la grasa neutra (triacilgliceridos) en el hígado y el plasma, pero solamente si la ciclodextrina es administrada a niveles de 20% w/w o mas. Si la α -ciclodextrina es menor a 20% del total de la dieta consumida, la S60-094912 reporta que no hay una diferencia significativa en la perdida de peso, según comparada con una dieta controlada. Similarmente, Suzuki y Sato, J. Nutri. Sci. Vitaminol 31:209-223 (1985) reportan que las ratas alimentadas con dietas que comprenden una mezcla de α -dextrina y de α -, β - y γ -ciclodextrinas (50:30:15:5% w/w) solamente mostraron una perdida de peso sustancialmente diferente a la del grupo controlado cuando por lo menos 58.5% w/w de la dieta consistía en una mezcla de ciclodextrina. En contraste, hemos encontrado que una perdida significativa de peso puede ser obtenida en sujetos con niveles mucho mas bajos de α -ciclodextrina si los sujetos están consumiendo dietas contentivas de grasas y las tasa de α -ciclodextrina ingerida a grasa ingerida en la dieta es suficiente para formar complejos de grasa y ciclodextrina. Naturalmente el cuerpo forma una emulsión fina de grasa en el agua, la que es necesaria para que la lipasa catalice la hidrólisis de la grasa. Sin querer estar atado por la teoría, el invento descrito en este altera este proceso mediante la formación de largos complejos de α -ciclodextrina y de grasa, de tal manera que la lipasa no pueda actuar en la grasa. Entonces la grasa de los productos alimenticios contentivos de grasa de este invento no esta biodisponible porque esta en forma de complejos α -ciclodextrina/grasa que son resistentes a la actividad de la lipasa.

Los niveles de ciclodextrina en los alimentos de este invento son mucho mas bajos a los niveles que en S60-94912 y Suzuki y Sato (J. Nutri Sci Vitaminol 1985 supra) se indican como necesarios para la perdida de peso. El total de ciclodextrina en los alimentos de este invento es menor que mas o menos 9% w/w preferiblemente menos que mas o menos 6% w/w, y mas preferiblemente menos que 3%, especialmente en el caso de los productos harinosos alimenticios consumibles de este invento. Los sujetos alimentados con una dieta que comprende los alimentos que contienen α -ciclodextrina de este invento, preferiblemente aquellos que comprenden las cantidades de α -ciclodextrina revelada en este y donde la tasa de α -ciclodextrina a grasa esta dentro de las tasas mostradas en este, muestran inter alia perdida de peso, aumento en los niveles HDL y una reducción en los trigliceridos de la sangre.

Sin querer estar atados por la teoría, los resultados presentados en este sugieren que la α -ciclodextrina es especialmente adecuada para reunir grasa en una composición alimenticia reduciendo entonces la biodisponibilidad de la grasa. Mediante la ingestión de α -ciclodextrina en cantidad apropiada con una comida contentiva de grasa, o poco antes o después de ingerir un alimento contentivo de grasa, un sujeto puede reunir la grasa ingerida e inhibir su absorción por el cuerpo. La cantidad de α -ciclodextrina debe ser suficiente para formar uniones con la grasa reduciendo entonces la biodisponibilidad de la grasa, preferiblemente la cantidad de α -ciclodextrina es suficiente para obtener una tasa de α -ciclodextrina a grasa de 1:20 a 1:3, preferiblemente 1:13 a 1:5 y mas preferiblemente mas o menos 1:9 de tal manera que las uniones de grasa y ciclodextrina se formen. Sin querer estar atados por la teoría, es la reducción en la biodisponibilidad de la grasa ingerida (la cantidad de grasa ingerida que es absorbida y esta entonces disponible al cuerpo para su uso) que resulta en e.g., la perdida de peso observado, el aumento en el colesterol HDL, disminución de los niveles de leptina y una disminución en los niveles de trigliceridos en el suero de la sangre.

Este invento también se relaciona con los métodos para unir las grasas contenidas en un producto alimenticio ingerido, especialmente un producto alimenticio alto en grasa,

reduciendo entonces la biodisponibilidad de la grasa ingerida. El método comprende ingerir una cantidad de α -ciclodextrina con un producto alimenticio de tal manera que la tasa de α -ciclodextrina a grasa sea mas o menos de 1:20 a mas o menos 1:3 w/w preferiblemente mas o menos 1:13 a mas o menos 1:5 w/w mas preferiblemente mas o menos 1:9 w/w. La α -ciclodextrina puede ser ingerida antes, concurrentemente o subsecuentemente a la ingestión del producto alimenticio. A tales tasas la grasa es unida con la α -ciclodextrina y la biodisponibilidad de la grasa ingerida es reducida. Alternativamente la α -ciclodextrina puede ser combinada con el producto alimenticio con anterioridad a su consumo en una cantidad tal que la tasa de α -ciclodextrina a grasa en el producto alimenticio ingerido sea mas o menos de 1:20 a mas o menos de 1:3 w/w w/w preferiblemente mas o menos de 1:13 a mas o menos de 1:5 w/w mas preferiblemente mas o menos de 1:9 w/w y el producto alimenticio que comprenda la α -ciclodextrina y la grasa es ingerido.

Este invento también se relaciona con los métodos para producir un producto alimenticio contentivo de grasa con biodisponibilidad reducida mediante la formación de uniones de α -ciclodextrina y grasa en el producto alimenticio, especialmente un producto alimenticio alto en grasa. El método comprende combinar α -ciclodextrina con un producto alimenticio bajo condiciones que favorezcan la formación de uniones de grasa y α -ciclodextrina, donde las condiciones eviten la formación de una emulsión fina de grasa dentro del producto. La cantidad de la α -ciclodextrina es tal que el producto alimenticio comprende una tasa de α -ciclodextrina a grasa mas o menos de 1:20 a mas o menos de 1:3 w/w preferiblemente mas o menos de 1:13 a mas o menos de 1:5 w/w mas preferiblemente mas o menos de 1:9 w/w. A tales tasas y bajo tales condiciones, la grasa es unida con la α -ciclodextrina, la biodisponibilidad de la grasa ingerida es reducida. El producto alimenticio puede ser un producto alimenticio harinoso e.g. barras de aperitivo, cereales de desayuno, pancakes, waffles, muffins, pasteles rellenos de frutas, tortillas, pedacitos de matiz, tortillas, galletas de aperitivo, panes, ponques, galletas o pies o productos alimenticios no harinosos, e.g. un producto alimenticio vegetal, leche o carne e.g. papas fritas, tempura, hamburguesas vegetarianas, frijoles refritos, humus, tahini, margarina y mantequilla de nueces, (e.g. maní, nuez, almendra, avellana), marzapán, papitas; leche, crema, pudín, mantequilla, helado y queso y productos procesados de queso, carne preparada de res, cordero, cerdo, aves o mariscos, e.g. salchichas, tajadas de deli, palos de pescado, chorizo y carne molida, e.g. masa de carne, pelotas de carne y hamburguesas, yogur y productos de yogur, y productos de huevos.

Entonces este invento también se relaciona con un método para promover la pérdida de peso o inhibir el aumento de peso en un sujeto comprendiendo administrar, a un sujeto necesitado, α -ciclodextrina, en cantidad y por un periodo suficiente para producir pérdida de peso o inhibir aumento de peso. Preferiblemente la α -ciclodextrina es administrada a un sujeto que consume una dieta de grasa promedio (mas o menos 100g grasa/día, mas o menos 33 g grasa/comida) donde la cantidad administrada al sujeto es tal que la tasa de α -ciclodextrina a grasa ingerida por comida, o diariamente, por el sujeto, es mas o menos de 1:20 a mas o menos de 1:3 w/w, preferiblemente la tasa es mas o menos de 1:13 a mas o menos de 1:5 w/w y mas preferiblemente mas o menos de 1:9 w/w. Una vez que el peso deseado es perdido, la α -ciclodextrina puede ser incluida en la dieta en una cantidad para inhibir o preferiblemente evitar el aumento de peso. Por una pérdida mas o menos de 1-1.5 lbs por semana para un sujeto cuyo consumo dietético es 100g grasa/día (mas o menos 33 g grasa/comida), la cantidad de α -ciclodextrina administrada es preferiblemente mas o menos 2g/comida, reduciendo entonces la biodisponibilidad de aproximadamente 54g de grasa por día.

El colesterol en el suero de la sangre es encontrado en combinación con proteínas de la sangre. De interés particular es la lipoproteína de alta densidad (HDL el buen colesterol) y de baja densidad. (LDLs el colesterol malo). Este invento se relaciona con un método para

aumentar el nivel de lipoproteína de alta densidad (HDL) en un sujeto que comprende administrar α -ciclodextrina a un sujeto necesitado de la misma, en cantidad y por un periodo suficiente para aumentar los niveles de HDL. Preferiblemente la cantidad de α -ciclodextrina administrada al sujeto es mas o menos cuatro a mas o menos once gramos por día. Preferiblemente, la α -ciclodextrina es administrada en una cantidad tal que la tasa α -ciclodextrina a grasa ingerida por comida, o diariamente, sea mas o menos de 1:20 a 1:3 w/w mas preferiblemente de 1:13-1:5 w/w o mas preferiblemente mas o menos de 1:9 w/w. La α -ciclodextrina puede ser administrada en una variedad de formas, e.g. una tableta, capsula, pastilla, elixir, galleta, bebida, o en un producto alimenticio, e.g., productos de pan, e.g., panecillos, rollos, bizcochos y cereales de desayuno, e.g. cereal de avena, crema de trigo, salvado de uvas pasas, pedacitos de matiz, u otros cereales listos para consumir, productos de carne y productos de leche, y especialmente los productos alimenticios consumibles de este invento. Preferiblemente la tableta, pastilla, capsula, elixir, wafer, bebida, u otro producto alimenticio consumible comprende una ciclodextrina que es predominantemente α -ciclodextrina, e.g., la ciclodextrina es por lo menos mas o menos de 90-98% α -ciclodextrina.

Es posible que los niveles totales de colesterol en la sangre se mantengan constantes a pesar de que los niveles de HDL sean elevados si hay una reducción en los niveles de LDL. Preferiblemente los niveles totales de colesterol son sustancialmente disminuidos o se mantienen sin cambio por los métodos de este invento. Entonces, este invento también se relaciona con un método para disminuir la tasa de colesterol/HDL en un sujeto que comprende administrar a un sujeto necesitado del mismo, α -ciclodextrina, en cantidad y por un periodo suficiente para reducir la tasa de colesterol/HDL. La α -ciclodextrina puede ser administrada en una variedad de formas, e.g. tableta, píldora, capsula, elixir, galleta, bebida, o en productos alimenticios, e.g., productos de pan, e.g., panecillos, rollos, bizcochos y cereales de desayuno, e.g. cereal de avena, crema de trigo, salvado de uvas pasas, pedacitos de matiz, u otros cereales listos para consumir, y especialmente los productos alimenticios consumibles de este invento. La tableta, pastilla, capsula, elixir, wafer, bebida, o productos alimenticios pueden contener α -ciclodextrina en combinación con otras ciclodextrinas, e.g., β y/o y ciclodextrinas o con n-dextrina. Preferiblemente la ciclodextrina en la tableta, pastilla, capsula, elixir, wafer, bebida, o los productos alimenticios es predominantemente α -ciclodextrina, e.g., la ciclodextrina es por lo menos mas o menos de 90-98% α -ciclodextrina.

Este invento también se relaciona con un método para reducir los niveles de triglicéridos en un sujeto que comprende administrar a un sujeto necesitado de la misma, una cantidad de α -ciclodextrina suficiente para reducir los niveles de triglicéridos. La cantidad de α -ciclodextrina administrada al sujeto es tal que la tasa de α -ciclodextrina a grasa ingerida por comida, o diariamente, por el sujeto, sea mas o menos de 1:20 a mas o menos de 1:3 w/w preferiblemente la tasa es mas o menos de 1:13 a mas o menos de 1:5 w/w y mas preferiblemente la tasa es mas o menos de 1:9 w/w. La α -ciclodextrina puede ser administrada en una variedad de formas, e.g. tableta, capsula, pastilla, elixir, galleta, bebida, o en productos alimenticios, e.g., productos de panadería, e.g., panecillos, rollos, bizcochos y cereal de desayuno, e.g. cereal de avena, crema de trigo, salvado de uvas pasas, pedacitos de matiz, u otros cereales listos para consumir, y especialmente los productos alimenticios consumibles de este invento. La tableta, pastilla, capsula, elixir, wafer, bebida, o productos alimenticios pueden contener α -ciclodextrina en combinación con otras ciclodextrinas, e.g., β y/o y ciclodextrinas o con n-dextrina, pero preferiblemente la ciclodextrina en la tableta, pastilla, capsula, elixir, wafer, bebida o producto alimenticio, es predominantemente α -ciclodextrina, e.g., la ciclodextrina es por lo menos mas o menos de 90-98% α -ciclodextrina.

El invento además se relaciona con un método para reducir los niveles de leptina en un sujeto que comprende administrar α -ciclodextrina a un sujeto necesitado de la misma en cantidad y por un periodo suficiente para reducir los niveles de leptina en el sujeto. La α -ciclodextrina puede ser administrada en una variedad de formas, e.g., una tableta, capsula,

pastilla, elixir, galleta, bebida, o en productos alimenticios, e.g., productos de panadería, e.g., panecillos, rollos, bizcochos y cereal de desayuno, e.g. cereal de avena, crema de trigo, salvado de uvas pasas, pedacitos de matiz, u otros cereales listos para consumir, y especialmente los productos alimenticios consumibles de este invento. La tableta, pastilla, capsula, elixir, wafer, bebida, o producto alimenticio pueden contener α -ciclodextrina en combinación con otras ciclodextrinas, e.g., β y/o y ciclodextrinas o con n-dextrina, pero preferiblemente la ciclodextrina en la tableta, pastilla, capsula, elixir, galleta, bebida, o producto alimenticio es predominantemente α -ciclodextrina, e.g., la ciclodextrina es por lo menos mas o menos 90-98% α -ciclodextrina.

Este invento también se relaciona con un método para suprimir el apetito mediante la administración de α -ciclodextrina a un sujeto necesitado, en cantidad y por un periodo suficiente para suprimir el apetito del sujeto. La cantidad de α -ciclodextrina administrada al sujeto es tal que la tasa de α -ciclodextrina a grasa ingerida por comida, o diariamente, por el sujeto, es mas o menos de 1:20 a mas o menos de 1:3 w/w, preferiblemente la tasa es mas o menos de 1:13 a mas o menos de 1:5 w/w y mas preferiblemente la tasa es mas o menos de 1:9 w/w. La α -ciclodextrina puede ser administrada en una variedad de formas, e.g. tableta, capsula, pastilla, elixir, galleta, bebida, o en productos alimenticios, e.g., productos de panadería, e.g., panecillos, rollos, bizcochos y cereal de desayuno, e.g. cereal de avena, crema de trigo, salvado de uvas pasas, pedacitos de matiz, u otros cereales listos para consumir, y especialmente los productos alimenticios consumibles de este invento. La tableta, pastilla, capsula, elixir, galleta, bebida o producto alimenticio pueden contener α -ciclodextrina en combinación con otras ciclodextrinas, e.g., β y/o y ciclodextrinas o con n-dextrina, pero preferiblemente la ciclodextrina en la tableta, pastilla, capsula, elixir, galleta, bebida, o producto alimenticio es predominantemente α -ciclodextrina, e.g., la ciclodextrina es por lo menos mas o menos 90-98% α -ciclodextrina.

Este invento ademas se relaciona con un método para reducir los niveles de insulina y la resistencia a la insulina en un sujeto que comprende administrar α -ciclodextrina a un sujeto necesitado de la misma, en una cantidad y por un periodo suficiente para reducir los niveles de insulina y la resistencia a la insulina en el sujeto. Preferiblemente la cantidad de α -ciclodextrina administrada al sujeto es tal que la tasa de α -ciclodextrina a grasa ingerida por comida, o diariamente, por el sujeto, este en una tasa mas o menos de 1:20 a mas o menos de 1:3 w/w, preferiblemente la tasa es mas o menos de 1:13 a mas o menos de 1:5 w/w y mas preferiblemente la tasa es mas o menos de 1:9 w/w. La α -ciclodextrina puede ser administrada en una variedad de formas, e.g. tableta, capsula, pastilla, elixir, galleta, bebida, o en productos alimenticios, e.g., productos de panadería, e.g., panecillos, rollos, bizcochos y cereal de desayuno, e.g. cereal de avena, crema de trigo, salvado de uvas pasas, pedacitos de matiz, u otros cereales listos para consumir, y especialmente los productos alimenticios consumibles de este invento. Preferiblemente la ciclodextrina en la tableta, pastilla, capsula, elixir, galleta, bebida, o productos alimenticios es predominantemente α -ciclodextrina, e.g., la ciclodextrina es por lo menos mas o menos de 90-98% α -ciclodextrina.

Este invento también se relaciona con un método para reducir la diarrea en un sujeto necesitado de la misma que comprende administrar al sujeto necesitado α -ciclodextrina, en cantidad y por un periodo suficiente para reducir la diarrea en el sujeto. Preferiblemente la cantidad de α -ciclodextrina administrada al sujeto es tal que la tasa de α -ciclodextrina a grasa ingerida por comida, o diariamente, por el sujeto, esta en una tasa mas o menos de 1:20 a mas o menos de 1:3 w/w preferiblemente la tasa es mas o menos de 1:13 a mas o menos de 1:5 w/w y mas preferiblemente la tasa es mas o menos de 1:9 w/w. La α -ciclodextrina puede ser administrada en una variedad de formas, e.g. tableta, capsula, pastilla, elixir, galleta, bebida, o en productos alimenticios, e.g., productos de panadería, e.g., panecillos, rollos, bizcochos y cereal de desayuno, e.g. cereal de avena, crema de trigo, salvado de uvas pasas, pedacitos de maiz, u otros cereales listos para consumir, y especialmente los productos

alimenticios consumibles de este invento. Preferiblemente la ciclodextrina en la tableta, pastilla, capsula, elixir, galleta, bebida, o los productos alimenticios es predominantemente α -ciclodextrina, e.g., la ciclodextrina es por lo menos mas o menos de 90-98% α -ciclodextrina.

Este invento también se relaciona con métodos para ampliar las propiedades organolépticas de un producto alimenticio contentivo de grasa sin reducir el porcentaje de grasa en el producto alimenticio o el contenido calórico resultante de la grasa, según ensayado por bomba calorimétrica. El método comprende adicionar α -ciclodextrina al alimento contentivo de grasa de tal manera que este presente durante el procesamiento y la ingestión final del producto alimenticio. La cantidad de α -ciclodextrina que se adiciona al producto alimenticio puede estar basada en la cantidad de grasa en el producto consumible terminado.

