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SEÑOR

SUPERINTENDENTE DE INDUSTRIA Y COMERCIO

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REF: EXPEDIENTE 00-068-859
TÍTULO SOLICITADO: "COMPOSICIÓN FARMACÉUTICA DE ORLISTAT
QUE CONTIENE TENSIOACTIVOS Y
DISPERSANTES"
SOLICITANTE: F. HOFFMANN-LA ROCHE AG.
APODERADO: GUSTAVO TAMAYO ARANGO
TRÁMITE: RECURSO DE REPOSICIÓN CONTRA LA
RESOLUCIÓN 7996 DE 23/03/2007, NOTIFICADA
POR EDICTO 6220 DESFIJADO EL 23/04/2007

JUAN PABLO REYES VILLAMIZAR, mayor y vecino de Bogotá D.C., identificado como aparece al pie de la firma, actuando en calidad de apoderado sustituto de la sociedad opositora **TECNOQUÍMICAS S.A.** y de representante legal suplente de la sociedad opositora **LAFRANCOL S.A.** en el asunto de la referencia, en los términos y para los efectos de la sustitución de poder y del certificado de existencia y representación legal adjuntos, manera respetuosa y estando en la debida oportunidad legal, manifiesto que interpongo **Recurso de Reposición** contra la resolución 7996 de 23/03/2007, por la cual su Despacho ha declarado infundada la oposición de mis representadas y ha resuelto otorgar privilegio de patente a la solicitud tramitada en el expediente 00-068-859.

I. PETICIÓN

Sírvase revocar íntegramente la resolución 7996 de 23/03/2007, y en su reemplazo, sírvase declarar fundada la oposición presentada con el lleno de los requisitos legales por parte de las sociedades **TECNOQUÍMICAS S.A.**, Y **LAFRANCOL S.A.**, procediendo en consecuencia a negar en todas sus reivindicaciones el privilegio de patente solicitado y ordenando el archivo del expediente respectivo.

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De manera expresa solicito que la resolución que resuelva el presente recurso considere y tenga en cuenta tanto los argumentos presentados en este memorial, como aquellos presentados en la debida oportunidad legal por el opositor.

II. ANTECEDENTES, MOTIVOS DE INCONFORMIDAD Y FUNDAMENTOS

En primer término me permito reiterar todos los argumentos y pruebas planteados por mis representadas en los escritos de oposición, de sustentación de oposición, y en los complementos de información radicados los días de 15-03-2004 y 15-03-2007 -sin que en apariencia éste último haya sido tenido en cuenta por el Despacho-, en relación con la carencia de Nivel Inventivo de que adolece la solicitud de patente indicada en la referencia.

Por razones de economía procesal me remito a los argumentos y pruebas aportados, en particular a la existencia de dos documentos anteriores a la fecha de prioridad de la presente solicitud, PCT/WO98/34607 y PCT/WO98/34630, los cuales revelan composiciones farmacéuticas que comprenden un inhibidor de lipasa gastrointestinal como Orlistat o tetrahidrolipstatina, y que tienen entre sus excipientes un agente tensoactivo y un agente dispersante, al igual que ocurre en las formulaciones reivindicadas en este expediente.

Ahora bien, es del caso reiterar lo expuesto en el complemento de información remitido el 15/03/2007, en el cual se llamaba la atención del Despacho en cuanto a que los tamaños de muestra que se utilizan para probar la efectividad en la supuesta reducción de efectos adversos (goteo de grasa anal), son totalmente inadecuados para el caso y no pueden por ello emplearse como demostración del supuesto aporte de la invención, considerando que respecto de formulaciones convencionales de Orlistat la medida de dichos efectos se ha realizado en grupos mayores y verdaderamente representativos de pacientes tratados con dicha sustancia, tal y como puede apreciarse al revisar "Complete Product Information (ORLISTAT) XENICAL®. Roche Pharmaceuticals. Copyright 1999-2005 Pg. 20. <http://www.rocheusa.com/products/xenical/pi.pdf>.