BREVE DESCRIPCION DE LAS FIGURAS

La Figura 1 muestra la masa total acumulada de alimento consumido por los cuatro grupos de ratas y demuestra que no hubo diferencia significativa en la masa de alimento consumido por los diferentes grupos.

La Figura 2 muestra la ingestión calórica acumulada de los cuatro grupos de ratas e indica que no hubo diferencia significativa en las calorías de alimentos que los dos pares de ratas (baja grasa y alta grasa) consumieron.

La Figura 3 ilustra el cambio en el peso corporal de los cuatro grupos de ratas adultas durante el total del periodo de estudio.

La Figura 4 muestra el contenido fecal de grasa de los cuatro grupos de ratas. Los grupos que comparten un sobrescripto común no son significativamente diferentes.

La Figura 5 muestra los parámetros de plasma sanguínea de cuatro grupos de ratas en el sacrificio. Las concentraciones de glucosa de plasma, colesterol y triglicéridos fueron medidas en todos los animales.

La Figura 6 compara los valores de leptina de plasma obtenida de los cuatro grupos de ratas.

La Figura 7 muestra los niveles de triglicéridos de suero de la sangre de voluntarios alimentados con un desayuno de alta grasa con un posterior ayuno por la noche.

La Figura 8 muestra el cambio en el peso corporal de un voluntario humano durante un periodo de seis meses aproximadamente.

La Figura 9A-9C muestra los resultados de un estudio in vitro de aceite vegetal (4g), agua (6g) (adicionado con colorante de alimentos para contraste) y cantidades variables de (A) α -ciclodextrina (100-2,000mg, derecha a izquierda), (B) β -ciclodextrina o γ -ciclodextrina. Una banda de material "similar a cera" haciendo capa entre el aceite y las fases acuosas es aparente en los tubos. El tamaño de esta banda aumenta con las mayores cantidades de α -ciclodextrina a un máximo en el tubo marcado 10% (400mg α -ciclodextrina/4g aceite). Notese el mayor tamaño (derecha a izquierda) de la capa blanca de α -ciclodextrina no reaccionada en el fondo de los tubos. El material es desplazado de la solución bien por el aceite o el complejo de α -ciclodextrina. Estos tubos fueron centrifugados para mejorar la definición de las capas. El complejo "similar a cera" es de tal consistencia que todos los tubos, excepto los dos lejanos a la derecha, pueden ser invertidos sin que goteen de la fase acuosa alrededor del complejo.

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DESCRIPCION DEL INVENTO

Este invento se relaciona con un producto alimenticio consumible contentivo de grasa que contiene α -ciclodextrina y con los métodos para su uso. Los productos alimenticios consumibles son adecuados para ser consumidos por mamíferos, e.g., un ratón, rata, un gato, un perro, una vaca, un caballo, un mico, un mono o un humano, y entonces incluyen e.g., un producto alimenticio para mascotas para un e.g. gato, perro o caballo o un producto alimenticio consumible para humanos. Los productos alimenticios consumibles de este invento comprenden α -ciclodextrina y grasa, preferiblemente la tasa de la cantidad de α -ciclodextrina a grasa es mas o menos de 1:20-1:3 w/w, mas preferiblemente la tasa de α -ciclodextrina a grasa es mas o menos de 1:13-1:5 w/w, y mas preferiblemente la tasa de α -ciclodextrina a grasa es mas o menos de 1:9 w/w. Preferiblemente el total de ciclodextrina en el producto alimenticio consumible es mas o menos de 9% w/w, mas preferiblemente el total de ciclodextrina en el producto alimenticio consumible es mas o menos de 6% y mas preferiblemente el total de ciclodextrina en los productos alimenticios es mas o menos de 3%. Preferiblemente las uniones de ciclodextrina y grasa son distribuidas igualmente a través del producto alimenticio. Preferiblemente los productos alimenticios consumibles de este invento son productos alimenticios altos en grasa que comprenden por contenido calórico mas o menos de 7% a mas o menos de 80% grasa, preferiblemente mas o menos de 20% a mas o menos de 70% grasa, mas preferiblemente mas o menos de 40% a mas o menos de 70% grasa, o por peso mas o menos de 5% w/w grasa a mas o menos de 50% w/w grasa preferiblemente mas o menos de 5-30% w/w grasa y mas preferiblemente mas o menos de 7% grasa a mas o menos de 25% grasa. Los métodos para determinar o calcular la cantidad de grasa en un producto alimenticio son bien conocidos en el arte. Vea por ejemplo el programa de soporte lógico "Procesador de Comida" por ESHA Research, Salem, OR, que se incorpora en este por referencia. Preferiblemente los productos alimenticios de este invento están hechos con menos de 2% ácido linolénico, mas preferiblemente menos de 0.2% ácido linolénico. Mas preferiblemente los productos alimenticios de este invento están hechos sin niveles detectables de ácido linolénico. Se ha mostrado que el ácido linolénico promueve la pérdida de peso pero a los niveles necesarios para promover la pérdida de peso, mas o menos de 2% la vida en estante de los productos que contienen ácido linolénico son reducidos debido a su tendencia a volverse rancios. Además, el ácido linolénico de alta pureza es muy costoso. Preferiblemente el ácido linolénico no es adicionado a los productos alimenticios de este invento, antes, durante o después de su preparación.

Varias formas de ciclodextrina están comercialmente disponibles. Por ejemplo, Wacker-Chemie GmbH produce una variedad de ciclodextrinas naturales y modificadas. La ciclodextrina es frecuentemente vendida como mezclas de α -, β - y γ -ciclodextrina y puede ser producida por una variedad de métodos. Generalmente las ciclodextrinas son producidas mediante el tratamiento de harinas, e.g. papas o maiz, con una ciclodextrina transferidora, la que es producida por una variedad de organismos, e.g., *Bacillus macerans*. La ciclodextrinas pueden ser aisladas de la harina tratada usando una variedad de métodos que combinan concentración, fraccionamiento, filtración, secado con regado, granulación, etc. Para una mas completa discusión de los métodos para la producción y aislamiento de ciclodextrinas vea e.g. Schmid "Preparación y producción industrial de ciclodextrinas", Química Supramolecular Comprensiva (1996), 3: 41-56. Eds. Szejtli, Jozsef, Osa, Tetsuo. Elsevier, Oxford, UK que se incorpora en este por referencia.

Los alimentos consumibles contentivos de grasa de este invento puede ser un producto alimenticio harinoso, e.g. barras de onces, cereales para el desayuno, pancakes, waffles, muffins, pasteles rellenos de frutas, tortillas, panes, ponques, galletas, o pies o productos alimenticios no harinosos, e.g. un producto vegetal preparado (vegetales según descritos en este incluye, vegetales, frutas y nueces), especialmente aquellos hechos con un

ingrediente graso, e.g. papas a la francesa, tempura, hamburguesas de vegetales, frijoles refritos, humus, tahini, margarina y mantequillas de nueces, (e.g., maní, anacardo, almendras, avellana), marzapán, papas fritas; un producto alimenticio lácteo e.g., leche, crema, pudín, mantequilla, helado, y productos de quesos y queso procesado; yogur y productos de yogur, productos de huevo y productos de carne, e.g. carne preparada, cordero, cerdo, aves o productos del mar, e.g., frankfurters, tajadas de deli, salchichas, palos de pescado, dedos de pollo, y carne molida, e.g., masa de carne, albóndigas y hamburguesas. Preferiblemente el producto lácteo es uno es uno donde los complejos de α -ciclodextrina/grasa están distribuidos a través del producto, preferiblemente un producto lácteo sólido o semisólido e.g. pudín, mantequilla, helado y queso y productos procesados de queso y yogur y preferiblemente las propiedades organolépticas del producto no sean adversamente afectadas. Los productos alimenticios de este invento puede también incluir entre otros, e.g., un producto alimenticio harinoso pre-empacado, e.g. un plato de pasta preparado pre-empacado como, e.g., lasagna, manicotti, espagueti en salsa, raviolis, tortellini, o macaroni y queso, o productos lácteos empacados, un producto vegetal preparado empacado, o un producto de carne preparado y pre-empacado, donde el producto alimenticio comprende α -ciclodextrina y grasa a las tasas señaladas en este. Preferiblemente, una servida del producto preparado suministra mas o menos de 160 mg a 11 mg α -ciclodextrina/servida, preferiblemente mas o menos de 1g a mas o menos de 7g/servida y mas preferiblemente mas o menos de 2- 4g por servida, y mas preferiblemente a mas o menos de 2-3g/servida. Un producto alimenticio pre-empacado puede ser encerrado en plástico, papel, cartón o metal, e.g., aluminio o papel metálico. El producto alimenticio pre-empacado puede ser empacado al granel, paquetes multi-servidas o empacados como servidas individuales.

Este invento también se relaciona con productos de confitería e.g. dulces duros tales como colombinas y mentas para el aliento o mentas para después de la comida, y condimentos, e.g., gravia, salsas, salsas para ensalada, mayonesa, etc., comprendiendo α -ciclodextrina. Preferiblemente, el producto de confitería es un producto que contiene grasa tal como, e.g., chocolates.

La α -ciclodextrina puede ser adicionada a un producto alimenticio consumible que es cocinado e.g., horneado, asado, o frito, o a un producto alimenticio consumible no cocinado, e.g., leche, crema, crema batida, untados batidos no lácteos o rellenos, yogur o una bebida, e.g., una leche malteada, sabajón, o un suave (bebida de fruta y yogur). La α -ciclodextrina puede ser adicionada al producto alimenticio en cualquier etapa de su preparación, e.g., la α -ciclodextrina puede ser mezclada con los ingredientes de tal manera que sea distribuida en el producto alimenticio y el producto puede entonces ser cocinado. Sin embargo, en algunos casos la α -ciclodextrina puede ser aplicada a la superficie del producto alimenticio, e.g., como derretido o cubierta, para obtener los niveles deseados de α -ciclodextrina a grasa.

Este invento también se relaciona con un método para promover la pérdida de peso o reducir el aumento de peso en un sujeto comprendiendo administrar a un sujeto necesitado de la misma, una cantidad de α -ciclodextrina suficiente para reducir el aumento de peso corporal o promover la pérdida de peso. Un método preferido comprende ingerir suficientes cantidades de α -ciclodextrina para unir una cantidad deseada de grasa en una comida contentiva de grasa, o cantidad deseada de grasa por día, para promover la pérdida de peso, reducir el aumento de peso o mantener el peso. Preferiblemente la pérdida de peso para un humano es mas o menos de 1-1.5lbs/semana. Un aspecto de este invento es un método que comprende ingerir suficiente cantidad de α -ciclodextrina para reunir la grasa en exceso de la cantidad deseada de grasa por comida o por día que un sujeto desea absorber. El método comprende determinar la cantidad de grasa que un sujeto desea absorber por comida por día, determinar la cantidad de grasa ingerida en exceso de la cantidad que el sujeto desea absorber, y después ingerir suficientes cantidades de α -ciclodextrina para reunir la grasa en exceso de

tal manera que solamente la cantidad deseada de grasa sea absorbida. Por ejemplo fundamentado en lo aquí mostrado que mas o menos 1 g de α -ciclodextrina puede reunir mas o menos 9g de grasa, la cantidad suficiente para promover una perdida de peso de 1-1.5 lbs/semana en un sujeto que consume una dieta diaria de 2500g/día, tal dieta comprendiendo mas o menos 100g grasa/día, la cantidad preferida de α -ciclodextrina ingerida es mas o menos 2g/comida tres comidas al día. Preferiblemente el total de α -ciclodextrina ingerida diariamente es mas o menos de 500g a mas o menos de 33g por día, mas preferiblemente de 5g a mas o menos de 20g por día, mas preferiblemente mas o menos de 6-11g/día. Preferiblemente la α -ciclodextrina es administrada con una comida de tal forma que la tasa de α -ciclodextrina a grasa ingerida que uno desea evitar que sea absorbida por el cuerpo sea mas o menos de 1:20 w/w a mas o menos de 1:3 w/w, preferiblemente la tasa es mas o menos de 1:13 w/w a mas o menos de 1.5 w/w, mas preferiblemente la tasa es mas o menos de 1:9 w/w. Un sujeto necesitado de la misma es uno que esta necesitado de ella o que desea perder peso o evitar el aumento de peso, e.g., uno que esta inclinado a aumentar de peso o que tiene ya sobrepeso o esta obeso. El sujeto también puede ser uno que consume una dieta diaria que comprende mas o menos 30% o mas grasas por caloría. La α -ciclodextrina puede ser administrada al sujeto en forma de polvo, una tableta, una capsula, una bebida u otro medio de entrega adecuado para el consumo, preferiblemente uno que no comprenda acido linolenico. La α -ciclodextrina puede ser administrada antes, concurrentemente a con posterioridad a la ingestión de una comida contentiva de grasa. Preferiblemente la α -ciclodextrina es administrada poco antes o concurrentemente con la ingestión de una comida contentiva de grasa. Mas preferiblemente la α -ciclodextrina es administrada a un sujeto humano mientras consume una comida contentiva de grasa. La α -ciclodextrina puede ser administrada en forma de un producto alimenticio, e.g., productos de pan, e.g. panecillos, rollos o bizcochos o un cereal de desayuno e.g., avena, crema de trigo, salvado de uvas pasas, pedacitos de matiz, u otro cereal listo para consumir, o preferiblemente en forma de los productos alimenticios de este invento. El sujeto puede ser un mamífero, e.g., ratón, rata, gato, perro, vaca, caballo, mico, mono o humano pero preferiblemente un humano y esta dentro de la habilidad del arte ajustar la cantidad total de α -ciclodextrina administrada al mamífero para reunir suficiente grasa para lograr la cantidad deseada de perdida de peso. Por ejemplo, 2g de α -ciclodextrina por comida reduce la biodisponibilidad de mas o menos de 18g de grasa por comida o mas o menos de 54g de grasa por día. Esto es igual a 1-1.5lbs de peso corporal por semana. Esta cantidad de grasa aproximadamente representa la mitad del consumo de grasa normal diaria para el promedio de Norteamericanos.

Este invento también se relaciona con métodos para reducir la biodisponibilidad de grasa en un producto alimenticio contentivo de grasa que comprende combinar una cantidad de una α -ciclodextrina con un producto alimenticio de tal manera que el producto alimenticio comprenda una tasa de α -ciclodextrina a grasa de mas o menos de 1:20 a mas o menos de 1:3 w/w, preferiblemente mas o menos de 1:13 a mas o menos de 1:5 w/w, mas preferiblemente mas o menos de 1:9 w/w. Preferiblemente el total de ciclodextrina en los productos alimenticios de este invento es menos de mas o menos de 9% w/w, mas preferiblemente menos de mas o menos 6% w/w y mas preferiblemente menos que mas o menos 3% w/w. Este método puede ser aplicado a una variedad de productos alimenticios contentivos de grasa, e.g., un producto alimenticio harinoso, un producto vegetal preparado, un producto lácteo, una carne preparada o producto del mar, gravia, salsas y salsas para ensalada. Por ejemplo, el producto alimenticio harinoso puede ser e.g. una barra de onces, un cereal de desayuno, pancakes, waffles, rollitos de pan, tortillas, tortillas de matiz, tortillas galletas, galletas, pan, ponques, galletas, rosquillas, zepolis y pies. Un producto alimenticio de este invento puede ser e.g. leche, crema, leche evaporada o condensada, pudin, mantequilla, helado, leche malteada, yogur y bebidas preparadas con yogur, e.g. un "suave" con yogur y fruta, y queso o productos procesados de queso o productos de huevo, e.g., una tortilla o pasta de huevo. El producto vegetal puede ser uno que es hecho con grasa como uno de los ingredientes, sopa de vegetales con base en crema, sopas con base en carne, o burger de

vegetales, o el producto vegetal puede ser uno que es frito en material que contiene grasa, e.g., papas fritas, papas o falafel, donde la cantidad de α -ciclodextrina en el producto es basada en el estimado de la cantidad de material contentivo de grasa que sera absorbida por el producto final. El producto de carne puede ser una carne preparada, cordero, cerdo, aves o producto de mariscos, e.g., salchichas alemanas, tajadas de deli, salchichas, dedos de pescado, dedos de pollo y carne molida para ser preparadas en, e.g., hamburguesas o rollo de carne. Este método también es aplicable a productos batidos o cubiertos, e.g., papas a la francesa, dedos de pescado, dedos de pollo o tempura, que son fritos y a batidos que son usados para cubrir los productos que son fritos en material contentivo de grasa. La cantidad de ciclodextrina en el batido de un producto batido esta basada en el estimado de la cantidad de material contentivo de grasa que sera absorbido por el por el producto cubierto de batido. El método también es aplicable a dulces y condimentos, e.g., chocolates, salsas, mayonesa y salsas para ensalada.

La α -ciclodextrina puede ser adicionada al producto alimenticio consumible en cualquier etapa de su producción y puede ser adicionado bajo condiciones que favorezcan la formación de complejos de α -ciclodextrina y grasa de tal manera que los complejos sean distribuidos a través del producto alimenticio consumible. Alternativamente, la α -ciclodextrina puede ser combinada con un producto alimenticio contentivo de grasa a medida que es consumido mediante la determinación de la cantidad aproximada de grasa del producto alimenticio y, posteriormente ingiriendo α -ciclodextrina en una cantidad suficiente para obtener una tasa de α -ciclodextrina a grasa ingerida de 1:20 a mas o menos de 1:13, preferiblemente de 1:13 a mas o menos de 1:5 y mas preferiblemente mas o menos de 1:9 w/w. Preferiblemente, el producto alimenticio que contiene grasa consumible comprende, por contenido calórico, 7-80% grasa, mas preferiblemente de 20-70% grasa y mucho mas preferiblemente 40-70% grasa, o por peso 5-50%, grasa, preferiblemente 7-25% grasa.

Este invento también se relaciona con métodos para reducir una condición patológica frecuentemente asociada con la obesidad y con el exceso de peso, e.g. tasa alta de colesterol/HDL, altos niveles de trigliceridos, altos niveles de leptina, altos niveles de insulina, y resistencia a la insulina, mediante la administración de α -ciclodextrina, a un sujeto necesitado de la misma, en cantidades suficientes y por un tiempo suficiente para reducir la condición patológica asociada con la obesidad y con el exceso de peso.

El colesterol en el suero de la sangre es encontrado en combinación con proteínas de la sangre. De interés particular son las lipoproteinas de alta intensidad (HDL) y de baja densidad (LDL). Este invento también se relaciona con un método para aumentar el nivel de colesterol lipoproteina de alta densidad (HDL) en un sujeto, comprendiendo la administración de α -ciclodextrina a un sujeto necesitado de la misma en cantidad suficiente, y por un periodo suficiente, para aumentar los niveles de HDL. Preferiblemente la cantidad de α -ciclodextrina administrada al sujeto es mas o menos de 500mg a mas o menos de 33 gramos por día, preferiblemente mas o menos de 3-21 g por día y mas preferiblemente mas o menos de 6-11 g por día. La α -ciclodextrina puede ser administrada antes, concurrentemente o subsecuentemente a la ingestión de una comida contentiva de grasa. El sujeto puede ser uno que consuma mas o menos 100g grasa/día. Preferiblemente la α -ciclodextrina es administrada al sujeto con una comida que contiene grasa. Una cantidad suficiente de α -ciclodextrina es mas o menos 165mg - 11g/comida, preferiblemente mas o menos 1-7g/comida o mas preferiblemente mas o menos 2-3.3g comida. La α -ciclodextrina puede ser administrada de cualquier forma adecuada, e.g. una tableta, pastilla, capsula, liquido u otro medio de entrega adecuado para consumo humano, o en forma de productos alimenticios, e.g., productos de pan, panecillos, rollos, bizcochos y cereal de desayuno, e.g., cereal de avena, crema de trigo, salvado de uvas pasas, pedacitos de maiz, u otro cereal listo para comer, y especialmente los productos alimenticios de este invento. Preferiblemente el tamaño de una servida del producto alimenticio, para uso en este método, contiene mas o menos 165mg - 11g/comida,

preferiblemente mas o menos 1-7g/comida o mas preferiblemente mas o menos 2-4g α -ciclodextrina. Preferiblemente la α -ciclodextrina es administrada al sujeto en cantidad tal que la tasa de α -ciclodextrina a grasa de mas o menos de 1:20 a mas o menos de 1:3 w/w, preferiblemente mas o menos de 1:13 a mas o menos de 1:5 w/w, mucho mas preferiblemente mas o menos de 1:9 w/w por comida, o diariamente.

Es posible que los niveles totales de colesterol en la sangre permanezcan constantes a pesar de que los niveles de HDL sean elevados, si hay una disminución en los niveles de LDL. Entonces otro aspecto de este invento es método para aumentar los niveles de HDL y reducir los niveles de LDL, reduciendo la tasa colesterol/HDL, y o reduciendo los niveles de colesterol en el sujeto necesitado del mismo, mediante la administración de α -ciclodextrina en cantidad y por un periodo suficiente para aumentar los niveles de HDL y/o reducir los niveles de LDL, disminuir la tasa total de colesterol/HDL y/o reducir colesterol. La disminución de LDL y el aumento de HDL reduce la tasa total de colesterol a HDL. Preferiblemente el nivel de colesterol total no es sustancialmente disminuido o aumentado.

La α -ciclodextrina puede ser administrada al sujeto en forma de polvo, tableta, una capsula, una bebida u otro medio de entrega adecuado para el consumo, preferiblemente uno que no comprenda acido linolenico. Una cantidad suficiente de α -ciclodextrina es mas o menos de 165mg-11g/comida, preferiblemente mas o menos mas o menos de 1-7g/comida o mas preferiblemente mas o menos de 2-3.3g/comida. Preferiblemente el total de α -ciclodextrina ingerida diariamente es mas o menos de 500mg a mas o menos de 33 g por día, mas preferiblemente mas o menos de 5 g a mas o menos de 20g por día, mucho mas preferiblemente mas o menos de 6-11g/día. Preferiblemente la α -ciclodextrina es administrada con la comida, de tal manera que la tasa de α -ciclodextrina a grasa sea mas o menos de 1:20 w/w a mas o menos de 1:3 w/w, preferiblemente la tasa es mas o menos de 1:13 w/w a mas o menos de 1:5 w/w, mucho mas preferiblemente la tasa es mas o menos de 1:9 w/w por comida.

Un sujeto necesitado de incrementar el nivel de HDL y/o disminuir los niveles de LDL, reduciendo la tasa colesterol/HDL o reduciendo los niveles de colesterol es uno que tiene, o tiene una predisposición a una tasa alta de niveles colesterol total a HDL. Los métodos para determinar el colesterol en la sangre, niveles HDL y LDL son bien conocidos en el arte y no necesitan ser elaborados en este. Sin embargo, para una discusión sobre los niveles de colesterol y los métodos para determinar el colesterol, los niveles HDL y LDL (ver e.g., Programa de expertos en la detección, evaluación y tratamiento de alto colesterol en la sangre en adultos. Resumen Ejecutivo del Tercer Reporte del Panel Nacional de Educación en la Detección, Evaluación y Tratamiento del Alto Colesterol en la Sangre en Adultos (Panel de Tratamiento de Adultos III), JAMA 285(19): 2486-97:2001, and: Manual de Prueba de Lipoproteína, Rifai N, Warnick GR and Dominiczak MH, eds. Chapters 9, 11 and 12. AACC Press, Washington DC, 2000 ambas incorporadas a este, por referencia.

Este invento también se relaciona con un método para reducir los trigliceridos en un sujeto que comprende administrar al sujeto necesitado del mismo una cantidad de α -ciclodextrina suficiente para reducir los niveles de trigliceridos. Un sujeto necesitado de esto es aquel que tiene altos niveles de trigliceridos, tiene una predisposición a niveles altos de trigliceridos o tiene una historia familiar de altos niveles de trigliceridos. Los altos niveles de trigliceridos están relacionados con una variedad de condiciones patológicas. Entonces, este invento también se relaciona con tratar una condición patológica, e.g., enfermedad cardiovascular, pancreatitis aguda, resistencia a la insulina y diabetes no controlada, y varias dislipidemias asociadas con altos niveles de trigliceridos, mediante la administración de α -ciclodextrina al sujeto necesitado de la misma en cantidades suficientes para reducir los niveles de trigliceridos en el sujeto. Aquellos con destreza en el arte están bien versados en los métodos para determinar los niveles de trigliceridos en un sujeto. Para una revisión de los

métodos para determinar los niveles de triglicéridos en la sangre ver e.g. manual de Prueba de Lipoproteína, Rifai N, Warnick GR and Dominiczak MH, eds. Chapter 10. AACC Press, Washington DC 2000, incorporado a este por referencia. La α -ciclodextrina puede ser administrada antes, concurrentemente o subsecuentemente a la ingestión de la comida contentiva de grasa. Mas preferiblemente, la α -ciclodextrina es administrada al sujeto con una comida contentiva de grasa. Una cantidad suficiente de α -ciclodextrina es mas o menos de 165mg-11g/comida, preferiblemente mas o menos de 1-7g/comida, o mucho mas preferiblemente mas o menos de 2-4g comida. Preferiblemente el total de α -ciclodextrina ingerida diariamente es mas o menos de 500mg a mas o menos de 33 g por día, mas preferiblemente mas o menos de 5g a mas o menos de 20g por día, mucho mas preferiblemente mas o menos de 6-11 g/día. Preferiblemente la tasa de α -ciclodextrina: grasa ingerida por comida o diariamente es mas o menos de 1:20 a mas o menos de 1:3 w/w, preferiblemente la tasa es mas o menos de 1:13 a mas o menos de 1:5 w/w y mas preferiblemente la tasa es mas o menos de 1:9 w/w. La α -ciclodextrina puede ser administrada al sujeto en forma de polvo, tableta, una capsula, una bebida u otros medio de entrega adecuado para el consumo, preferiblemente uno que no comprenda acido linolenico. La α -ciclodextrina puede ser administrada al sujeto en forma de un producto alimenticio, particularmente un producto alimenticio de este invento.

Este invento ademas se relaciona con un método para reducir los niveles de leptina en un sujeto que comprende administrar α -ciclodextrina a un sujeto necesitado de la misma en cantidad suficiente para reducir los niveles de leptina en el sujeto. La α -ciclodextrina puede ser administrada antes, concurrentemente o subsecuentemente a la ingestión de la comida contentiva de grasa. Preferiblemente la α -ciclodextrina es administrada poco antes o concurrentemente con la comida contentiva de grasa. Mas preferiblemente la α -ciclodextrina es administrada al sujeto con una comida contentiva de grasa. La cantidad de α -ciclodextrina ingerida por comida es preferiblemente mas o menos de 165mg-11g/comida, mas preferiblemente de 1-7g/comida y mas preferiblemente de 2-3.3g/comida. Preferiblemente el total de α -ciclodextrina ingerida diariamente es mas o menos de 500mg a mas o menos de 33 g por día, mas preferiblemente mas o menos de 5g a mas o menos de 20g por día mas preferiblemente mas o menos 6-11g/día. Preferiblemente la cantidad de α -ciclodextrina administrada diariamente al sujeto y la grasa ingerida diariamente por el sujeto esta en una tasa mas o menos de 1:20 a mas o menos de 1.3 w/w, preferiblemente la tasa es mas o menos de 1:13 a mas o menos de 1:5 w/w, y mucho mas preferiblemente la tasa es mas o menos de 1:9 w/w. Un sujeto necesitado en reducir la leptina es uno que tiene altos niveles de leptina, tiene una predisposición a la resistencia a la leptina. Los niveles de leptina pueden ser determinados usando cualquier método conocido en el arte para determinar los niveles de leptina. Para una revisión de varios ensayos para determinar la resistencia a la leptina ver e.g., Maffei et al., Nature Med 1:1155-161 (1995) incorporado a este por referencia. La α -ciclodextrina puede ser administrada al sujeto en forma de polvo, tableta, capsula, bebida, confitería u otros medio de entrega adecuado para el consumo humano, preferiblemente uno que comprenda menos de 2% acido linolenico, mas preferiblemente uno que comprenda menos de 0.2% de acido linolenico, mas preferiblemente uno que no comprenda acido linolenico. La α -ciclodextrina puede ser administrada al sujeto en forma de un producto alimenticio, preferiblemente un producto alimenticio de este invento.

Este invento ademas se relaciona con un método para reducir los niveles de insulina en la sangre y la resistencia a la insulina en un sujeto, comprendiendo administrar α -ciclodextrina a un sujeto necesitado de la misma en cantidad suficiente para reducir los niveles de insulina en la sangre del sujeto. La resistencia a la insulina es típicamente la causa de la diabetes Tipo II. La resistencia a la insulina puede ser estimada por la tasa de triglicéridos/HDL-colesterol y la tasa de glucosa/insulina. Un sujeto necesitado de la misma es uno que muestra altos niveles de insulina, tiene diabetes Tipo II o que tiene una predisposición para desarrollar diabetes Tipo II, o que tiene una historia familiar de altos

niveles de insulina o diabetes Tipo II. Cualquier método rutinariamente usado para determinar los niveles de insulina puede ser usado en este para ensayar y monitorear los niveles de insulina y la resistencia. Ver por ejemplo Berson et al. (Eds) Métodos de Investigación y Diagnostico Endocrinológico, ch 3, Part III, Vol 28. American Elsevier Publishing Co., New York, 1973, incorporado en este por referencia, para una descripción de ensayos para determinar los niveles de insulina. La α -ciclodextrina puede ser administrada antes, concurrentemente o subsecuentemente a la ingestión de la comida contentiva de grasa. Preferiblemente la α -ciclodextrina es administrada poco antes o concurrentemente con la ingestión de la comida contentiva de grasa. Mas preferiblemente la α -ciclodextrina es administrada al sujeto con una comida contentiva de grasa. La cantidad de α -ciclodextrina ingerida por comida es preferiblemente mas o menos de 165mg-11g/comida, mas preferiblemente mas o menos mas o menos de 1-7g/comida y mas preferiblemente mas o menos de 2-3.3g/comida. El total de α -ciclodextrina ingerida diariamente es mas o menos de 500mg a mas o menos de 33 g por día, preferiblemente mas o menos de 5g a mas o menos de 20g por día, y mucho mas preferiblemente mas o menos de 6-11g/día. Preferiblemente la cantidad de α -ciclodextrina administrada diariamente al sujeto esta basada en la grasa ingerida diariamente por el sujeto, y esta a una tasa mas o menos de 1:20-1:3 w/w, preferiblemente la tasa es mas o menos de 1:13 - 1:5 w/w, y mucho mas preferiblemente la tasa es mas o menos de 1:9 w/w. La α -ciclodextrina puede ser administrada al sujeto en forma de polvo, tableta, gel, capsula, un liquido u otro medio de entrega adecuado para consumo humano, preferiblemente uno que no comprenda acido linolenico. La α -ciclodextrina puede ser administrada al sujeto en forma de un producto alimenticio, preferiblemente un producto alimenticio de este invento.

Este invento también se relaciona con un método para reducir la diarrea en un sujeto necesitado de ello, comprendiendo administrar al sujeto necesitado de ello, α -ciclodextrina en cantidad y por un periodo suficiente para reducir la diarrea en el sujeto. El sujeto puede ser un mamífero, e.g., ratón, rata, gato, perro, vaca, caballo, mico, mono, o humano. Tal sujeto puede ser uno que esta predispuesto a diarrea, o actualmente sufre de diarrea, e.g., el sujeto puede ser un paciente propenso a la colecistectomía o que tenga diarrea, un paciente que sufra de diarrea agravada por la grasa, o un paciente que tenga diverticulitis aguda o subaguda., las fases agudas de ciertas condiciones inflamatorias del intestino, e.g., colitis ulcerativa o enfermedad de Crohn y después de algunos tipos de cirugía intestinal, e.g., colostomía o ileostomía. La α -ciclodextrina puede ser administrada en forma de un producto alimenticio, preferiblemente un producto alimenticio de este invento por ejemplo un producto alimenticio harinoso o no harinoso de este invento. La α -ciclodextrina también puede ser administrada al sujeto en forma de polvo, tableta, una capsula, gel, un liquido u otro medio de entrega adecuado para el consumo. La α -ciclodextrina puede ser administrada con una comida a mas o menos e.g. de 165mg-11g/comida, preferiblemente mas o menos de 1-7g/comida y mas preferiblemente mas o menos de 2-3.3g/comida. Preferiblemente el total de α -ciclodextrina ingerida diariamente es mas o menos de 500mg a mas o menos de 33 g por día, mas preferiblemente mas o menos de 5 g a mas o menos de 20g por día, mas preferiblemente de 6-11g/día. La tasa de α -ciclodextrina ingerida a grasa ingerida por comida, o diariamente, preferiblemente por comida, es mas o menos de 1:20-1:3 w/w, preferiblemente la tasa es mas o menos de 1:13-1:5 w/w, mas preferiblemente la tasa es mas o menos de 1:9 w/w. La α -ciclodextrina puede ser administrada antes, concurrentemente a subsecuentemente a la ingestión de la comida contentiva de grasa. Preferiblemente la α -ciclodextrina es administrada poco antes o concurrentemente de la ingestión de la comida contentiva de grasa.

La adición de α -ciclodextrina a un producto alimenticio para mascotas mantiene o promueve buena calidad de excrementos de la mascota y/o mejora la calidad de los excrementos de la mascota. La buena calida de excrementos en una mascota es un trato deseable según es percibido por el propietario de la mascota en que no solamente es generalmente estéticamente mas satisfactorio pero también es un indicador de la buena salud

de la mascota. Como tal, este invento también se relaciona con un producto alimenticio para mascotas que comprende α -ciclodextrina en cantidad suficiente para mantener o promover buena calidad de los excrementos de una mascota y/o mejorar la calidad de los excrementos de una mascota. Los excrementos que tienen buena calidad son firmes y bien formados al mantener su forma. Un excremento con contenido de humedad, de tal manera que la forma no sea mantenida (banquillo suelto o diarrea), o un contenido de humedad de tal manera que el excremento sea duro y seco, no son excrementos de buena calidad. La comida de mascotas es preferiblemente comida para mascotas empacada. El empaque puede ser de plástico, papel, cartón o metal, e.g., aluminio o hoja de metal. La comida de mascota puede ser comida de mascota húmeda, tal como aquellas empacadas en tarros o hojas de metal o una comida seca de mascota, tal como aquellas empacadas en papel o cartón, e.g., kible o bizcochos. Preferiblemente la comida de mascota es comida desarrollada para un gato, perro, vaca o caballo. Este invento también se relaciona con un método para mantener o promover buena calidad de excrementos de una mascota y/o mejorar la calidad de los excrementos de una mascota mediante la administración de α -ciclodextrina a una mascota, preferiblemente una mascota necesitada de la misma, en cantidad y por un periodo suficiente para mantener o promover buena calidad de excrementos de la mascota y/o mejorar la calidad del excremento de la mascota. La α -ciclodextrina puede ser administrada con una comida a mas o menos e.g. 165mg-11g/comida, preferiblemente mas o menos de 1-7g/comida, y mucho mas preferiblemente mas o menos de 2-3.3g/comida. Preferiblemente el total de α -ciclodextrina ingerida diariamente es mas o menos de 500mg a mas o menos de 33 g por día, mas preferiblemente mas o menos de 5g a mas o menos de 20g por día, mas preferiblemente de 6-11g/día. La tasa de α -ciclodextrina ingerida a grasa ingerida por comida, o diariamente, preferiblemente por comida, es mas o menos de 1:20 - 1:3 w/w, preferiblemente la tasa es mas o menos de 1:13-1:5 w/w, mas preferiblemente la tasa es mas o menos de 1:9 w/w. La α -ciclodextrina puede ser administrada antes, concurrentemente a subsecuentemente a la ingestión de la comida contentiva de grasa. Preferiblemente la α -ciclodextrina es administrada poco antes o concurrentemente con la ingestión de la comida contentiva de grasa. La α -ciclodextrina puede ser administrada a la mascota en forma de pastilla, galleta, tableta, capsula etc. o en forma de un producto alimenticio para mascotas, particularmente un producto alimenticio para mascotas de este invento, incluyendo alimentos húmedos para mascotas tales como empacados en un tarro o en hojas de metal o comida seca para mascotas tales como aquellas empacadas en un contenedor de papel o cartón e.g. kible o bizcocho. Una mascota necesitada de la misma es una que tiene excrementos pobremente formados o con predisposición a tener excrementos pobremente formados, e.g., una mascota con diarrea o con predisposición a la diarrea.

En los métodos de este invento, la α -ciclodextrina puede ser administrada en forma de unidad de dosis de una sola dosis fundamentalmente consistiendo en α -ciclodextrina. La unidad de única dosis puede ser en forma de polvo, tableta, capsula, gel, pelota, liquido, etc. por cualquier medio que es rutinariamente usado en el arte. La α -ciclodextrina puede ser incorporada en el polvo, tableta, gel, capsula, pelota, liquido, etc. con otros aditivos comúnmente usados, e.g., colorantes, antioxidantes, llenadores, almidones, azucars, agentes antibacteriales o antihongos, preservativos, estabilizantes o emulsificadores. La α -ciclodextrina puede ser combinada con cualquier transportador farmacéutico aceptable para administración oral, e.g. puede ser encerrado en una capsula de gelatina suave o dura, comprimida en tabletas, o directamente incorporada en la dieta del individuo.