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295**Table 11 Commonly Observed Adverse Events**

Adverse Event	Year 1		Year 2	
	XENICAL* % Patients (N=1913)	Placebo* % Patients (N=1466)	XENICAL* % Patients (N=613)	Placebo* % Patients (N=524)
Oily Spotting	26.6	1.3	4.4	0.2
Flatus with Discharge	23.9	1.4	2.1	0.2
Fecal Urgency	22.1	6.7	2.8	1.7
Fatty/Oily Stool	20.0	2.9	5.5	0.6
Oily Evacuation	11.9	0.8	2.3	0.2
Increased Defecation	10.8	4.1	2.6	0.8
Fecal Incontinence	7.7	0.9	1.8	0.2

* Treatment designates XENICAL three times a day plus diet or placebo plus diet

Si se compara lo anterior con el número de pacientes supuestamente utilizados en los estudios realizados en soporte de la solicitud en trámite (equivalente internacional WO 01/19340), es necesario concluir que tales valores, en cuanto al número de voluntarios, son estadísticamente inadecuados sobre todo si se tiene en cuenta que el porcentaje de aparición de estos efectos adversos en pacientes es bastante bajo (específicamente 26.6 % para el goteo anal de grasa), con lo que la probabilidad de que se noten en una muestra tan pequeña (entre 4 y 18) se ve seriamente disminuida, y por lo tanto, los resultados arrojados por estos ensayos carecen de validez estadística, que se transmite a la demostración del supuesto efecto mejorado frente al goteo anal que se intenta defender con estos estudios.

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Table 1: In vivo results

Example	Orlistat dose (mg)	Excreted fat (%) ⁽¹⁾	n ⁽²⁾	Free oil in stool samples ⁽³⁾
Reference	120 mg (Xenical®)	41.8 ± 11.5	18	9/18
1	60 mg	64.5 ± 3.0	5	1/5
2	60 mg	72.0 ± 3.4	5	0/5
3	60 mg	61.1 ± 10.0	4	0/5
4	30 mg	39.9 ± 11.4	5	0/5
5	30 mg	57.6 ± 27.8	5	0/5
6	60 mg	53.7 ± 13.0	5	0/5
7	30 mg	26.5 ± 9.9	5	0/5

⁽¹⁾ percentage of excreted fat as percentage of fat intake.

⁽²⁾ number of volunteers subjected to the experiments

⁽³⁾ number of stool samples containing free oil/number of volunteers

Al reiterar la falta de soporte estadístico de los estudios llevados a cabo en la solicitud en trámite, me permito llamar la atención del Despacho en cuanto a la "solución del problema técnico" de la invención, explicada en la página 5 del escrito de 04-10-2006 presentado por el solicitante, en donde se afirma que *"una composición farmacéutica que contenga Orlistat, un dispersante y un tensioactivo, en donde los dispersante y tensioactivos específicamente definidos permiten que dicha formulación presente una mayor eficiencia asociada a una reducción de los efectos colaterales, que entre ellos incluye el goteo anal..."* (cursiva fuera del texto):

- La solicitud internacional WO 00/009122 de título "Pharmaceutical composition containing lipase inhibitors" publicada el 24 de febrero de 2000 y con prioridades EP 98115311.7 de 14-08-1998 y EP 99109516.7 de 12-05-1999, publicada y con fechas de prioridad anteriores a la solicitud internacional WO 01/19340 (publicada el 22-03-2001; Prioridad EP 99118180.1 de 13-09-1999) equivalente a la solicitud colombiana en trámite (publicada el 30-07-2002 y prioridad EP 99118180.1 de 13-09-1999), revela:

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"Anal leakage of oil (oily spotting) is an adverse effect which is occasionally observed in patients treated with lipase inhibitors. This phenomenon reflects physical separation of some liquid unabsorbed dietary fat from the bulk of unabsorbable solids in the lower large intestine. This physical separation and thus anal leakage of oil can be prevented with the pharmaceutical compositions of the present invention.

Surprisingly, it has now been found that the separation of unabsorbed oil from the feces and thus anal oil leakage can be reduced or prevented, when a lipase inhibitor such as orlistat is administered in combination with low amounts of one or more poorly digestible, poorly fermentable, hydrophilic and/or hydrocolloidal food grade thickeners and/or emulsifiers."

Pese a la fecha de publicación del documento citado, es necesario concluir que "el problema técnico" de goteo anal de grasa de la solicitud colombiana en trámite ya se estaba resolviendo cuando se presentó la Solicitud Internacional WO 00/009122.

- Por su parte, la patente americana RE33996 de título "Compositions of treating hypercholesterolemia", publicada el 14-07-1992 se refiere a una composición para el tratamiento de la hipercolesterolemia que comprende un poliol de éster de ácido graso líquido y un agente antigoteo anal como por ejemplo un ácido graso saturado.