Específicamente, la α -ciclodextrina puede ser incorporada con excipientes y usada en forma de tabletas digestivas, capsulas, elixires, suspensiones, siropes, wafers y similares. La α -ciclodextrina puede ser mezclada con otras formas de alimento y aumentadores de sabores farmacéuticos aceptables. Los transportadores farmacéuticos aceptables y las formulaciones son descritas, por ejemplo, en Remington's Ciencias Farmacéuticas (19th ed.) (Genarro, ed. (1995) Mack Publishing Co., Easton, Pa), incorporada a este por referencia. Preferiblemente,

la formulación es tal que la α -ciclodextrina es liberada en el estomago para mezclarse con el alimento ingerido, de tal manera que uniones de la α -ciclodextrina y grasa sean formados de tal forma que la α -ciclodextrina: los complejos grasos estén ya formados cuando el quimo es empujado al yeyuno y es mezclado con bicarbonato y lipasa.

Debido a que solamente una cantidad relativamente pequeña de ciclodextrina total (e.g. menos que mas o menos de 9% w/w preferiblemente menos que mas o menos de 6% w/w, mucho mas preferiblemente menos que mas o menos de 3% w/w) es adicionada a los productos alimenticios para lograr la tasa deseada de α -ciclodextrina a grasa, la α -ciclodextrina puede ser adicionada a la composición de la comida, en vez de usar α -ciclodextrina como un llenador para reemplazar una cantidad igual de los ingredientes secos en el producto alimenticio. Entonces el contenido calórico de los productos alimenticios de este invento, según determinado por bomba calorimétrica, no es sustancialmente alterado por la adición de ciclodextrina total. Aun si los ingredientes secos son removidos del producto alimenticio para compensar por la relativa poca cantidad de ciclodextrina adicionada al producto alimenticio (menos que mas o menos de 9% preferiblemente menos que mas o menos de 6% w/w, mas preferiblemente menos que mas o menos de 3% w/w), el contenido calórico del alimento no sera sustancialmente reducido.

Este invento también se relaciona con métodos para mejorar las propiedades organolépticas de un producto alimenticio consumible contentivo de grasa, sin reducir el contenido calórico (como ensayado por bomba calorimétrica) o sustancialmente reducir el porcentaje de grasa en el producto alimenticio. El método comprende adicionar α -ciclodextrina al producto alimenticio contentivo de grasa durante la preparación del producto. La cantidad de α -ciclodextrina adicionada a los alimentos esta basada en la cantidad de grasa en el producto terminado. Los productos alimenticios de este invento típicamente tienen una tasa de α -ciclodextrina a grasa mas o menos de 1:20-1:3 w/w, preferiblemente mas o menos de 1:13-1:5 w/w, y mas preferiblemente mas o menos de 1:9 w/w. La cantidad total de ciclodextrina adicionada al producto es típicamente menos de 9% w/w, preferiblemente menos de 6% w/w y mas preferiblemente menos de 3% w/w. Los productos hechos con tan poco como 0.7% w/w α -ciclodextrina han aumentado las propiedades organolépticas, e.g., un sabor mas dulce y una textura mas suave. El producto alimenticio consumible contentivo de grasa puede comprender por contenido calórico 7-80% grasa, preferiblemente 20-70% o, mucho mas preferiblemente 40-70% grasa, o por peso 5-50% w/w grasa o preferiblemente 7-25% w/w grasa. Este método puede ser aplicado a una variedad de productos alimenticios contentivos de grasa, e.g. un producto alimenticio harinoso, un producto vegetal preparado, un producto lácteo, una carne de res preparada o mariscos, sopas y condimentos e.g., gravia, salsas, mayonesa, salsa para ensaladas, etc. Por ejemplo, el producto alimenticio harinoso puede ser e.g. barra de merienda, cereal de desayuno, pancake, waffle, muffin, tortilla, tortillas de matiz, galleta de merienda, pan, ponqué, galleta, donald, zeppoli y pie u otra fruta o producto de panadería lleno de nueces. Un producto lácteo de este invento puede ser e.g. leche, crema, leche evaporada o condensada, pudin, mantequilla, helado, leche malteada y sopas a base de crema o sopas, yogur y bebidas preparadas con yogur, e.g., frutas y "suave" yogur, y queso o productos de queso procesados, o productos de huevo, e.g., una tortilla o pasta de huevo. El producto vegetal puede ser uno que es hecho con grasa como uno de los ingredientes e.g., humus, tahini, margarina y mantequillas de nueces, o puede ser uno que es frito en un material contentivo de grasa, e.g., papas fritas, vegetales tempura, o falafel, donde la cantidad de una α -ciclodextrina en el producto frito esta basada en la cantidad de material contentivo de grasa que es estimado que es contenido en el producto frito, después de ser frito. El producto de carne puede ser carne preparada, cordero, cerdo, aves o productos del mar, e.g., frankfurters, tajadas de deli, salchichas, barras de pescado, dedos de pollo y carne molida para ser hechas en, e.g., hamburguesas, bolas de carne o masa de carne. El método también es aplicable a batidos que son usados para cubrir productos, e.g. papas fritas o tempura, para ser fritadas en material contentivo de grasa, e.g., manteca o

aceite. Además el método es aplicable a jabones, y condimentos, e.g., gravias, salsas y salsas de ensalada, donde la tasa de α -ciclodextrina a grasa descrito supra puede mejorar la textura y/o sabor del producto. Los productos de este invento frecuentemente tienen un sabor comparable al de productos similares hechos sin α -ciclodextrina y/o tienen una textura mas suave y un sabor mas dulce. Además, la inclusión de α -ciclodextrina en leche evaporada o condensada produce un producto mas blanco según comparado con productos similares sin α -ciclodextrina.

Este invento también se relaciona con un método para reducir la cantidad de tiempo requerido para preparar crema batida, que comprende adicionar α -ciclodextrina a la crema antes o durante la batida. La α -ciclodextrina es adicionada en cantidad suficiente para reducir la cantidad de tiempo necesario para hacer crema batida. Preferiblemente la cantidad de α -ciclodextrina es suficiente para obtener una tasa de α -ciclodextrina a grasa en la crema mas o menos de 1:20 - 1:3 w/w, preferiblemente mas o menos de 1:13-1:5 w/w y mucho mas preferiblemente mas o menos de 1:9 w/w. Reduciendo la cantidad de tiempo necesario para que se forme crema batida reduce la cantidad de energía necesaria para correr el mezclador, lo que cuando calculado en una escala comercial resulta en grandes ahorros monetarios tanto en electricidad y mano de obra. La crema batida queda suave y acucharada y el suero no se separa del resto de los componentes.

Se ambiciona en este que la crema batida que contiene α -ciclodextrina pueda ser usada como cubierta en otro material contentivo de grasa, que puede o puede no contener α -ciclodextrina, y la cantidad de α -ciclodextrina en la crema batida sera suficiente para unir la grasa al otro material contentivo de grasa cuando consumido, reduciendo entonces también la biodisponibilidad.

EJEMPLOS

EJEMPLO 1

Las Figuras 9A-9C muestran los resultados de un estudio in vitro de aceite vegetal (4g), agua (6g) (adicionado con color para alimentos para contraste) y cantidades variadas de (A) α -ciclodextrina (100-2,000mg, derecha a izquierda), (B) β -ciclodextrina o (C) γ -ciclodextrina. Una banda de material "similar a cera" que divide el aceite y las fases acuosas es aparente en los tubos. El tamaño de esta banda aumenta con mayores cantidades de α -ciclodextrina, a un máximo en el tubo marcado 10% (400mg α -ciclodextrina/4g aceite). Notese el mayor tamaño (derecha a izquierda) de una capa blanca de α -ciclodextrina no reaccionada en el fondo de los tubos. Este material es desplazado de la solución, bien por el aceite o por el complejo α -ciclodextrina-aceite. Estos tubos fueron centrifugados para mejorar la definición de las capas. El complejo "similar a cera" es de tal consistencia que todos los tubos en el 9A, excepto los mas lejanos a la derecha, pueden ser invertidos sin goteo de la fase acuosa alrededor del complejo.

El tamaño de poro de la α -ciclodextrina es significativamente mas pequeño que el tamaño de poro de la β -ciclodextrina y γ -ciclodextrina. Entonces, uno no esperaría una α -ciclodextrina una moléculas de triglicéridos porque las moléculas no cabrían en ese poro de la α -ciclodextrina. Sin embargo, la cantidad de grasa unida en los tubos que contienen el aceite/ β -ciclodextrina (Figura 9B) y la mezcla aceite/ γ -ciclodextrina (Figura 9C) es significativamente menor que lo visto en los tubos que contienen la mezcla aceite/ α -ciclodextrina (Figura 9A). Esta diferencia es aun mas dramática en la Figura 9C, donde es vagamente notoria una banda de material similar a cera. La sustancia blanca en el fondo de los tubos es ciclodextrina precipitada.

EJEMPLO 2 ESTUDIOS EN ANIMALES

Para examinar el efecto de la α -ciclodextrina en el aumento de peso corporal y en los niveles de plasma lípido en animales alimentados con dietas altas en grasa y dietas bajas en grasa, adelantamos un estudio de alimentación, a corto plazo, usando ratas Wistar. Cuarenta y dos ratas Wistar machos, de 10 semanas de edad, fueron obtenidas de Harlan-Sprague Dawley. Después de una semana de adaptación, mientras eran alimentadas con la dieta baja en grasas controlada (LF), fueron divididas en dos grupos iguales, uno de dieta baja en grasa (LF) y otro de dieta alta en grasa (HF). Estos dos grupos fueron además divididos en dos subgrupos. Dos grupos fueron alimentados la dieta LF o HF y sirvieron como controles para los otros dos grupos de ensayo que fueron alimentados con la dieta LF o la dieta HF conteniendo α -ciclodextrina, donde la cantidad de α -ciclodextrina era tal que la tasa de α -ciclodextrina a grasa en el alimento era de 1:10 w/w. La dieta LF fue formulada en conformidad con la dieta AIN-93M y contiene 4% (w/w) aceite de soya como la fuente de grasa. La dieta HF era una modificación de la dieta LF con 40% aceite de soya. Entonces, el grupo LF que recibía la α -ciclodextrina (LF-ciclodextrina) ingirió 0.4g de α -ciclodextrina/100g de alimento, y el grupo HF que recibió α -ciclodextrina (HF-ciclodextrina) comió 4g α -ciclodextrina/100g de alimento. La densidad calórica de las 4 dietas fueron: LF: 3.96 kcal/g; LF-ciclodextrina: 3.66 kcal/g; HF: 5.70 kcal/g; HF-ciclodextrina: 5.59 kcal/g.

Las ratas fueron alojadas en pares, por cinco semanas, antes de ser colocadas en cajas metabólicas individuales en la sexta semana de estudio. Todos los excrementos de las ratas fueron recogidos durante los tres días finales de estudio. Al final de la sexta semana del periodo de estudio las ratas fueron sacrificadas, por decapitación, después de una breve exposición a gas dióxido de carbono. Fue recogida la sangre del tronco y del hígado en cada animal. El resto del cuerpo fue viscerado, y toda la grasa visible de la cavidad interna fue recogida y pesada. La carcasa fue congelada para análisis de su composición corporal, en una fecha posterior.

Consumo de Alimento y Energía:

La cantidad de alimento ingerido por los animales fue monitoreado por las primeras cinco semanas del estudio y de esta información el consumo calórico fue calculado. Esta información aparece presentada en la Tabla 1 y Figuras 1 y 2 como un promedio para cada grupo $\pm$ SD.

Tabla 1: Consumo total de alimento y de calorías en los 4 grupos de ratas durante las primeras 5 semanas del estudio (media $\pm$ SD).

Grupo	Total alimento ingerido	Consumo calórico (Kcal)
LF	779 $\pm$ 40	2,970 $\pm$ 154
LF-ciclodextrina	786 $\pm$ 87	2,978 $\pm$ 332
HF	753 $\pm$ 70	4,072 $\pm$ 921
HF-ciclodextrina	769 $\pm$ 107	3,986 $\pm$ 560

No hubo diferencia estadística entre ninguno de los grupos, en relación con la cantidad (g) de alimento ingerido. Debido al mayor contenido calórico de la dieta HF, las ratas en los grupos 2 HF significativamente consumieron mas calorías, comparado con aquellas de los 2 grupos alimentados con LF. Debe ser notado que el consumo calórico entre los dos grupos HF o los dos grupos LF no fue afectado por la ingestión de α -ciclodextrina. Esta información muestra que (1) todas las ratas fueron saciadas con la cantidad de alimento ingerido, y (2) que si la α -ciclodextrina estaba uniendo una parte de la grasa y entonces evitando que la grasa fuera digerida por las ratas, las ratas no estaban consumiendo mas alimento para compensar por ello. No hay diferencia estadística entre los grupos en lo pertinente a consumo de agua.

Cambio en el peso corporal:

La Figura 1 ilustra el cambio en el peso corporal de los cuatro grupos de ratas en crecimiento durante la totalidad del periodo en estudio. Según habíamos previamente demostrado (Jen *Physical Behav* 42:551-556 (1988) y Jen et al. *Int. J Obesity* 19:699-708 (1995) incorporado en este por referencia), los animales que recibieron la dieta HF ganaron mas peso que aquellos que recibieron la dieta LF. Interesantemente, la Figura 3 demuestra que los animales que recibieron una dieta comprendiendo α -ciclodextrina y grasa, a una tasa de 1:10 w/w, ganaron peso a una tasa menor en relación con su respectivo grupo de control. A pesar de que el grupo de control en la dieta HF aparecen estar todavía ganando peso a una tasa significativa, la tasa de ganancia de peso de los otros tres grupos parece haber llegado a un tope. En este ejemplo los animales alimentados con la dieta de α -ciclodextrina/alta muestran haber ganado peso a una tasa casi idéntica a la de los animales que recibieron la dieta baja en grasa (4% w/w) sin α -ciclodextrina. Entonces, mediante la adición de la α -ciclodextrina a la dieta de los animales, donde la cantidad de α -ciclodextrina esta basada en la cantidad de grasa en la dieta, en este ejemplo 4% w/w α -ciclodextrina y 40% w/w grasa, la tasa de aumento de peso es significativamente inhibida. Esto aparece en claro contraste con estudios anteriores, donde la composición de ciclodextrina adicionada a la dieta de las ratas no tuvo ningún efecto en la tasa de ganancia de peso hasta que el porcentaje de composición de ciclodextrina en el alimento fue al menos de 58.5% w/w.

Composición corporal:

El análisis de la composición corporal revela que adicionar α -ciclodextrina a la dieta LF no afecto el contenido corporal. Sin embargo, la α -ciclodextrina adicionada a la dieta HF redujo significativamente la masa de grasa corporal (LF: 48.3 ± 2.4 g, LF-ciclodextrina: 51 ± 6.5 g; HF: 71.3 ± 5.8 g; HF-ciclodextrina: 55.6 ± 2.4 g, media $\pm$ SE). Esto implica que la α -ciclodextrina es mas efectiva en reducir la grasa corporal cuando la grasa dietética es alta.

Estoquiometria:

Shimada et al. (Shimada et al. "Estructura de la inclusión de uniones de ciclodextrinas con trigliceridos en la interfase de aceite/agua vegetal" *J. Food Sci.* 1992; 57(3):655-656) ha reportado que dos moléculas de complejo de α -ciclodextrina con un acido graso libre (FFA) mientras que Szejtli (Szejtli J. "Utilizacion de ciclodextrinas en productos y procesos industriales" *J. Mater. Chem.* 1997;7:575-587) sugiere que este fenómeno es dependiente del largo de la cadena de ácidos grasos y que es posible para 3-4 moléculas de α -ciclodextrina unirse con cada uno de los tres ácidos grasos de la molécula de triglicerido. Estos resultados sugieren que 9-12 moléculas de α -ciclodextrina serán necesarias para completamente unir una molécula de triglicerido. Si este fuera el caso, seria difícil imaginar ser capaz de alimentar suficiente α -ciclodextrina a un animal para unir suficientes trigliceridos para lograr una diferencia significativa en el peso corporal, debido a que los trigliceridos y la α -ciclodextrina tienen pesos moleculares similares. Sin embargo, de los datos mostrados en este, donde e.g., una dieta comprendiendo 4% α -ciclodextrina y 40% grasa inhibe el aumento de peso y reduce la masa de grasa corporal, siendo que los pesos moleculares son muy similares, hemos calculado que una molécula de α -ciclodextrina puede unir aproximadamente nueve moléculas de trigliceridos, el equivalente a 27 ácidos grasos libres. Entonces podemos directamente convertir esto a uniones de 1 gramo de α -ciclodextrina aproximadamente 9 gramos de triglicerido. Sin querer estar atados por la teoría, la diferencia en la tasa de las moléculas de α -ciclodextrina necesarias para unir un triglicerido, basados en lo revelado en Shimada o Szejtli, y la tasa de α -ciclodextrina a grasa revelada en este como formando uniones con grasa, sugiere que la α -ciclodextrina cataliza la formación de grandes partículas de trigliceridos cubiertos con α -ciclodextrina en forma de una miscelánea muy estable, reduciendo entonces la biodisponibilidad de grasas en esas partículas. Hemos podido

demostrar que cuando el aceite de oliva purificado es pre-mezclado con α -ciclodextrina, la actividad lipolítica de la lipasa porcina pancreática es significativamente disminuida. A medida que estas partículas son formadas en el medio de la chime, una "sopa" muy compleja, las partículas pueden ser análogas a partículas de lipoproteína en la corriente sanguínea. Esto también explicaría porque la flora bacteriana parece no poder metabolizar los complejos grasos de α -ciclodextrina que llegan del intestino delgado.

Contenido Graso Fetal:

El total de las determinaciones de lípido fueron adelantadas en los excrementos recogidos, usando técnicas estándar Folch et al. J. Biol. Chem 226: 497-509 (1957) incorporado por referencia. Los resultados (Figura 4) indican un aumento significativo en la grasa fetal en la HF-ciclodextrina ($p < 0.05$) pero no en las ratas alimentadas LF-ciclodextrina. En promedio este aumento fue aproximadamente de 25%. Estos datos indican que la α -ciclodextrina redujo la biodisponibilidad de la grasa, evitando que la grasa fuera absorbida cuando el consumo de grasa era alto, y además, evito que esta fuera metabolizada por la flora intestinal de el intestino grueso de los animales. La última observación fue confirmada por inspección visual del excremento. Todo el material recogido parecía tener una forma y consistencia normales, no había indicación de diarrea.