Las reivindicaciones 1, 4 y de esta patente revelan:

1. A composition of matter, comprising:

- (a) an edible, non-absorbable, non-digestible liquid polyol fatty acid polyester having at least 4 fatty acid ester groups, wherein the polyol is selected from the group consisting of sugars and sugar alcohols containing from 4 to 8 hydroxyl groups and wherein each fatty acid group has from about 8 to about 22 carbon atoms; and
- (b) sufficient anti-anal leakage agent to prevent leakage of said liquid polyester through the anal sphincter, wherein the anti-anal leakage agent is a member selected from the group consisting of: edible C₁₂ and higher saturated fatty acids, and their edible salts; edible, digestible sources of C₁₂ and higher saturated fatty acids, other than tristearin or C₁₈ saturated fatty acid esters of 1,3-propanediol; edible, non-absorbable, non-digestible solid polyol fatty acid polyesters having at least 4 fatty acid ester groups, wherein the polyol is selected from the group consisting of sugars and sugar alcohols containing from 4 to 8 hydroxyl groups and wherein each fatty acid group is a saturated fatty acid group having from about 8 to

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about 22 carbon atoms; and edible, non-digestible esters of alpha-branched chain C₁₀ -C₁₈ fatty acids.

4. A composition according to claim 3 wherein the polyol is a member selected from the group consisting of erythritol, xylitol, sorbitol, glucose and sucrose.

13. A composition according to claim 12 wherein the anti-anal leakage agent is a lower alkyl ester of C₁₂ -C₂₄ saturated fatty acids, or mixtures thereof.

14. A composition according to claim 12 wherein the anti-anal leakage agent comprises substantially saturated triglyceride esters of C₁₂ -C₂₄ fatty acids, or mixtures thereof, *other than tristearin*.

Como puede apreciarse, en el estado del arte existen solicitudes anteriores y composiciones farmacéuticas divulgadas las cuales, pese a no resultar idénticas a la reveladas en la solicitud en trámite, sí plantean las mismas soluciones al problema técnico ahora planteado por el solicitante, en lo que se refiere a disminuir los efectos secundarios o adversos de la composición, entre los que resalta la pérdida anal.

Por lo expuesto respetuosamente llamo la atención sobre el hecho de que la solicitud de la referencia, en todas sus reivindicaciones, no cumple con los requisitos dispuestos en la Decisión 486 de 2000, por tal razón no puede ser objeto de privilegio de patente de invención.

III. ANEXOS

1. La solicitud internacional internacional WO 00/009122 de título "Pharmaceutical composition containing lipase inhibitors" publicada el 24 de febrero de 2000 y con prioridades EP 98115311.7 de 14-08-1998 y EP 99109516.7 de 12-05-1999, páginas 1 a 5.
2. La patente americana US RE 33996 de título "Compositions of treating hypercholesterolemia", publicada el 14-07-1992.

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Señor Superintendente,

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JUAN PABLO REYES VILLAMIZAR

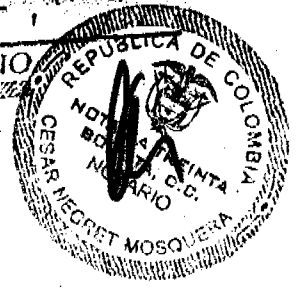
C.C. 80.419.709 de Usaquén

T.P.A. 92.189 del C.S.J.

NOTARIA TREINTA DE BOGOTÁ, D.C.

Este memorial dirigido a SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
fué presentado personalmente ante el suscrito Notario por
JUAN PABLO REYES VILLAMIZAR
Identificado (s) con Cds. Nos. 80.419.709 USQUÉN
T. P. de Abogado No: 92.189 C.S.J.
Bogotá, D.C. de 30 ABR. 2007
Diligenció *[Handwritten signature]*

EL NOTARIO



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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : A61K 31/365, 9/00, A61P 3/04		A1	(11) International Publication Number: WO 00/09122 (43) International Publication Date: 24 February 2000 (24.02.00)
(21) International Application Number: PCT/EP99/05607 (22) International Filing Date: 2 August 1999 (02.08.99) (30) Priority Data: 98115311.7 14 August 1998 (14.08.98) EP 99109516.7 12 May 1999 (12.05.99) EP (71) Applicant: F. HOFFMANN-LA ROCHE AG [CH/CH]; Grenzacherstrasse 124, CH-4070 Basle (CH). (72) Inventors: HUG, Manuela; Obere Schanzstrasse 6A, D-79576 Weil am Rhein (DE). MAERKI, Hans-Peter; Seltisbergerstrasse 75, CH-4059 Basle (CH). MEIER, Marcel; Bahnhofstrasse 11, CH-4133 Pratteln (CH). (74) Agent: WITTE, Hubert; Grenzacherstrasse 124, CH-4070 Basle (CH).			(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, 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, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published With international search report.

(54) Title: PHARMACEUTICAL COMPOSITIONS CONTAINING LIPASE INHIBITORS

(57) Abstract

Orally administrable pharmaceutical composition containing an inhibitor of gastrointestinal lipase, one (or more) additive(s) of the group consisting of poorly digestible, poorly fermentable, hydrophilic and/or hydrocolloidal food grade thickeners and emulsifiers, and auxiliary excipients.

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PHARMACEUTICAL COMPOSITIONS CONTAINING LIPASE INHIBITORS

The present invention relates to pharmaceutical compositions containing an inhibitor of gastrointestinal lipases, one (or more) additive(s) of the group consisting of poorly digestible, poorly fermentable, hydrophilic and/or hydrocolloidal food grade thickeners and emulsifiers, and excipients.

An example of an inhibitor of gastrointestinal lipases is orlistat, previously known as tetrahydrolipstatin or THL. Orlistat reduces the absorption of dietary fat. Its use for the control or prevention of obesity and hyperlipidaemia is described in US patent 4 598 089.

Anal leakage of oil (oily spotting) is an adverse effect which is occasionally observed in patients treated with lipase inhibitors. This phenomenon reflects physical separation of some liquid unabsorbed dietary fat from the bulk of unabsorbable solids in the lower large intestine. This physical separation and thus anal leakage of oil can be prevented with the pharmaceutical compositions of the present invention.

In the US patent 5 447 953 it has been demonstrated that by combining a lipase inhibitor with substantial amounts of water-insoluble crude fibers, the inhibiting effect on fat absorption can be increased. This synergistic effect is likely attributable to acceleration of gastrointestinal transit of food by the water-insoluble fiber component. The consequent shortening of the time period available for fat digestion combined with the reducing effect on lipase activity intensifies the inhibitory effect on fat absorption.

Surprisingly, it has now been found that the separation of unabsorbed oil from the feces and thus anal oil leakage can be reduced or prevented, when a lipase inhibitor such as orlistat is administered in combination with low amounts of one or more poorly digestible, poorly

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fermentable, hydrophilic and/or hydrocolloidal food grade thickeners and/or emulsifiers.

5 The invention is also concerned with the use of poorly digestible, poorly fermentable hydrophilic and/or hydrocolloidal food grade thickeners and/or emulsifiers for the combined simultaneous, separate or chronologically spaced use with lipase inhibitors, e.g. orlistat, in the treatment of obesity and hyperlipaemia.

10 The invention is further concerned with the use of the above thickeners and/or emulsifiers for treating or preventing the syndrome of anal leakage of oil occurring after the administration of a lipase inhibitor, such as orlistat, or after ingestion of food containing poorly absorbable or non-absorbable fats or oils or undigestible oily fat substitutes.

15 Further examples of lipase inhibitors which can be used in the scope of the present invention are lipstatin, panclicins, hesperidin, ebelactones, esterastin and their derivatives, and valilactone.

20 As thickeners there can be cited water soluble natural, synthetic or semisynthetic polysaccharides, such as methylcellulose, xanthan gum, psyllium seed, ispaghula husk, plantago ovata seeds, karaya gum and mixtures of such compounds:

Methyl cellulose is the methyl ether of cellulose. It is slowly soluble in water, giving a viscous, colloid solution.

25 Xanthan gum is a biosynthetic hydrocolloidal high molecular weight exopolysaccharide produced by pure culture fermentation of *Xanthomonas campestris*. It contains D-glucose, D-mannose, and D-glucuronic acid as the dominant hexose units and is manufactured as the sodium, potassium, or calcium salt.

30 Psyllium seed husk, seed coat is a source of soluble fibre. It comprises cellulose containing walls of endosperm, and mucilage containing epidermis of small dried ripe seeds. A colorless transparent mucilage forms upon contact with water.