Niveles de Glucosa de Plasma, Colesterol y Triglicéridos:

Las concentraciones de glucosa de plasma, colesterol y triglicéridos fueron medidas en todos los animales sacrificados, usando técnicas estándar de laboratorio clínico, como pueden ser encontradas en Libro de Texto de Tietz de Química Clínica, segunda edición. Burtis CA and Ashwood ER eds., W.B. Saunders Company A Division of Harcourt Brace & Company, 1994, Philadelphia, incorporada en este por referencia. (Figura 5). En promedio, la α -ciclodextrina pareció haber disminuido los niveles de plasma total de colesterol mas o menos en 10%. Esta disminución no fue estadísticamente significativa durante el corto periodo de estudio; esperamos que con periodos de alimentación mas largos los niveles de colesterol continúen disminuyendo. Los niveles de colesterol HDL también disminuyeron pero en menor proporción, aproximadamente 6-8% de niveles de colesterol LDL, en todos los animales fueron muy bajos para medirlos confiablemente, debido a que en las ratas la mayoría del colesterol es llevado en la fracción de colesterol HDL y muy poco es llevado en la fracción de colesterol LDL. Los niveles de triglicéridos fueron significativamente disminuidos ($p < 0.05$) en mas o menos en 30%, en los animales que recibieron la α -ciclodextrina. Los niveles de glucosa no fueron significativamente afectados por la alimentación HF o con α -ciclodextrina, en contraste con los resultados reportados en la solicitud japonesa de Patente S60-94912, donde los altos niveles de ciclodextrina (19.5%, 39%, 58.5% o 78% w/w CD: alimento total) redujeron significativamente la glucosa sanguínea.

Resistencia a la Insulina:

Un aumento en la resistencia a la insulina, elevados triglicéridos en la sangre y disminución en los niveles de colesterol HDL, son todos factores de riesgo del Síndrome X. Las tasa de insulina/glucosa, así como las tasas de triglicéridos/HDL fueron calculados para suministrar indicaciones sobre la resistencia a la insulina y el riesgo al Síndrome X. (Szejtli J. Matter. Chem. 1997;7:575-587 incorporado a este por referencia). A pesar que debido al corto periodo del estudio la alimentación HF no indujo significativamente a una resistencia a la insulina, apareció una tendencia en esa dirección. Similarmente, los animales con ciclodextrina-HF mostraron una tendencia hacia una disminuida resistencia a la insulina. Esperamos, basados en los datos humanos abajo presentados, que cuando el periodo de alimentación sea aumentado, la resistencia a la insulina se volverá significativa y la α -

ciclodextrina puede significativamente disminuir la resistencia a la insulina vista en las ratas alimentadas HF. La reducción en las tasas de colesterol triglicéridos/HDL por α -ciclodextrina indicaron una disminución significativa en el riesgo de Síndrome X.

Leptina:

La leptina es una hormona de proteína con importantes efectos en la regulación del peso corporal, el metabolismo y la función reproductiva. La leptina es predominantemente segregada por el adipocitos, apoyando la idea de que el peso corporal es designado como el total de masa de grasa del cuerpo. Entonces, analizamos los niveles de plasma leptina en los animales alimentados con las dietas LF y HF $\pm$ α -ciclodextrina usando técnicas estándar.

La Figura 6 compara los valores de plasma leptina obtenidos de los cuatro grupos de ratas, donde los niveles de leptina fueron determinados mediante el uso de un kit RIA para ratas leptina (Linco Research, St. Charles, MO), siguiendo las instrucciones del productor, que se incorporan en este por referencia. La cantidad de leptina presente en el plasma de las ratas HF ($18.1 \pm 32 \text{ ng/mL}$) es estadísticamente mayor ($p < 0.001$) que aquella de las ratas LF ($7.5 \pm 1.9 \text{ ng/mL}$). La concentración de plasma leptina de las ratas HF-ciclodextrina ($9.6 \pm 1.8 \text{ ng/mL}$) no es estadísticamente diferente al de las ratas LF. Debido a que la adiposa es la fuente de tejido para la leptina, los datos sugieren que hay mas grasa corporal en las ratas HF en relación con los otros tres grupos. Debido a que la leptina reduce el consumo de alimento y el peso corporal, los mayores niveles de leptina indican un estado de resistencia a la leptina en las ratas alimentadas HF. Sin embargo, cuando la α -ciclodextrina fue adicionada a la dieta HF, las ratas que consumían esta dieta tuvieron, significativamente, un menor nivel de leptina. Esto demuestra que la masa corporal de grasa fue reducida en las ratas HF-ciclodextrina, y sugiere que la resistencia a la leptina en estas ratas es disminuida. Estos resultados sugieren que estas ratas son mas sensibles a los efectos de la leptina, y entonces, el futuro reaumento de peso puede ser mas difícil. Cuando la leptina por gramo de tejido adiposo fue calculada, fue revelado que tanto la dieta grasa y como la α -ciclodextrina tenían efectos independientes en los niveles sanguíneos de leptina (LF: $0.11 \pm 0.02 \text{ ng/mL/g}$ de tejido adiposo; LF-CD: 0.075 ± 0.01 ; HF 0.24 ± 0.03 ; HF-CD: 0.17 ± 0.03 ; efecto dieta $p < 0.001$; efecto CD $p < 0.001$). En las ratas alimentadas con la dieta HF adicionada con α -ciclodextrina, la reducción de los niveles de leptina en la sangre fue mayor que aquella que puede ser contabilizada por la disminución en la masa grasa corporal. Entonces, la α -ciclodextrina reduce los niveles de leptina en la sangre y reduce la resistencia a la leptina, además de aquella inducida por reducción en el peso/grasa corporal. Resultados similares fueron obtenidos de estudios humanos (ver ejemplo 4).

EJEMPLO 3: DATOS CLINICOS INICIALES

Efecto de la α -ciclodextrina en los niveles de triglicéridos en el suero de la sangre

Para determinar el efecto de la α -ciclodextrina en los niveles de triglicéridos, ocho voluntarios fueron alimentados, por dos días consecutivos, con una tortilla de dos huevos con queso (54g) y una leche malteada, conteniendo un total de 47g de grasa después de un ayuno de una noche. En la primera noche la comida también contenía aproximadamente 5g de α -ciclodextrina. Las muestras de sangre (10ml) de cada voluntario tomadas en la habitación vía un catéter intravenoso, inmediatamente antes de la comida (tiempo cero), y a las 1, 2, y 3 horas después de la comida, fue consumido y fueron ensayados para niveles de triglicéridos en el suero de la sangre. La muestra a la hora cero fue usada como base para calcular el porcentaje de cambio en los niveles triglicéridos en el suero de la sangre de los voluntarios humanos, a la una, dos y tres horas. La Figura 7 ilustra los datos recogidos de los voluntarios. Es de anotar que el aumento esperado en los niveles de los triglicéridos en el suero de la sangre es menor cuando la α -ciclodextrina fue mezclada con el alimento que

cuando no esta presente, a pesar de que la diferencia fallo en tener un nivel significativo ($p > 0.08$) debido a altas variaciones entre los individuos y el pequeño numero de individuos incluidos en este estudio.

La Figura 7 también contiene datos de tres voluntarios que tomaron parte en un estudio anterior de dos horas, con una comida mas pequeña (marcada "a"). El estudio anterior de las dos horas también demuestra que el cambio en los niveles de trigliceridos es menor cuando la α -ciclodextrina es incluida en la comida.

Efectos de la perdida de peso

Para determinar si la α -ciclodextrina adicionada a una dieta alta en grasa resultaría en perdida de peso, la α -ciclodextrina fue adicionada a una dieta alta en grasa de un sujeto en examen, i.e. un voluntario humano, hombre de 50 años de edad, cinco pies y siete pulgadas de altura, con un peso inicial de 267 libras. La α -ciclodextrina fue adicionada a la dieta del sujeto, en proporción de un gramo de α -ciclodextrina por cada nueve gramos de grasa que se estimo que eran consumidos por el sujeto. La Figura 8 demuestra el cambio en el peso corporal del sujeto en un periodo de 200 días, aproximadamente 6 meses. A los 6 meses el peso corporal del sujeto fue reducido en 32 libras. Además de la perdida de peso, dentro de las primeras dos semanas del estudio la elevada presión sanguínea del sujeto bajo al punto en que se vio obligado a disminuir en un tercio el bloqueador beta prescrito. Sus trigliceridos sanguíneos fueron también ensayados durante este tiempo y sus niveles de trigliceridos en el suero de la sangre disminuyeron en 23% en el primer mes y 46% para el final de los seis meses. Los efectos de la α -ciclodextrina, en varios parámetros, se muestran en la tabla 2.

Parametro	Base	1 mes	6 meses
Colesterol (mmol/L)	4.76	4.76	4.0
HDL colesterol (mmol/L)	0.97	1.00	1.11
Colesterol/LDL	4.91	4.76	4.41
Trigliceridos (mmol/L)	2.76	2.13	1.50
Resistencia a la insulina	2.85	2.13	1.35
Indice de masa corporal		39.17	37.27
Grasa corporal (%)		33.5	30.0
Cintura (cm)		124	117
Cadera (cm)		127	117
Energía dietética Kcal/d		1,656	1,795
Grasa total (g/d)		112	103
Proporción de grasa (%)		60.9	51.7
Carbohidratos totales (g/d)		56	84
Proporción de carbohidratos (%)		13.5	18.7
Proteínas totales (%)		106	133
Proporción de proteínas (%)		25.6	29.6

La α -ciclodextrina fue también adicionada a la dieta de dos voluntarios adicionales. La α -ciclodextrina fue adicionada en proporción tal que cada comida comprendiera mas o menos 2g de α -ciclodextrina. La Tabla 3 muestra los efectos de la α -ciclodextrina en disminuir los niveles de colesterol, LDL, tasa colesterol/HDL y trigliceridos en el suero de la sangre. Se anota que ambos voluntarios, así como el voluntario inicial, estaban y todavía siguen tomando uno de los farmacéuticos estatín para reducir los trigliceridos en el suero de la sangre. Los tres voluntarios estaban tomando diferentes estatínes. Además, el voluntario "FK" estaba tomando 3g/d niacina, que redujo a 50% en las primeras dos semanas del estudio debido a los efectos secundarios no placenteros de este medicamento.

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TABLA 3

Voluntario	Periodo Meses	Colesterol	Colesterol/HDL	LDL	TG
FK	2.5	-18.5%	-16.1%	-25.6%	-22.2%
JA	6	-10.2	-8.8	-15.0	-37.5%

EJEMPLO 4: NIVELES DE INSULINA y LEPTINA

Muestras de sangre fueron tomadas de los dos sujetos adicionales del Ejemplo 3, en diferentes periodos de tiempo, y ensayados para niveles de insulina y de leptona por el método de Linco Research (St. Charles, MO), usando ensayos radioinmunes de insulina y de leptina humanas.

Los resultados de este análisis, presentados en la Tabla 4, demuestra que la disminución en los niveles de insulina y de leptina son mayores que la que puede ser contabilizada por reducción del peso corporal.

Tabla 4	Días en dieta	Peso Corporal (lb/kg)	Insulina (uU/ml)	Leptina (ng/ml)
Sujeto 1	0	196/89.09	14	3.6
	55	188/85.45	13	2.9
	112	180/81.82	8	1.6
	% disminución	5.0%	42.9%	55.6%
Sujeto 2	0	232/105.45	26	6.1
	28	230/104.55	28	6.0
	62	220.5/100.23	16	3.9
	% disminución	5.0%	38.5%	36%

EJEMPLO 5

Un perro macho de dieciocho meses, adulto castrado de parentesco desconocido, con diarrea crónica, fue purgado dos veces y colocado en comida hipoalergica en un esfuerzo por controlar la diarrea. Sin embargo, la diarrea crónica no fue aliviada y el perro dejo de comer por uno o dos días, en tres ocasiones diferentes.

El perro fue entonces tratado con α -ciclodextrina de la siguiente manera: el perro fue puesto en una dieta comprendiendo una cucharada (2.5g) de α -ciclodextrina mezclada con dos tazas de comida seca, dos veces al día por dos semanas y media. Basados en el contenido de grasa de la comida, la tasa de α -ciclodextrina a grasa era de mas o menos 1:9. La diarrea crónica del perro fue eliminada durante este periodo excepto por un episodio agudo de excremento sueltos después de un día de bañarse en un río, pero desde entonces el excremento se ha formado.

El perro fue entonces alimentado con una dieta idéntica, que no comprendía α -ciclodextrina, por 4 días. Muy rápidamente el perro perdió el apetito, restringió por si mismo el alimento consumido a la mitad y comenzó a comer pasto, el pasto ayuda amarrar el excremento. La diarrea volvió.

La α -ciclodextrina 5(g) fue reintroducida en el alimento del perro y la diarrea fue de nuevo eliminada.

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EJEMPLO 6: PRODUCTOS ALIMENTICIOS

La cantidad de α -ciclodextrina incorporada en los alimentos de este invento esta basada en la cantidad de grasa contenida en el producto alimenticio. Lo siguiente describe una variedad de productos alimenticios convencionales contentivos de grasa donde la α -ciclodextrina ha sido adicionada en conformidad con este invento. La tabla 5 indica el peso total de los productos alimenticios y la cantidad de α -ciclodextrina, grasa y carbohidratos en los productos descritos en este ejemplo comparados con los productos descritos en otras referencias.

A. Galletas expreso de chocolate con pedacitos de chocolate

260g	harina pastelera
75g	polvo de cocoa
3.8g	polvo para hornear
2.8g	sal
226g	margarina
150g	azúcar
180ml (165g)	molaza o azúcar carmelita
28g	α -ciclodextrina
5g	extracto de vainilla
22g	expreso (temperatura ambiente)
2	huevos
115g	pedazos de chocolate

La harina, cocoa, polvo para hornear y sal fueron mezclados conjuntamente y después fue la margarina, azúcar, molaza (o azúcar carmelita), α -ciclodextrina, vainilla y expreso fueron adicionados a la mezcla. Unos huevos algo batidos fueron revueltos a la mezcla, y los pedacitos de chocolate fueron doblados en esa. Unas cucharadas grandes de la mezcla fueron puestas en un papel para galletas, un poco engrasado, y después fue horneada por mas o menos 15 minutos en un horno convencional o 10-12 minutos en un horno convencional precalentado a 375°F. Las galletas fueron cocinadas en una bandeja de alambre.

La mayoría de los catadores a ciegas encontraron que las galletas horneadas no eran distinguibles de aquellas preparadas con la misma receta, sin adicionarles la α -ciclodextrina. Aquellos que detectaron una diferencia prefirieron las que incluían la α -ciclodextrina por la manera como describieron que era: mas rica, suave, de mas sabor y humedad, con una textura mas placentera a la boca que las galletas sin la α -ciclodextrina.

B. Galletas de miel de harina de avena

42g	mantequilla
110g	azúcar morena
85g	miel
1	huevo
15g	agua
58g	harina
2.5g	sal
0.75g	soda para hornear
81g	avena enrollada
4g	α -ciclodextrina

En un mezclador, preferiblemente con una paleta adicionada, los ingredientes húmedos, mantequilla, azúcar morena, miel, huevo y agua, fueron conjuntamente mezclados.

Los ingredientes secos restantes, excepto la avena enrollada, fueron cernidos en un perol. La avena enrollada fue entonces agregada a los ingredientes secos. Los ingredientes mojados y secos fueron entonces conjuntamente mezclados y alícuotas del batido fueron depositados en una lamina para galletas engrasada, y horneadas por 12-15 minutos en un horno convencional precalentado a 350°F por 8-10 minutos en un horno convencional. Las galletas cocinadas fueron enfriadas en una bandeja de alambre.

La mayoría de los catadores a ciegas encontraron que las galletas horneadas eran indistinguibles de aquellas preparadas con la misma receta, sin la adición de α -ciclodextrina. Aquellos que detectaron una diferencia prefirieron aquellas que incluían la α -ciclodextrina, siendo estas descritas como mas ricas, suaves, mas sabor y humedad y con una textura mas placentera a la boca que las galletas sin la α -ciclodextrina.

C. Barras de cinco capas

69g	migajas de laminillas de matiz
100g	azúcar
113g	mantequilla o margarina
115g	pedacitos de chocolate
115g	pedacitos de mantequilla y azúcar morena
124g	laminillas de nuez de coco
63g	nueces partidas
1 lata	(14oz, 400g) de leche condensada endulzada
36g	α -ciclodextrina

Las migajas de laminillas de matiz, azúcar, mantequilla derretida y 18g α -ciclodextrina fueron conjuntamente mezcladas en una vasija para hornear de 13x9x2 pulgadas, revueltas entre si. La mezcla fue presionada uniformemente y firmemente en el fondo de la vasija para formar una costra.

Los pedacitos de chocolate, pedacitos de mantequilla y azúcar morena, coco y nueces partidas fueron regadas en forma uniforme en las capas sobre la costra y 14 oz (400g) de leche condensada endulzada, mezclada con 18 g de α -ciclodextrina, fue regada uniformemente en las 5 capas, y después horneadas a 350°F por 23 minutos, o hasta estar un poco carmelita en los bordes. El producto fue completamente enfriado y cortado en 24 pedazos.

La mayoría de los catadores a ciegas encontraron que las barras horneadas no eran distinguibles de las preparadas con la misma receta sin la adición de α -ciclodextrina. Aquellos que detectaron una diferencia prefirieron aquella que incluía la α -ciclodextrina, las que fueron descritas como mas ricas, suaves, mas sabor, mas dulces y húmedas con una textura mas placentera a la boca que las barras sin la α -ciclodextrina. Es anotado que la leche condensada endulzada conlleva un cambio significativo al mezclarla con la α -ciclodextrina. Típicamente, la leche condensada endulzada es muy gruesa, lo que hace difícil verterla, y tiene un color blanco no llamativo. Al mezclarla con la α -ciclodextrina se vuelve mas suave y mas fluida en su naturaleza, ademas de cambiar su apariencia a un color muy blanco brillante.

D. Macaroni con queso

98g	mantequilla
29g	harina
484g	crema media y media
4g	sal
0.53g	pimienta blanca molida

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6g	salsa chili
106g	queso parmesano rallado
57g	queso cheddar rallado
50g	queso fontina rallado
50g	queso gruyere rallado
450g	macaroni
3g	ajo tajado
25g	migajas de pan frescas
3g	condimento
33g	α -ciclodextrina
$\frac{1}{2}$	cucharadita condimento
33g	α -ciclodextrina

29g de harina y 33g de α -ciclodextrina fueron adicionadas a 56g de mantequilla, derretida, y cocinado por 3 minutos. La mitad y mitad fue adicionada lentamente a la mantequilla derretida y a la mezcla de harina, y después cocinada, revoviendola frecuentemente hasta que engrosara, por 4 a 5 minutos. La mezcla fue removida del calor y la sal, pimienta, salsa picante y la mitad del parmesano rallado fueron adicionados a la mezcla y revueltos hasta que el queso se derritió.

El macaroni fue cocinado en agua hirviendo y el macaroni cocinado fue combinado con mantequilla y ajo tajado. La mezcla de queso fue adicionada al macaroni. Los quesos restantes fueron mezclados y adicionados a la mezcla de macaroni, las migajas de pan fueron puestas en capas en el macaroni y queso y horneadas por 40-45 minutos.

Los catadores a ciegas encontraron que la comida preparada con la α -ciclodextrina era mas cremosa y húmeda que la misma comida sin la α -ciclodextrina.