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Ispaghula husk is psyllium hydrophilic mucilloid. It comprises the epidermis and collapsed adjacent layer of Plantago species, e.g. Pl. psyllium. It swells rapidly upon contact with water to form a stiff mucilage.

5 Plantago ovata seeds (seed husk and seed coat) is a source of soluble fibre. It comprises cellulose containing walls of endosperm, and mucilage containing epidermis of small dried ripe seeds. A colorless transparent mucilage forms upon contact with water.

10 Karaya gum is a hydrocolloidal exudate or gum from Sterculia species. It forms a homogenous adhesive gelatinous mass upon contact with water.

Examples of these types of thickeners are contained in OTC products and/or food additives, such as:

15 METHOCEL A4M, a trademark of Dow Chemical Co. for a high viscosity methyl cellulose,

KELTROL TF, a trademark of Merck & Co. Inc., Rahway NJ, for xanthan gum,

MUCILAR; psyllium seed (Psyllii seminis testa), a product of Spirig AG, CH-4622 Egerkingen,

20 METAMUCIL, ispaghula husk (Ispaghulae testae pulvis) a product of Procter & Gamble, CH-1211 Geneve 2,

AGIOCUR, plantago ovata seeds, a product of Madaus AG, D-5000 Köln 91,

25 NORMACOL MITE, a trademark of Norgine Ltd., Great Britain, for karaya gum,

POLY-KARAYA, a trademark of Delalande for karaya gum of Interdelta SA, CH-1701 Fribourg.

30 A further example of a thickener is FIBERCON (polycarbophil), a trademark of Lederle Laboratories Division, American Cyanamid Co., Pearl River NY, for the calcium salt of a synthetic loosely crosslinked hydrophilic resin of the polycarboxylate type.

As emulsifiers which can be utilized in the compositions of the invention, there can be cited saccharose polyesters, such as Ryoto Sugar

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Esters, e.g. Ryoto Sugar Ester S-170. Ryoto Sugar Esters are a trade name of Mitsubishi-Kasi Foods Corp., Chuo-Ku, Tokyo 104, for sucrose fatty acid esters. Ryoto Sugar Ester S-170 contains sucrose stearic acid polyesters.

5 Examples of excipients which can be used in the pharmaceutical compositions of the invention are binders, diluents and lubricants, such as AVICEL, polyvinyl pyrrolidone (povidone), talc, stearic acid and sodium stearyl fumarate; sweeteners, such as sorbitol, glucose, saccharose, saccharine-sodium salt and sodium cyclamate; flavour
10 agents, such as passion fruit, citron and limette; flavour enhancers, such as citric acid, monosodium citrate, sodium chloride and chinine sulfate; effervescing agents, such as sodium bicarbonate and tartaric acid; disintegrants, such as sodium starch glycolate; antimicrobial agents, such as p-hydroxybenzoic acid methyl or propyl ester;
15 detergents, such as sodium lauryl sulfate, and colouring agents, such as β -carotene.

 AVICEL essentially comprises microcrystalline cellulose. It is available from FMC Corporation, Pharmaceutical Division, 1735 Market Street, Philadelphia, PA 19103, e.g. as AVICEL RC-591 or
20 CL-611, which are mixtures of microcrystalline cellulose (about 92%) and carboxymethylcellulose sodium (about 8%), AVICEL PH 101 or PH 105, which is microcrystalline cellulose with an average particle size of 50 or 20 μ , respectively; AVICEL CE-15 a mixture of microcrystalline cellulose and guar gum.

25 As indicated above, anal leakage of oil, occasionally observed with the therapeutic use of lipase inhibitors such as orlistat, can be reduced or prevented with the pharmaceutical compositions of the invention. This is illustrated by the following in vivo experiments:

 Rats maintained on high fat diet were used as model. Inhibition of
30 fat absorption by diet-admixed orlistat provoked anal leakage of liquid oil. However, the amount of oil leakage could not easily be determined. Due to coprophagia and extensive grooming activity the rats distributed the oil to a large extent over their fur. Moreover, this stressful condition of unsuccessful grooming provoked considerable excitation of the



US00RE33996E

United States Patent

[19]

[11] E

Patent Number: Re. 33,996

Jandacek

[45] Reissued Date of Patent: Jul. 14, 1992

[54] COMPOSITIONS FOR TREATING
HYPERCHOLESTEROLEMIA

[75] Inventor: Ronald J. Jandacek, Cincinnati, Ohio

[73] Assignee: The Procter & Gamble Company,
Cincinnati, Ohio

[21] Appl. No.: 346,662

[22] Filed: May 3, 1989

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4,005,196 1/1977 Jandacek et al.
4,034,083 7/1977 Mattson

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Primary Examiner—Sam Rosen

Attorney, Agent, or Firm—Eric W. Guttag; Ronald L.
Hemingway; Richard C. Witte

[57]

ABSTRACT

Anti-anal leakage agents are used in combination with
liquid polyol fatty acid polyesters to provide pharma-
ceutical and food compositions for treating and/or pre-
venting hypercholesterolemia while avoiding undesired
anal leakage of the liquid polyesters.

76 Claims, No Drawings

Related U.S. Patent Documents

Reissue of:

[64] Patent No.: 4,005,195
Issued: Jan. 25, 1977
Appl. No.: 657,528
Filed: Feb. 12, 1976[51] Int. Cl.³ A61K 31/23; A61K 31/70[52] U.S. Cl. 514/23; 514/53;
514/552; 514/558; 514/560

[58] Field of Search 514/552, 558, 23

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3,849,554 11/1974 Winitz

COMPOSITIONS FOR TREATING HYPERCHOLESTEROLEMIA

Matter enclosed in heavy brackets [] appears in the original patent but forms no part of this reissue specification; matter printed in *italics* indicates the additions made by reissue.

BACKGROUND OF THE INVENTION

The present invention relates to certain edible, but non-absorbable and non-digestible, liquid polyesters which can be used as low calorie fat substitutes in foods and as pharmaceutical compositions. The polyesters herein interfere with the body's absorption of cholesterol and thereby provide a means for treating hypercholesterolemia. It has now been determined that the liquid polyesters herein can also cause an undesired anal leakage effect. By the present invention, certain agents are added to the polyester compositions to avoid this undesired effect. Highly preferred compositions for treating hypercholesterolemia and/or hyperlipidemia comprising the polyesters and anti-anal leakage agent are provided.

High blood cholesterol (hypercholesterolemia) is recognized as being a risk factor in cardiovascular disease which comprises a major health care problem today. Epidemiological studies have demonstrated that, with few exceptions, populations consuming large quantities of saturated fat and cholesterol have a relatively high concentration of serum cholesterol and a high mortality rate from coronary heart disease. While it is recognized that other factors can also contribute to the development of cardiovascular disease, there appears to be a causal relationship between the concentration of serum cholesterol, in which hypercholesterolemia results in the accumulation of undesirable amounts of cholesterol in various parts of the circulatory system (atherosclerosis) or in soft tissues (xanthomatosis), and coronary disease and coronary mortality rates.

A variety of dietary and drug regimens have been suggested for alleviating or preventing hypercholesterolemia.

By providing a fat substitute which is non-absorbable and non-digestible, the total content of cholesterol in the body can be lowered. Mineral oil is a well-known laxative and has been suggested for use as a fat substitute and as a kind of "intestinal solvent" to dissolve cholesterol and cause its removal in body wastes. However, mineral oil has never been accepted for these uses. Moreover, mineral oil is partially absorbed by the body and undesirably deposits in the liver.

In the present invention, liquid, non-absorbable, non-digestible polyesters of sugars (or sugar alcohols) are used as fat substitutes in foods and, conveniently, in unit dose forms as therapeutic compositions. The polyesters herein are fat-like in their physical properties and are excellent fat substitutes for use in low calorie foods and diets. Moreover, the polyesters herein efficiently inhibit absorption of cholesterol by the body and, in contrast with mineral oil, are not absorbed and/or deposited in the liver during usage in a treatment/prevention regimen with persons having or likely to develop hypercholesterolemia.

The anal leakage effect of the liquid polyesters of the type disclosed herein can be overcome by adding an

anti-anal leakage agent of the type disclosed hereinafter to the liquid polyesters, or to foods containing same.

The following references are relevant to the present invention.

The copending application of Mattson, Ser. No. 628,265, filed Nov. 3, 1975, entitled COMPOSITIONS FOR INHIBITING ABSORPTION OF CHOLESTEROL, discloses vitamin-fortified liquid and solid polyesters of the general type employed herein, their use as anti-hypercholesterolemic and anti-hyperlipidemic agents, and their stool-softening laxative effect.