Tabla 5	Peso total g	CHO total, g	Grasa total, g	α -CD adicio, g	α -CD como % total de wt	α -CD como % total de CHO	α -CD como % total de grasa	Kcal grasa (%)	grasa wt/ wt total (%)	Kcal CHO (%)	CHO wt/ wt total (%)
Tortilla de queso	162	5	30	3.5	2.2%	70%	11.7%		68%	5%	3.1%
Mantequilla de maní 34 (2 cuch	34	8	16	2.0	5.9%	25%	12.5%		70%	15%	23.5%
Bola de carne	1659	146	317	36	2.2%	24.7%	11.4%		69%	14%	8.8%
Macaroni w/4 quesos	1586	395	293	33	2.1%	8.4%	11.3%		51%	31%	24.9%
Barras de cinco capas	1241	702	292	35	2.8%	5.0%	12%		46%	49%	56.6%
Pudin de pan francés de manzana	1365	295	112	10.5	0.8%	3.6%	9.4%		42.4%	49.6%	21.6%
Galletas de miel con avena	492	308	48	3.5	0.7%	1.1%	7.3%		24%	69%	62.6%
Galletas expreso de chocolate con	1020	556	231	28	2.8%	5.0%	12.2%		46%	49%	54.5%

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pedazos de chocol										
Biscoti	1323	870	108	12	0.9%	1.4%	11.1%	20%	71%	65.8%
Ponqué de mantequilla solicitud japonesa S60-94912	470	170	141	50 (CD comp)2	10.6% (CD comp)2 3.2% α -CD	29.4% (CD comp)2 8.8% α -CD	35.5% (CD comp)2 10.6% α -CD	64%	31%	36.2%
Pasta china solicitud japonesa S60-94912	1336	535	22.15	300 (CD comp)2	22.5% (CD comp)2 7.5% α -CD	56.1% (CD comp)2 18.7% α -CD	1364% (CD comp)2 454% α -CD	7%	72%	74.9%
Bizcochos solicitud japonesa S60-94912	2015	1400	400	500 (CD comp)2	24.8% (CD comp)2 7.4% α -CD	35.7% (CD comp)2 10.7% α -CD	125% (CD comp)2 37.5% α -CD	45%	49%	69.5%

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Existe una relación clara entre el aumento de peso, la obesidad y una variedad de desórdenes patológicos, e.g., diabetes, resistencia a la insulina, enfermedad cardiovascular, niveles elevados de lípido en la sangre, apnea del sueño, artritis, ciertos tipos de cáncer y elevadas tasas de mortalidad (Solomon and Manson, "Obesidad y mortalidad: una revisión de la información epidemiológica". *Ann J. Clin Nutr.* 1997;66:1044S-1050S). Los costos totales por cuidados de salud y por la pérdida de productividad, por desórdenes relacionados con la obesidad, llegan a \$117 billones en el 2000 (Sobrepeso y obesidad: en una mirada. Oficina del Cirujano General, 2001) Se ha reportado que los cambios en el índice de masa corporal (BMI) preceden a la diabetes (Resnick et al., "Relación del aumento de peso y pérdida de peso en los riesgos subsecuentes de diabetes en adultos con sobrepeso" *J Epidemiol Community Health* 2000;54:596-602), y por cada kg de aumento de peso corporal la prevalencia de la diabetes aumenta en 9% (Mokdad et al. "Inclinaciones de la diabetes en los E.U.: 1990-1998". *Diabetes Care* 2000;23:1278-1283). A pesar de que la diabetes clase II es asociada con exceso el peso corporal, otras anomalías metabólicas observadas en la obesidad pueden contribuir a la diabetes tipo II. Los individuos obesos tienden a ser hiperlipidémicos, hiperinsulémicos y resistentes a la insulina, todos los que han mostrado aumentar el riesgo de desarrollar de desarrollar diabetes Tipo II (Kissebah et al. *Riesgos a la Salud de la Obesidad. Med Clin North Am* 1989; 73:111-138; Kreisberg et al., *Secreción de insulina de la obesidad. N. Engl J. Med* 1967; 276:314-319, y; Olefsky J. *Resistencia a la insulina y acción de insulina: una perspectiva in vitro y in vivo. Diabetes* 1981;30:148-162). Entonces, una disminución en la severidad de cualquiera de estas anomalías también reducirá el riesgo de desarrollar diabetes Tipo II. Los productos de este invento tienen propiedades organolépticas deseadas por los consumidores, y también promueven la pérdida de peso y otros beneficios para la salud.

REIVINDICAMOS

1. Un producto alimenticio harinoso consumible que comprende α -ciclodextrina y grasa, donde dicho producto alimenticio tiene una tasa de α -ciclodextrina a grasa de 1:20 w/w a mas o menos de 1:3 w/w de dicho producto alimenticio, y donde dicho producto alimenticio comprende menos que mas o menos 9% w/w de ciclodextrina total.
2. El producto alimenticio harinoso consumible de la reivindicación 1, que comprende por lo menos mas o menos 7% a mas o menos 80% grasa por contenido calórico.
3. El producto alimenticio harinoso consumible de la reivindicación 1 que comprende menos mas o menos 6% w/w de ciclodextrina total.
4. El producto alimenticio harinoso consumible de la reivindicación 1 donde el producto alimenticio es cocinado.
5. Un producto alimenticio no harinoso consumible que comprende complejos de α -ciclodextrina y grasa, donde dicho producto alimenticio no harinoso tiene una tasa de α -ciclodextrina a grasa de 1:20 w/w a mas o menos 1:3 w/w de dicho producto alimenticio.
6. El producto alimenticio no harinoso consumible de la reivindicación 5 donde dicho producto alimenticio no harinoso es un producto alimenticio lácteo, carne o vegetal.
7. El producto alimenticio no harinoso consumible de la reivindicación 6 que comprende menos de mas o menos 9% de ciclodextrina total.
8. El producto alimenticio no harinoso consumible de la reivindicación 5 que comprende

5% a 50% grasa w/w.

9. Un método para aumentar las propiedades organolépticas de un producto alimenticio consumible contentivo de grasa que comprende adicionar α -ciclodextrina a dicho producto alimenticio contentivo de grasa de tal manera que el producto alimenticio tenga una tasa de α -ciclodextrina a grasa de mas o menos 1:20-1:3 w/w y donde dicho producto alimenticio comprenda menos de mas o menos 9% w/w de ciclodextrina total.
10. El método de la reivindicación 9, donde la α -ciclodextrina es sustancialmente α -ciclodextrina pura.
11. El método de la reivindicación 9, donde dicho producto alimenticio consumible comprende mas o menos 7% a mas o menos 80% de grasa por contenido calórico.
12. El método de la reivindicación 9, donde el producto alimenticio consumible contentivo de grasa es un producto alimenticio harinoso consumible.
13. Un método para reducir la biodisponibilidad de grasa en un producto alimenticio consumible contentivo de grasa que comprende determinar la cantidad de grasa en un producto alimenticio consumible contentivo de grasa y combinar la α -ciclodextrina con el producto alimenticio consumible contentivo de grasa de tal manera que el producto alimenticio consumible contentivo de grasa comprenda una tasa de α -ciclodextrina a grasa de mas o menos 1:20 a mas o menos 1:3 w/w donde dicha α -ciclodextrina no es removida de dicho producto alimenticio antes de su consumo.
14. El método de la reivindicación 13, donde el producto alimenticio consumible es un producto alimenticio harinoso consumible.
15. El método de la reivindicación 13, donde el producto alimenticio consumible es un producto consumible lácteo, carne o vegetal.
16. El método de la reivindicación 13 donde el producto alimenticio consumible comprende mas o menos 7% a 80% de grasa w/w por contenido calórico.
17. El método de la reivindicación 13 donde la α -ciclodextrina es administrada en forma de una pastilla, tableta, polvo, capsula, liquido o confitura.
18. Un método para aumentar el nivel de colesterol lipoproteína de alta densidad (HDL) en un sujeto necesitado del mismo, que comprende administrar la α -ciclodextrina a un sujeto necesitado de la misma, en cantidad suficiente para aumentar los niveles de HDL.
19. El método de la reivindicación 18 donde mas o menos 165mg a 11g de α -ciclodextrina es administrada a dicho sujeto con una comida contentiva de grasa.
20. El método de la reivindicación 18, donde dicho sujeto consume mas o menos 100g de grasa por día.
21. El método de la reivindicación 18, donde la α -ciclodextrina esta en una cantidad tal que esta en una tasa de 1:20 a mas o menos 1:3 de grasa ingerida diariamente por el sujeto.
22. El método de la reivindicación 18, donde los niveles de colesterol total no son

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aumentados en ese sujeto.

23. El método de la reivindicación 18, donde la α -ciclodextrina es administrada de una forma escogida del grupo consistente en una tableta, polvo, capsula, liquido y una confitura.
24. El método de la reivindicación 18, donde la α -ciclodextrina es administrada al sujeto en forma de un producto alimenticio harinoso consumible de la reivindicación 1.
25. El método de la reivindicación 1 donde mas o menos 500mg a 33g de α -ciclodextrina es administrada diariamente al sujeto necesitado de la misma para aumentar el nivel de lipoproteína de alta densidad (HDL).
26. Un método para reducir la tasa de colesterol/HDL en un sujeto que comprende administrar a un sujeto necesitado del mismo una cantidad de α -ciclodextrina, donde la cantidad de α -ciclodextrina administrada a dicho sujeto y la grasa ingerida diariamente por dicho sujeto este en una tasa de mas o menos 1:20 a mas o menos 1:3 w/w.
27. El método de la reivindicación 26, donde la α -ciclodextrina es administrada en una forma escogida de un grupo que consiste en una tableta, polvo, capsula, liquido y confitura.
28. El método de la reivindicación 26 donde la α -ciclodextrina es administrada al sujeto en forma de un producto alimenticio de la reivindicación 1.
29. El método de la reivindicación 26 donde mas o menos 500mg a 33g de α -ciclodextrina es administrada diariamente al sujeto necesitado de la misma, para reducir la tasa de colesterol/HDL.
30. Un método para promover la perdida de peso en un sujeto necesitado de la misma, que comprende administrar a un sujeto necesitado de lo mismo una cantidad de α -ciclodextrina donde la cantidad de α -ciclodextrina administrada a dicho sujeto y la cantidad de grasa ingerida que ese sujeto desea para evitar que sea absorbida, están a una tasa de mas o menos 1:20 a mas o menos 1:3 w/w.
31. El método de la reivindicación 30 donde dicho sujeto consume una dieta diaria que comprende por lo menos 30% de grasa por contenido calórico.
32. El método de la reivindicación 30, donde la α -ciclodextrina es administrada en forma de una tableta, polvo, capsula, liquido o confitura.
33. El método de la reivindicación 30, donde la α -ciclodextrina es administrada al sujeto en forma de un producto alimenticio harinoso consumible de la reivindicación 1.
34. El método de la reivindicación 30, donde mas o menos 500mg a 33g de α -ciclodextrina es administrada diariamente al sujeto necesitado de la misma para promover la perdida de peso.
35. Un método para reducir los niveles de trigliceridos en un sujeto que comprende administrar a un sujeto necesitado de lo mismo, una cantidad de α -ciclodextrina donde la cantidad de α -ciclodextrina administrada a dicho sujeto y la grasa ingerida diariamente por dicho sujeto, están a una tasa de mas o menos 1:20 a mas o menos 1:3 w/w.

36. El método de la reivindicación 35, donde la α -ciclodextrina es administrada al sujeto en forma de una tableta, polvo, capsula, liquido o confitura.
37. El método de la reivindicación 35, donde la α -ciclodextrina es administrada al sujeto necesitado de la misma en forma de un producto alimenticio harinoso consumible de la reivindicación 1.
38. El método de la reivindicación 35 donde mas o menos 500mg a 33g de α -ciclodextrina es administrada diariamente al sujeto necesitado de la misma.
39. Un método para reducir los niveles de leptina, niveles de insulina, o resistencia a la insulina, en un sujeto que comprende administrar α -ciclodextrina al sujeto necesitado de la misma, en cantidad suficiente para reducir los niveles de leptina, los niveles de insulina o la resistencia a la insulina por ese sujeto.
40. El método de la reivindicación 39, donde la cantidad de α -ciclodextrina administrada a dicho sujeto y la grasa ingerida diariamente por dicho sujeto, están a una tasa de mas o menos 1:20 a mas o menos 1:3 w/w.
41. El método de la reivindicación 39, donde la α -ciclodextrina es administrada en forma de tableta, polvo, capsula, liquido o confitura.
42. El método de la reivindicación 39, donde la α -ciclodextrina es administrada al sujeto en forma de un producto alimenticio harinoso consumible de la reivindicación 1.
43. El método de la reivindicación 39, donde mas o menos 500mg a 33g de α -ciclodextrina es administrada diariamente al sujeto necesitado de la misma.
44. Un método para reducir la diarrea en un sujeto, que comprende administrar al sujeto necesitado de la misma, α -ciclodextrina en cantidad suficiente para reducir la diarrea en dicho sujeto.
45. El método de la reivindicación 44 donde dicho sujeto es un sujeto con colecistectomía o un paciente que sufre de diarrea agravada por la gordura.
46. El método de la reivindicación 44, donde la α -ciclodextrina es administrada en forma del producto alimenticio harinoso consumible de la reivindicación 1.
47. El método de la reivindicación 44 donde la α -ciclodextrina es administrada en forma de una pastilla, capsula, wafer, tableta, polvo, liquido o confitura.
48. El método de la reivindicación 44, donde mas o menos 500mg a 33g de α -ciclodextrina es administrada diariamente al sujeto necesitado de la misma.
49. El método de la reivindicación 44, donde la cantidad de α -ciclodextrina administrada a dicho sujeto y la grasa ingerida diariamente por dicho sujeto, están en una tasa de mas o menos 1:20 a mas o menos 1:3 w/w.
50. El método de la reivindicación 18, donde la α -ciclodextrina es administrada al sujeto en forma del producto alimenticio no harinoso consumible de la reivindicación 5.
51. El método de la reivindicación 26 donde la α -ciclodextrina es administrada al sujeto en forma del producto alimenticio no harinoso consumible de la reivindicación 5.

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52. El método de la reivindicación 30, donde la α -ciclodextrina es administrada al sujeto en forma del producto alimenticio no harinoso consumible de la reivindicación 5.
53. El método de la reivindicación 35, donde la α -ciclodextrina es administrada al sujeto en forma del producto alimenticio no harinoso consumible de la reivindicación 5.
54. El método de la reivindicación 39, donde la α -ciclodextrina es administrada al sujeto en forma del producto alimenticio no harinoso consumible de la reivindicación 5.
55. El método de la reivindicación 44, donde la α -ciclodextrina es administrada en forma del producto alimenticio no harinoso consumible de la reivindicación 5.
56. El método de la reivindicación 44, donde el producto alimenticio consumible comprende mas o menos 20% a 70% grasa w/w o calorías.
57. El método de la reivindicación 54, donde el producto alimenticio consumible comprende mas o menos 40% a 70% grasa w/w o calorías.
58. El método de la reivindicación 44, donde el sujeto es un mamífero.
59. El método de la reivindicación 58, donde el mamífero es seleccionado del grupo que consiste en humano, caballo, vaca, perro o gato.
60. El método de la reivindicación 59, donde la α -ciclodextrina es administrada en forma de alimento para mascotas.
61. Un método para reducir la cantidad de tiempo necesario para producir crema batida que comprende adicionar α -ciclodextrina a la crema durante o antes de batir dicha crema, donde la α -ciclodextrina es adicionada en cantidad suficiente para reducir la cantidad de tiempo necesario para producir crema batida.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/23291

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 47/00
US CL : 424/439, 484, 489, 499

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 424/439, 484, 489, 499

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
US Patents, US PG-Publications, Derwent, JPO, EPO, Medline, CAPLUS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	JP 60-094912 A (SUIKO SUGAR REFINING CO LTD.) 28 May 1985 (28.05.95), entire document	1-61
Y	JP 62-011072 A (KOKUSAI KK) 20 January 1987 (20.02.87), entire document	1-61

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"B" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"A" document member of the same patent family

Date of the actual completion of the international search

26 January 2004 (26.01.2004)

Date of mailing of the international search report

08 MAR 2004

Name and mailing address of the ISA/US

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PCT**NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT
OR THE DECLARATION**

(PCT Rule 44.1)

Applicant's or agent's file reference AIC 201.1PCT	Date of Mailing (day/month/year) 08 MAR 2004
International application No. PCT/US03/23291	FOR FURTHER ACTION See paragraphs 1 and 4 below International filing date (day/month/year) 29 July 2003 (29.07.2003)
Applicant ARTGEN COMPLEXUS, INC.	

1. ☒ The applicant is hereby notified that the international search report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

Where? Directly to the International Bureau of WIPO, 34, chemin des Colombettes
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 740.14.33

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. Reminders

Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90 *bis*.1 and 90 *bis*.3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later); otherwise the applicant must, within 20 months from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of 30 months (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the ISA/US
Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
Facsimile No. (703) 305-3230

Authorized officer
James L. Evans
Telephone No. 703-308-1235

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference AJC 201.1PCT	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. PCT/US03/23291	International filing date (day/month/year) 29 July 2003 (29.07.2003)	(Earliest) Priority Date (day/month/year) 19 August 2002 (19.08.2002)
Applicant ARTGEN COMPLEXUS, INC.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 2 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the Report

a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing:



contained in the international application in written form.



filed together with the international application in computer readable form.



furnished subsequently to this Authority in written form.



furnished subsequently to this Authority in computer readable form.



the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.



the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

2. ☐ Certain claims were found unsearchable (See Box I).

3. ☐ Unity of invention is lacking (See Box II).

4. With regard to the title,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

5. With regard to the abstract,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No. 1



as suggested by the applicant.



None of the figures



because the applicant failed to suggest a figure.



because this figure better characterizes the invention.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/23291

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 47/00
US CL : 424/439, 484, 489, 499

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 424/439, 484, 489, 499

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
US Patents, US PG-Publications, Derwent, JPO, EPO, Medline, CAPlus

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	JP 60-094912 A (SUIKO SUGAR REFINING CO LTD.) 28 May 1985 (28.05.95), entire document.	1-61
Y	JP 62-011072 A (KOKUSAI KK) 20 January 1987 (20.02.87), entire document.	1-61

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"A" document member of the same patent family

Date of the actual completion of the international search

26 January 2004 (26.01.2004)

Date of mailing of the international search report

08 MAR 2004

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (703) 305-3230

Authorized officer

Charles L. Evans

Telephone No. 703-308-1235

PATENT COOPERATION TREATY

103 1

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:
MARY ANNE SCHOFIELD
FULBRIGHT & JAWORSKI, LLP
MARKET SQUARE
801 PENNSYLVANIA AVENUE, N.W.
WASHINGTON, DC 20004-2623

PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing
(day/month/year)

06 JUL 2004

Applicant's or agent's file reference

AJC 201.1 PCT

IMPORTANT NOTIFICATION

International application No.