The concurrently-filed application of Jandacek and Mattson, Ser. No. 657,529, filed Feb. 12, 1976, P&G Attorney's Docket No. 2309, entitled VITAMINIZED COMPOSITIONS FOR TREATING HYPERCHOLESTEROLEMIA, discloses ternary compositions comprising fat-soluble vitamins, anti-anal leakage agents and a liquid polyester of the type employed herein.

U.S. Pat. No. 3,600,186 (1971) to Mattson and Volpenhein discloses low calorie food compositions containing polyol polyesters of the general type employed herein, and their use in combination with hardstocks which are fatty acid sources. The anti-anal leakage effect of fatty acids is not noted.

The copending application of Mattson and Volpenhein, entitled PHARMACEUTICAL COMPOSITIONS FOR INHIBITING ABSORPTION OF CHOLESTEROL, Ser. No. 425,010, filed Dec. 14, 1973, now U.S. Pat. No. 3,954,976 discloses and claims sugar polyesters of the general type employed herein for the treatment and/or prevention of hypercholesterolemia. A variety of optional carriers are mentioned, including the fatty acid, stearic acid. The anti-anal leakage effect of stearic acid is not mentioned.

U.S. Pat. No. 1,656,474 (1928) to Dubin discloses edible fat compositions consisting of ethyl and glycerol esters of odd chain fatty acids in combination with fat-soluble vitamins.

Mattson and Nolen, The Journal of Nutrition Vol. 102, No. 9, September 1972, at pages 1171-1175, report on the lack of absorbability of sugar polyesters of the general type employed herein in rats.

Fallet, Glueck, Mattson and Lutmer, Clinical Research XXIII No. 3, page 319A (1975) report the lowering of both serum cholesterol and vitamin A and E levels in subjects receiving sugar polyesters of the present type.

U.S. Pat. No. 2,962,419 (1960) to Minich relates to neopentyl fatty esters and their use as fat substitutes.

U.S. Pat. No. 3,160,565 (1964) to H. E. Duell relates to sugar mono-, di- and tri-esters and their use as carriers for varying orally-administered medicinals.

U.S. Pat. No. 3,849,554 (1974) to Winitz discloses means for reducing blood serum cholesterol by injecting diets comprising a fatty acid source, said diets being low in sucrose.

U.S. Pat. No. 2,893,990 (1959) to Hass, et al., discloses fatty acid mono- and di-esters of sucrose which aid in the absorption of fat from the digestive tract.

U.S. Pat. No. 3,158,490 (1964) to Baur and Lutton discloses non-cloudy salad oils containing esters of disaccharides in which there are not more than five unesterified hydroxy groups. See also U.S. Pat. Nos. 3,059,009 (1962) and 3,059,010 (1962) to Schmid and Baur.

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U.S. Pat. No. 2,997,492 (1961) to Martin is directed to a method of making partial fatty acid esters of hexitols. U.S. Pat. No. 2,997,491 (1961) to Huber is directed to the synthesis of partial fatty esters of inositol. The general methods of synthesis disclosed in these patents can be used to prepare the liquid polyesters herein. Preferred methods of synthesis are fully disclosed hereinafter.

SUMMARY OF THE INVENTION

Administration of anti-hypercholesterolemic amounts of a composition comprising a liquid polyester of the type described herein to an animal (especially humans) afflicted with or susceptible to hypercholesterolemia is an effective means of controlling the body's cholesterol level. Unfortunately, administration of cholesterol-controlling amounts of the liquid polyesters can result in an undesired "laxative" effect, namely, leakage of the liquid polyester through the anal sphincter. By combining the polyester compositions with an anti-laxative agent, especially a C₁₂, or higher, saturated fatty acid, or edible source which provides such fatty acids in the gut, this undesired laxative effect is prevented. (By "anti-anal leakage agent", or "AAL" agent, herein is meant those materials which prevent frank leakage of the liquid polyesters. The natural stool-softening effect of the polyesters is not substantially affected, nor is it a problem.)

The present invention encompasses compositions of matter which comprise a liquid, non-absorbable, nondigestible polyol fatty acid polyester of the type described hereinafter, and an anti-laxative, or "stiffening", amount of an anti-laxative agent, especially sources of C₁₂, or higher, fatty acids. The compositions can be used as fat substitutes in cooking or can be self-administered to reduce the body's cholesterol level. Such compositions also find use as diet aids for the hyperlipidemic individual.