PCT/US03/23291

International filing date (day/month/year)

29 July 2003 (29.07.2003)

Priority date (day/month/year)

19 August 2002 (19.08.2002)

Applicant

ARTJEN COMPLEXUS, INC.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US

Mail Stop PCT, Attn: IPEA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (703) 305-3230

Authorized officer

BLESSING FUBARA

Telephone No. 703-306-1234

Form PCT/IPEA/416 (July 1992)

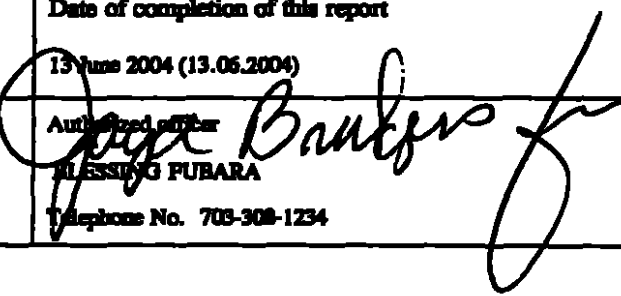
106

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference AJC 201.1 PCT	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US03/23291	International filing date (day/month/year) 29 July 2003 (29.07.2003)	Priority date (day/month/year) 19 August 2002 (19.08.2002)
International Patent Classification (IPC) or national classification and IPC IPC(7): A61K 47/00 and US Cl.: 424/439, 484, 489, 499		
Applicant ARTSEN COMPLEXUS, INC.		
1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36. 2. This REPORT consists of a total of <u>3</u> sheets, including this cover sheet. ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT). These annexes consist of a total of <u>0</u> sheets. 3. This report contains indications relating to the following items: - I ☒ Basis of the report - II ☐ Priority - III ☐ Non-establishment of report with regard to novelty, inventive step and industrial applicability - IV ☐ Lack of unity of invention - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement - VI ☐ Certain documents cited - VII ☐ Certain defects in the international application - VIII ☐ Certain observations on the international application		
Date of submission of the demand 19 March 2004 (19.03.2004)	Date of completion of this report 13 June 2004 (13.06.2004)	
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1430 Alexandria, Virginia 22313-1430 Facsimile No. (703) 305-3230	Authorized officer  BLESSING PUBARA Telephone No. 703-308-1234	

I. Basis of the report

1. With regard to the elements of the international application:*

- ☒ the international application as originally filed.
- ☒ the description:
pages 1-45 as originally filed
pages NONE filed with the demand
pages NONE filed with the letter of _____.
- ☒ the claims:
pages 46-51 as originally filed
pages NONE as amended (together with any statement) under Article 19
pages NONE filed with the demand
pages NONE filed with the letter of _____.
- ☒ the drawings:
pages 1-8 as originally filed
pages NONE filed with the demand
pages NONE filed with the letter of _____.
- ☐ the sequence listing part of the description:
pages NONE as originally filed
pages NONE filed with the demand
pages NONE filed with the letter of _____.

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages NONE
- ☐ the claims, Nos. NONE
- ☐ the drawings, sheets/fig NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

108106

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US05/23291

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims 1-61	YES
	Claims NONE	NO
Inventive Step (IS)	Claims 1-61	YES
	Claims NONE	NO
Industrial Applicability (IA)	Claims 1-61	YES
	Claims NONE	NO

2. CITATIONS AND EXPLANATIONS

Claims 1-61 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest food product that comprises the combination of alpha cyclodextrin and fat in the amounts recited in the claims.

The JP 60-094912 discloses a composition for reducing fat where the composition comprises 30:15:5 alpha cyclodextrin: beta cyclodextrin: gamma cyclodextrin. The food product of the JP reference appears not to teach the presence of fat in composition.

Claims 1-61 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

The demand must be filed directly with the competent International Preliminary Examining Authority or, if two or more Authorities are competent, with the one chosen by the applicant. The full name or two-letter code of that Authority may be indicated by the applicant on the line below:

IPEA/ US

PCT

CHAPTER II

DEMAND

under Article 31 of the Patent Cooperation Treaty.
The undersigned requests that the international application specified below be the subject of international preliminary examination according to the Patent Cooperation Treaty.

For International Preliminary Examining Authority use only	
Identification of IPEA	Date of receipt of DEMAND
Box No. I IDENTIFICATION OF THE INTERNATIONAL APPLICATION	
Applicant's or agent's file reference AJC 201.1 PCT/10304772	
International application No. PCT/US03/23291	International filing date (day/month/year) 29/07/03
(Earliest) Priority date (day/month/year) 19/08/02	
Title of invention COMPOSITIONS COMPRISING DIETARY FAT COMPLEXER AND METHODS FOR THEIR USE	
Box No. II APPLICANT(S)	
Name and address: (Family name followed by given names; for a legal entity, full official designation. The address must include postal code and name of country.)	
ARTJEN COMPLEXUS, INC. 510 Westcourt Place 251 Goyeau Street Windsor, Ontario N9A 6V2 CANADA	
Telephone No. (248) 701-4722	
Facsimile No. (248) 737-6480	
Teleprinter No.	
Applicant's registration No. with the Office	
State (that is, country) of nationality: CA	State (that is, country) of residence: CA
Name and address: (Family name followed by given names; for a legal entity, full official designation. The address must include postal code and name of country.)	
JEN, Catherine 5159 Provincial Drive Bloomfield Hills Michigan 48302 UNITED STATES OF AMERICA	
State (that is, country) of nationality: US	State (that is, country) of residence: US
Name and address: (Family name followed by given names; for a legal entity, full official designation. The address must include postal code and name of country.)	
ARTISS, Joseph D. 3117 Curry Avenue Windsor, Ontario N9E 2T2 CANADA	
State (that is, country) of nationality: CA	State (that is, country) of residence: CA
☐ Further applicants are indicated on a continuation sheet.	

Box No. III AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCEThe following person is ☒ agent ☐ common representativeand ☒ has been appointed earlier and represents the applicant(s) also for international preliminary examination.☐ is hereby appointed and any earlier appointment of (an) agent(s)/common representative is hereby revoked.☐ is hereby appointed, specifically for the procedure before the International Preliminary Examining Authority, in addition to the agent(s)/common representative appointed earlier.Name and address: (Family name followed by given name; for a legal entity, full official designation.
The address must include postal code and name of country.)

SCHOFIELD, Mary Anne
FULBRIGHT & JAWORSKI, LLP
Market Square
801 Pennsylvania Avenue, N.W.
Washington, D. C. 20004-2623
UNITED STATES OF AMERICA

Telephone No.

(202) 662-0200

Facsimile No.

(202) 662-4643

Teleprinter No.

Agent's registration No. with the Office
36,669☐ Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.**Box No. IV BASIS FOR INTERNATIONAL PRELIMINARY EXAMINATION****Statement concerning amendments:***

1. The applicant wishes the international preliminary examination to start on the basis of:

☒ the international application as originally filed

the description ☒ as originally filed
☐ as amended under Article 34

the claims ☒ as originally filed
☐ as amended under Article 19 (together with any accompanying statement)
☐ as amended under Article 34

the drawings ☒ as originally filed
☐ as amended under Article 34

2. ☐ The applicant wishes any amendment to the claims under Article 19 to be considered as reversed.3. ☐ The applicant wishes the start of the international preliminary examination to be postponed until the expiration of the applicable time limit under Rule 69.1(d).4. ☐ The applicant expressly wishes the international preliminary examination to start earlier than at the expiration of the applicable time limit under Rule 54bis.1(a).

* Where no check-box is marked, international preliminary examination will start on the basis of the international application as originally filed or, where a copy of amendments to the claims under Article 19 and/or amendments of the international application under Article 34 are received by the International Preliminary Examining Authority before it has begun to draw up a written opinion or the international preliminary examination report, as so amended.

Language for the purposes of international preliminary examination: English

☒ which is the language in which the international application was filed.☐ which is the language of a translation furnished for the purposes of international search.☐ which is the language of publication of the international application.☐ which is the language of the translation (to be) furnished for the purposes of international preliminary examination.**Box No. V ELECTION OF STATES**

The filing of this demand constitutes the election of all Contracting States which are designated and are bound by Chapter II of the PCT.

Box No. VI CHECK LIST

The demand is accompanied by the following elements, in the language referred to in Box No. IV, for the purposes of international preliminary examination:

- | | | | |
|--|---|---|--------|
| 1. translation of international application | : | 0 | sheets |
| 2. amendments under Article 34 | : | 0 | sheets |
| 3. copy (or, where required, translation) of amendments under Article 19 | : | 0 | sheets |
| 4. copy (or, where required, translation) of statement under Article 19 | : | 0 | sheets |
| 5. letter | : | 0 | sheets |
| 6. other (specify) | : | 0 | sheets |

For International Preliminary Examining Authority use only

received	not received
----------	--------------

- | | |
|--------------------------|--------------------------|
| ☐ | ☐ |
| ☐ | ☐ |
| ☐ | ☐ |
| ☐ | ☐ |
| ☐ | ☐ |
| ☐ | ☐ |

The demand is also accompanied by the item(s) marked below:

- | | |
|--|--|
| 1. ☒ fee calculation sheet | 5. ☐ statement explaining lack of signature |
| 2. ☐ original separate power of attorney | 6. ☐ sequence listing in computer readable form |
| 3. ☐ original general power of attorney | 7. ☐ tables in computer readable form related to a sequence listing |
| 4. ☐ copy of general power of attorney; reference number, if any: | 8. ☐ other (specify): |

Box No. VII SIGNATURE OF APPLICANT, AGENT OR COMMON REPRESENTATIVE

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the demand).


SCHOFIELD, Mary Anne
Registration No. 36,669

For International Preliminary Examining Authority use only

1. Date of actual receipt of DEMAND:

2. Adjusted date of receipt of demand due to CORRECTIONS under Rule 60.1(b):

3. ☐ The date of receipt of the demand is AFTER the expiration of 19 months from the priority date and item 4 or 5, below, does not apply.

☐ The applicant has been informed accordingly.

4. ☐ The date of receipt of the demand is WITHIN the time limit of 19 months from the priority date as extended by virtue of Rule 80.5.

5. ☐ Although the date of receipt of the demand is after the expiration of 19 months from the priority date, the delay in arrival is EXCUSED pursuant to Rule 82.

6. ☐ The date of receipt of the demand is AFTER the expiration of the time limit under Rule 54bis.1(a) and item 7 or 8, below, does not apply.

7. ☐ The date of receipt of the demand is WITHIN the time limit under Rule 54bis.1(a) as extended by virtue of Rule 80.5.

8. ☐ Although the date of receipt of the demand is after the expiration of the time limit under Rule 54bis.1(a), the delay in arrival is EXCUSED pursuant to Rule 82.

For International Bureau use only

Demand received from IPRA on:

PCT

FEE CALCULATION SHEET

Annex to the Demand

International application No. PCT/US03/23291 Applicant's or agent's file reference AJC 201.1 PCT/10304772 Applicant ArtJen Complexus, Inc.	For International Preliminary Examining Authority use only Date stamp of the IPEA								
CALCULATION OF PRESCRIBED FEES 1. Preliminary examination fee \$600 P 2. Handling fee (<i>Applicants from certain States are entitled to a reduction of 75% of the handling fee. Where the applicant is (or all applicants are) so entitled, the amount to be entered at H is 25% of the handling fee.</i>) \$148 H 3. Total of prescribed fees Add the amounts entered at P and H and enter total in the TOTAL box \$748 TOTAL									
MODE OF PAYMENT <table style="width: 100%;"> <tr> <td>☐ authorization to charge deposit account with the IPEA (see below)</td> <td>☐ cash</td> </tr> <tr> <td>☒ cheque</td> <td>☐ revenue stamps</td> </tr> <tr> <td>☐ postal money order</td> <td>☐ coupons</td> </tr> <tr> <td>☐ bank draft</td> <td>☐ other (specify):</td> </tr> </table>		☐ authorization to charge deposit account with the IPEA (see below)	☐ cash	☒ cheque	☐ revenue stamps	☐ postal money order	☐ coupons	☐ bank draft	☐ other (specify):
☐ authorization to charge deposit account with the IPEA (see below)	☐ cash								
☒ cheque	☐ revenue stamps								
☐ postal money order	☐ coupons								
☐ bank draft	☐ other (specify):								
AUTHORIZATION TO CHARGE (OR CREDIT) DEPOSIT ACCOUNT (This mode of payment may not be available at all IPEAs) ☐ Authorization to charge the total fees indicated above. ☒ (This check-box may be marked only if the conditions for deposit accounts of the IPEA so permit) Authorization to charge any deficiency or credit any overpayment in the total fees indicated above. IPEA/ <u>US</u> Deposit Account No.: <u>06-2375</u> Date: <u>March 19, 2004</u> Name: <u>Mary Anne Schofield</u> Signature: <u><i>Mary Anne Schofield</i></u>									

PATENT COOPERATION TREATY

PCT/US03/23291

111

PCT

From the INTERNATIONAL BUREAU

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

To:

SCHOFIELD, Mary Anne
Fulbright & Jaworski, LLP
Market Square
801 Pennsylvania Avenue, N.W.
Washington, DC 20004-2623
United States of America

Date of mailing (day/month/year)

04 November 2003 (04.11.03)

Applicant's or agent's file reference

AJC 201.1PCT

International application No.

PCT/US03/23291

IMPORTANT NOTIFICATION

International filing date (day/month/year)

29 July 2003 (29.07.03)

1. The following indications appeared on record concerning:



the applicant



the inventor



the agent



the common representative

Name and Address

ARTGEN COMPLEXUS, INC.

State of Nationality

State of Residence

Telephone No.

Facsimile No.

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:



the person



the name



the address



the nationality



the residence

Name and Address

ART JEN COMPLEXUS, INC.

State of Nationality

State of Residence

Telephone No.

Facsimile No.

Teleprinter No.

RECEIVED

NOV 03 2003

3. Further observations, if necessary:

FULBRIGHT & JAWORSKI

4. A copy of this notification has been sent to:



the receiving Office



the designated Offices concerned



the International Searching Authority



the elected Offices concerned



the International Preliminary Examining Authority



other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 338.71.40

Authorized officer

Kiwa MPAY

Telephone No. (41-22) 338 9087

PATENT COOPERATION TREATY

112 M

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

NOTIFICATION OF RECEIPT
OF DEMAND BY COMPETENT INTERNATIONAL
PRELIMINARY EXAMINING AUTHORITY

(PCT Rules 59.3(e) and 61.1(b), first sentence
and Administrative Instructions, Section 601(a))

To:
MARY ANNE SCHOFIELD
FULBRIGHT & JAWORSKI, LLP
MARKET SQUARE
801 PENNSYLVANIA AVENUE, N.W.
WASHINGTON, DISTRICT OF COLUMBIA
20004-2823

Date of mailing
(day/month/year)

13 MAY 2004

Applicant's or agent's file reference
AJC 201.1 PCT/10304772

IMPORTANT NOTIFICATION

International application No.
PCT/US03/23291

International filing date (day/month/year)
29 Jul 2003

Priority date (day/month/year)
19 Aug 2002

Applicant
ARTJEN COMPLEXUS, INC.

1. The applicant is hereby notified that this International Preliminary Examining Authority considers the following date as the date of receipt of the demand for international preliminary examination of the international application:

19 Mar 2004

2. That date of receipt is:

- ☒ the actual date of receipt of the demand by this Authority (Rule 61.1(b)).
- ☐ the actual date of receipt of the demand on behalf of this Authority (Rule 59.3(e)).
- ☐ the date on which this Authority has, in response to the invitation to correct defects in the demand (Form PCT/IPEA/404), received the required corrections.

3. ☐ **ATTENTION:** That date of receipt is **AFTER** the expiration of 19 months from the priority date. Consequently, the election(s) made in the demand does (do) not have the effect of postponing the entry into the national phase until 30 months from the priority date (or later in some Offices) (Article 39(1)). Therefore, the acts for entry into the national phase must be performed within 20 months from the priority date (or later in some Offices) (Article 22). For details, see the *PCT Applicant's Guide*, Volume II.

- ☐ (If applicable) This notification confirms the information given by telephone, facsimile transmission or in person on:

4. Only where paragraph 3 applies, a copy of this notification has been sent to the International Bureau.

Name and mailing address of the IPEA/ Mail Stop PCT, Commissioner for Patents P.O. Box 1450, Alexandria, VA 22313-1450	Authorized officer Nhu Thuy Tran
Facsimile No. 703-305-3230 Form PCT/IPEA/402 (July 1998)	Telephone No. 703-605-1537

From the INTERNATIONAL BUREAU

PCT

NOTICE INFORMING THE APPLICANT OF THE
COMMUNICATION OF THE INTERNATIONAL
APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

To:

RECEIVED

MAR 11 2004

SCHOFIELD, Mary Anne
Fulbright & Jaworski, LLP
Market Square
801 Pennsylvania Avenue, N.W.
Washington, DC 20004-2623
ETATS-UNIS D'AMERIQUE

FULBRIGHT & JAWORSKI

Date of mailing (day/month/year) 26 February 2004 (26.02.2004)		
Applicant's or agent's file reference AJC 201.1PCT		IMPORTANT NOTICE
International application No. PCT/US2003/023291	International filing date (day/month/year) 29 July 2003 (29.07.2003)	Priority date (day/month/year) 19 August 2002 (19.08.2002)
Applicant ART JEN COMPLEXUS, INC. et al		

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this notice:

AU, AZ, BY, CH, CN, CO, DZ, EP, HU, JP, KG, KP, KR, MD, MK, MZ, RU, TM, US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:

AE, AG, AL, AM, AP, AT, BA, BB, BG, BR, BZ, CA, CR, CU, CZ, DE, DK, DM, EA, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, ID, IL, IN, IS, KE, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MG, MN, MW, MX, NI, NO, NZ, OA, OM, PG, PH, PL,
PT, RO, SC, SD, SE, SG, SK, SL, SY, TJ, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW

The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this notice is a copy of the international application as published by the International Bureau on 26 February 2004 (26.02.2004) under No. WO 2004/016101

4. TIME LIMITS for filing a demand for international preliminary examination and for entry into the national phase

The applicable time limit for entering the national phase will, subject to what is said in the following paragraph, be 30 MONTHS from the priority date, not only in respect of any elected Office if a demand for international preliminary examination is filed before the expiration of 19 months from the priority date, but also in respect of any designated Office, in the absence of filing of such demand, where Article 22(1) as modified with effect from 1 April 2002 applies in respect of that designated Office. For further details, see *PCT Gazette* No. 44/2001 of 1 November 2001, pages 19926, 19932 and 19934, as well as the *PCT Newsletter*, October and November 2001 and February 2002 issues.

In practice, time limits other than the 30-month time limit will continue to apply, for various periods of time, in respect of certain designated or elected Offices. For regular updates on the applicable time limits (20, 21, 30 or 31 months, or other time limit), Office by Office, refer to the *PCT Gazette*, the *PCT Newsletter* and the *PCT Applicant's Guide*, Volume II, National Chapters, all available from WIPO's Internet site, at <http://www.wipo.int/pct/en/index.html>.

For filing a demand for international preliminary examination, see the *PCT Applicant's Guide*, Volume I/A, Chapter IX. Only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination (at present, all PCT Contracting States are bound by Chapter II).

It is the applicant's sole responsibility to monitor all these time limits.

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Authorized officer

Gijsbertus Beijer - Carlos Roy

Facsimile No.(41-22) 740.14.35

Telephone No.(41-22) 338.91.11

PATENT COOPERATION TREATY

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PCT

From the INTERNATIONAL BUREAU

NOTIFICATION CONCERNING
SUBMISSION OR TRANSMITTAL
OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

To:

SCHOFIELD, Mary Anne
Fulbright & Jaworski, LLP
Market Square
801 Pennsylvania Avenue, N.W.
Washington, DC 20004-2623
United States of America

Date of mailing (day/month/year) 01 October 2003 (01.10.03)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference AJC 201.1PCT	
International application No. PCT/US03/23291	
International publication date (day/month/year) Not yet published	
International filing date (day/month/year) 29 July 2003 (29.07.03)	Priority date (day/month/year) 19 August 2002 (19.08.02)
Applicant ARTGEN COMPLEXUS, INC. et al	

1. The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
2. This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.
3. An asterisk(*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.
4. The letters "NR" appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

<u>Priority date</u>	<u>Priority application No.</u>	<u>Country or regional Office or PCT receiving Office</u>	<u>Date of receipt of priority document</u>
19 Augu 2002 (19.08.02)	60/404,366	US	17 Sept 2003 (17.09.03)
11 Apri 2003 (11.04.03)	60/461,847	US	17 Sept 2003 (17.09.03)
14 July 2003 (14.07.03)	60/486,440	US	17 Sept 2003 (17.09.03)

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 338.71.40

Authorized officer

JEANNEROT Jocelyn (Fax 338-71-30)

Telephone No. (41-22) 338 8958

PATENT COOPERATION TREATY

115

PCT

From the INTERNATIONAL BUREAU

NOTIFICATION OF RECEIPT OF
RECORD COPY

(PCT Rule 24.2(a))

To:

SCHOFIELD, Mary Anne
Fulbright & Jaworski, LLP
Market Square
801 Pennsylvania Avenue, N.W.
Washington, DC 20004-2623
United States of America

Date of mailing (day/month/year) 01 October 2003 (01.10.03)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference AJC 201.1PCT	International application No. PCT/US03/23291

The applicant is hereby notified that the International Bureau has received the record copy of the international application as detailed below.

Name(s) of the applicant(s) and State(s) for which they are applicants:

ARTGEN COMPLEXUS, INC. (for all designated States except US)

JEN, Catherine et al (for US)

International filing date : 29 July 2003 (29.07.03)

Priority date(s) claimed : 19 August 2002 (19.08.02)

11 April 2003 (11.04.03)

14 July 2003 (14.07.03)

Date of receipt of the record copy
by the International Bureau : 15 September 2003 (15.09.03)

List of designated Offices :

AP : GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW

EA : AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

EP : AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

OA : BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

National : AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ,

EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,

LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ,

TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RECEIVED

OCT 21 2003

FULBRIGHT & JAWORSKI

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer: JEANNEROT Jocelyn (Fax 338-71-30)
Facsimile No. (41-22) 338.71.40	Telephone No. (41-22) 338 8958

Continuation of Form PCT/IB/301

NOTIFICATION OF RECEIPT OF RECORD COPY

116

Date of mailing (day/month/year) 01 October 2003 (01.10.03)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference AJC 201.1PCT	International application No. PCT/US03/23291

ATTENTION

The applicant should carefully check the data appearing in this Notification. In case of any discrepancy between these data and the indications in the international application, the applicant should immediately inform the International Bureau.

In addition, the applicant's attention is drawn to the information contained in the Annex, relating to:

- ☒ time limits for entry into the national phase - see updated important information (as of April 2002)
- ☐ confirmation of precautionary designations (if applicable)
- ☐ requirements regarding priority documents (if applicable)

A copy of this Notification is being sent to the receiving Office and to the International Searching Authority.

INFORMATION ON TIME LIMITS FOR ENTERING THE NATIONAL PHASE

The applicant is reminded that the "national phase" must be entered before each of the designated Offices indicated on the cover sheet of this Notification by paying national fees and furnishing translations, as prescribed by Articles 22 and 39 and the applicable national laws. In addition, the applicant may also have to comply with other special requirements applicable in certain Offices. It is the applicant's responsibility to ensure the necessary steps to enter the national phase are taken in a timely fashion. Most Offices do not issue reminders to applicants in connection with the entry into the national phase.

The applicable time limit for entering the national phase will, subject to what is said in the following paragraph, be 30 MONTHS from the priority date, not only in respect of any elected Office where a demand for international preliminary examination is filed before the expiration of 18 months from the priority date (see Article 39(1)), but also in respect of any designated Office, in the absence of filing of such demand, where Article 22(1) as modified with effect from 1 April 2002 applies in respect of that designated Office. For further details, see PCT Gazette No. 44/2001 of 1 November 2001, pages 19926, 19932 and 19934, as well as the PCT Newsletter, October and November 2001 and February 2002 issues.

In practice, time limits other than the 30-month time limit will continue to apply, for various periods of time, in respect of certain designated or elected Offices. For regular updates on the applicable time limits (20, 21, 30 or 31 months, or other time limit), Office by Office, refer to the PCT Gazette ("Section IV" part published on a weekly basis), to the PCT Newsletter (on a monthly basis) and to the relevant National Chapters in Volume II of the PCT Applicant's Guide (the paper version of which is updated usually twice a year and the Internet version of which is updated usually on a weekly basis). Finally, a cumulative table of all applicable time limits for entering the national phase is available from WIPO's Internet site, via links from various pages the site including those of the Gazette, Newsletter and Guide, at <http://www.wipo.int/pct/en/index.html>.

Information about the requirements for filing a demand for international preliminary examination is set out in the PCT Applicant's Guide, Volume I/A, Chapter IX. Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination (at present, all PCT Contracting States are bound by Chapter II).

CONFIRMATION OF PRECAUTIONARY DESIGNATIONS

This notification lists only specific designations made under Rule 4.9(a) in the request. It is important to check that these designations are correct. Errors in designations can be corrected where precautionary designations have been made under Rule 4.9(b). The applicant is hereby reminded that any precautionary designations may be confirmed according to Rule 4.9(c) before the expiration of 15 months from the priority date (this time limit may not be extended). If it is not confirmed, it will automatically be regarded as withdrawn by the applicant. There will be no reminder and no invitation. Confirmation of a designation consists of the filing of a notice specifying the designated State concerned (with indication of the kind of protection or treatment desired) and the payment of the designation and confirmation fees. The Notice of confirmation and payment must reach the receiving Office within the 15-month time limit.

REQUIREMENTS REGARDING PRIORITY DOCUMENTS

For applicants who have not yet complied with the requirements regarding priority documents, the following is recalled.

Where the priority of an earlier national, regional or international application is claimed, the applicant must submit a copy of the said earlier application, certified by the authority with which it was filed ("the priority document") to the receiving Office (which will transmit it to the International Bureau) or directly to the International Bureau, before the expiration of 18 months from the priority date, provided that any such priority document may still be submitted to the International Bureau before that date of international publication of the international application, in which case that document will be considered to have been received by the International Bureau on the last day of the 18-month time limit (Rule 17.1(a)).

Where the priority document is issued by the receiving Office, the applicant may, instead of submitting the priority document, request the receiving Office to prepare and transmit the priority document to the International Bureau. Such request must be made before the expiration of the 18-month time limit and may be subjected by the receiving Office to the payment of a fee (Rule 17.1(b)).

If the priority document concerned is not submitted to the International Bureau or if the request to the receiving Office to prepare and transmit the priority document has not been made (and the corresponding fee, if any, paid) within the applicable time limit indicated under the preceding paragraphs, any designated State may disregard the priority claim, provided that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within the time limit which is reasonable under the circumstances.

Where several priorities are claimed, the priority date to be considered for the purposes of computing the 18-month time limit is the filing date of the earliest application whose priority is claimed.

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
26 February 2004 (26.02.2004)

PCT

(10) International Publication Number
WO 2004/016101 A3

(51) International Patent Classification⁷: A61K 47/00

48302 (US). ARTISS, Joseph, D. [CA/CA]; 3117 Curry Avenue, Windsor, Ontario N9E 2T2 (CA).

(21) International Application Number:
PCT/US2003/023291

(74) Agent: SCHOFIELD, Mary Anne, Fulbright & Jaworski, LLP, Market Square, 801 Pennsylvania Avenue, N.W., Washington, DC 20004-2623 (US).

(22) International Filing Date: 29 July 2003 (29.07.2003)

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/404,366 19 August 2002 (19.08.2002) US
60/461,847 11 April 2003 (11.04.2003) US
60/486,440 14 July 2003 (14.07.2003) US

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(71) Applicant (*for all designated States except US*): ART JEN COMPLEXUS, INC. [CA/CA]; 510 Westcourt Place, 251 Goyeau Street, Windsor, Ontario N9A 6V2 (CA).

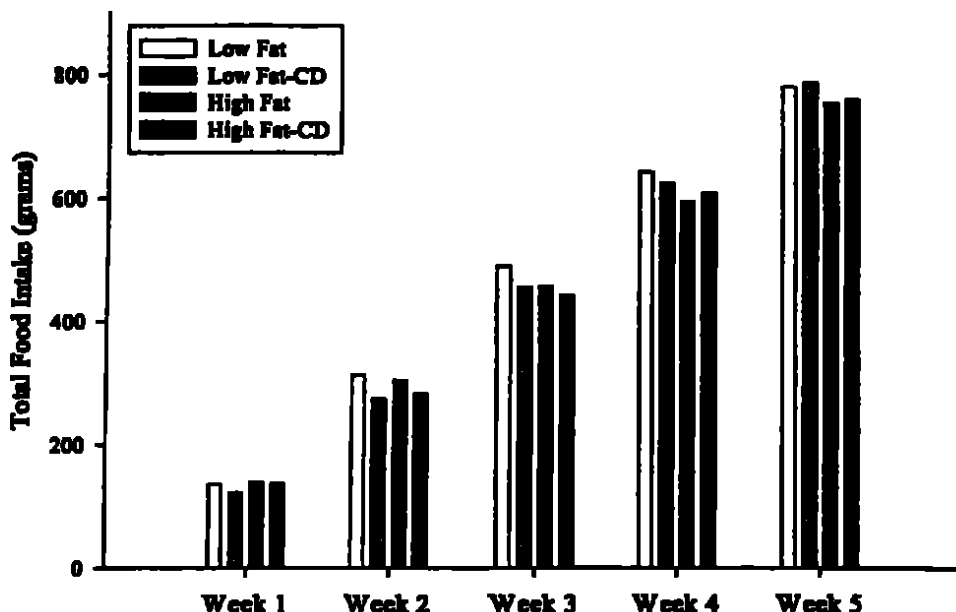
(72) Inventors; and

(75) Inventors/Applicants (*for US only*): JEN, Catherine [US/US]; 5159 Provincial Drive, Bloomfield Hills, MI

Published:
— with international search report

[Continued on next page]

(54) Title: COMPOSITIONS COMPRISING DIETARY FAT COMPLEXER AND METHODS FOR THEIR USE



(57) Abstract: This invention relates to fat containing consumable food products comprising α -cyclodextrin. The food products have reduced levels of bioavailable fat but have substantially the same fat, cholesterol and caloric content as a like food without α -cyclodextrin. The invention also relates to methods for reducing the bioavailability of fats in fat containing food products without reducing caloric intake as determined by bomb calorimetry and to methods for increasing high density lipoproteins in a subject and reducing or controlling weight by administering the food products of this invention.

WO 2004/016101 A3

(19) World Intellectual Property
Organization
International Bureau



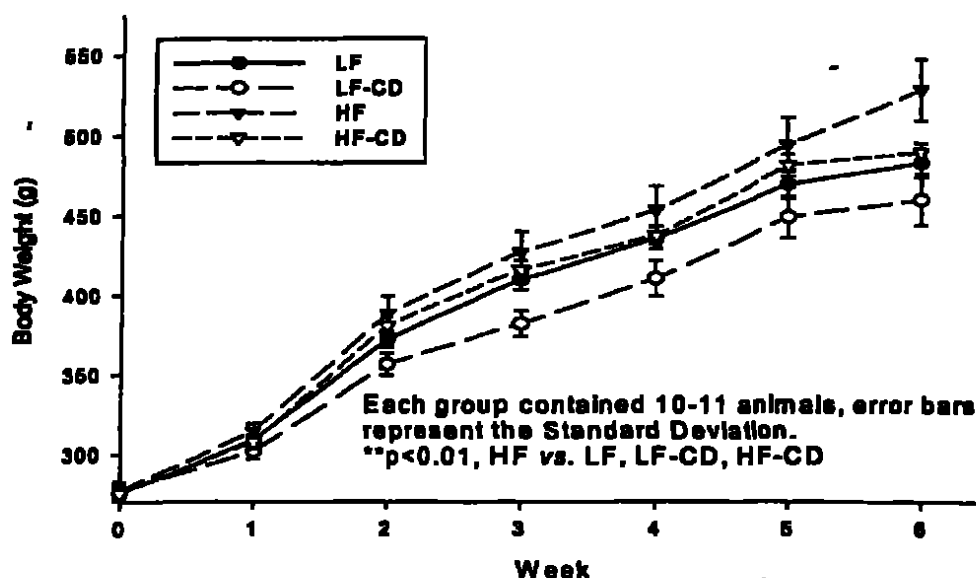
(43) International Publication Date
26 February 2004 (26.02.2004)

PCT

(10) International Publication Number
WO 2004/016101 A2

- (51) International Patent Classification⁷: A23L
- (21) International Application Number: PCT/US2003/023291
- (22) International Filing Date: 29 July 2003 (29.07.2003)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/404,366 19 August 2002 (19.08.2002) US
60/461,847 11 April 2003 (11.04.2003) US
60/486,440 14 July 2003 (14.07.2003) US
- (71) Applicant (for all designated States except US): ART JEN COMPLEXUS, INC. [CA/CA]; 510 Westcourt Place, 251 Goyeau Street, Windsor, Ontario N9A 6V2 (CA).
- (72) Inventors; and
- (73) Inventors/Applicants (for US only): JEN, Catherine [US/US]; 5159 Provincial Drive, Bloomfield Hills, MI 48302 (US). ARTISS, Joseph, D. [CA/CA]; 3117 Curry Avenue, Windsor, Ontario N9E 2T2 (CA).
- (74) Agent: SCHOFIELD, Mary Anne; Fulbright & Jaworski, LLP, Market Square, 801 Pennsylvania Avenue, N.W., Washington, DC 20004-2623 (US).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:
— without international search report and to be republished upon receipt of that report
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: COMPOSITIONS COMPRISING DIETARY FAT COMPLEXER AND METHODS FOR THEIR USE



(57) Abstract: This invention relates to fat containing consumable food products comprising α -cyclodextrin. The food products have reduced levels of bioavailable fat but have substantially the same fat, cholesterol and caloric content as a like food without α -cyclodextrin. The invention also relates to methods for reducing the bioavailability of fats in fat containing food products without reducing caloric intake as determined by bomb calorimetry and to methods for increasing high density lipoproteins in a subject and reducing or controlling weight by administering the food products of this invention.

REQUISITOS NECESARIOS PARA PRESENTACION Y AGILIZACION DEL
 TRAMITE

	JOYER	RADICADOR
PATENTE DE INVENCION ✓		
MODELO DE UTILIDAD	()	()
Indicacion de que se solicita la concesión de una patente	()	()
Datos de identificación del solicitante o de la persona que se presenta a la solicitud	()	()
- Descripción de la invención	()	()
- Dibujos de ser estos pertinentes	()	()
- Comprobante de Pago de las tasas establecidas	()	()
COMPLETA ()	INCOMPLETA ()	()
DISEÑO INDUSTRIAL ()		
- Indicación de que se solicita el registro de Diseño Industrial	()	()
- Datos de identificación del solicitante o de la persona que presenta la solicitud	()	()
- Representación gráfica o fotográfica del Diseño Industrial o muestra del Material que incorpora el diseño	()	()
- Comprobante de pago de las tasas establecidas	()	()
COMPLETA ()	INCOMPLETA ()	()
ESQUEMA DE TRAZADO ()		
- Indicación de que solicita el registro de un Esquema de Trazado	()	()
- Datos de identificación del solicitante o de la persona que presenta la solicitud	()	()
- Representación gráfica del esquema de trazado	()	()
- Comprobante de pago de las tasas establecidas	()	()
COMPLETA ()	INCOMPLETA ()	()

Firma Responsable *Claudia M Neiva*

Fecha





121

Industria y Comercio
SUPERINTENDENCIA

2020
Bogotá, D.C.,

Doctor:
CAMILO ALVAREZ
Apoderado
ART JEN COMPLEXUS, INC.

Oficio N° 12380

ASUNTO:	Radicación N°	05-12002
	Solicitud internacional	PCT/US03/023291
	Fecha inicio fase nacional	22/03/2005
	Trámite	011
	Evento	379
	Actuación	430
	Folios	001

Como resultado del examen de forma, realizado con fundamento en el artículo 38 de la Decisión 486 de la Comisión de la Comunidad Andina, artículo 27 del Tratado de Cooperación en Materia de Patentes (PCT), regla 51 bis del Reglamento y Circular Única de la Superintendencia de Industria y Comercio, se le comunica que:

- Los dibujos deberán traer su correspondiente traducción para trámites posteriores de publicación y título.

En cumplimiento de lo dispuesto por el artículo 39 de la Decisión 486, se le requiere para que dentro del término de dos meses siguientes a la fecha de notificación del presente oficio, complete los requisitos anteriormente enunciados. En caso de no dar cumplimiento al presente requerimiento, la solicitud se considerará abandonada y perderá su prelación.

Notifíquese el presente oficio conforme a lo dispuesto en el numeral 5.2, literal e), del capítulo quinto del título primero de la Circular Única N° 10 de 2001.


ALIX CARMENZA CESPEDES DE VERGEL
Jefe de la División de Nuevas Creaciones.

El anterior requerimiento fue notificado por fijación en lista de fecha, 11 MAR 2005.

202030

Carrera 13 No. 27-00 Piso 5 y 10
Conmutador: 334 12 21-2-3-4
Fax: 281 31 25 e-mail: info@sic.gov.co
Santa Fe de Bogotá D.C. - Colombia