The present invention also encompasses non-laxative pharmaceutical compositions in effective unit dosage amounts for inhibiting the absorption of cholesterol, said compositions comprising from about 1 gram to about 5 grams of the liquid polyesters herein and sufficient AAL agent, especially a C₁₂, or higher, saturated fatty acid, or edible source thereof, to prevent anal leakage in humans ingesting said compositions.

The polyester materials herein are non-absorbable and non-digestible fat-like materials and are suitable for use as fat substitutes in low calorie fat-containing food compositions. Accordingly, the present invention also encompasses low calorie fat-containing food compositions comprising non-fat ingredients and fat ingredients wherein from about 10% to about 100% of the total fat ingredients comprise the liquid, non-absorbable, non-digestible polyesters of the type disclosed hereinafter, said compositions also containing an effective amount of an AAL agent, especially a C₁₂, or higher, saturated fatty acid, or an edible source of fatty acids, which prevents an undesired anal leakage effect.

The present invention also encompasses methods for inhibiting the absorption of cholesterol without causing an anal leakage effect, comprising systemically (generally, orally) administering to animals susceptible to or afflicted with hypercholesterolemia successive therapeutically effective doses of the compositions of the foregoing type.

It is to be understood that the edible, non-absorbable, non-digestible polyester materials herein are liquids at

body temperature, i.e., have a melting point of ca. 37° C. or below. (Edible, non-absorbable, non-digestible polyester materials that are solid at body temperature do not exhibit the undesirable anal leakage effects noted with the liquid polyesters. Indeed, such solid polyesters can be used as one type of AAL agent herein.) In general, the liquid polyesters are those which are made from unsaturated fatty acids, whereas the solid polyesters are substantially saturated.

DETAILED DESCRIPTION OF THE INVENTION

The consumption of diets containing sucrose polyesters (SPE) has been shown to result in the desirable decrease in absorption of dietary cholesterol in animals; see Mattson, Mandacek and Glucek, Clinical Research 23 445A (1975). Similar results have been noted in humans.

In studies of the foregoing type, rats which ingested about 300 mg. to about 3000 mg. total liquid polyester per day and human volunteers who ingested from about 10 grams to about 50 grams total liquid polyester per day exhibited undesired anal leakage of the polyesters. Further studies indicated that this anal leakage effect was a direct result of the passage of the polyesters through the anal sphincter. Briefly, this undesired effect is not unlike the effect which can be caused by the ingestion of excessive amounts of mineral oil. It has now been determined that this undesirable effect can be obviated by combining the liquid polyester compositions with certain AAL agents.

The types of AAL agents which can be used herein to overcome the above-described anal leakage problem without interfering with the beneficial effects of the present compositions are disclosed immediately hereinafter.

Anti-Anal Leakage Agents

One class of materials which provide the anti-anal leakage effect herein includes fatty acids having a melting point of ca. 37° C., or higher, and ingestible, digestible sources of such fatty acids. The fatty acid AAL agents include, for example, the C₁₂-C₂₄ saturated fatty acids, and ingestible, digestible sources thereof.

While not intending to be limited by theory, it appears that the foregoing type of AAL agent functions via the formation of calcium or magnesium fatty acid soaps in the gut. These soaps apparently interact with the liquid polyesters herein and impart a "stiffening" effect thereto. Once "stiffened", or partly solidified, in the gut, the polyesters do not leak through the anal sphincter. The antihypercholesterolemic effect of the liquid polyesters is not diminished.

Non-limiting examples of saturated fatty acids and sources thereof which can be used as the AAL agent herein include the free saturated fatty acids per se, compounds such as esters (e.g., triglycerides) that yield such saturated fatty acids on hydrolysis in the gut, soaps of the fatty acids such as the sodium, potassium, etc., water-soluble soaps, as well as the calcium and magnesium water-insoluble soaps.

Highly preferred herein for their anti-anal leakage effect are the C₁₆-C₂₂, most preferably C₁₆-C₁₈, saturated fatty acids, or edible sources thereof.

Specific examples of materials useful as the foregoing type of AAL agent herein include natural or processed fats yielding C₁₂-C₂₄ saturated fatty acids in the gut, e.g., materials such as cocoa butter, palm oil, palm ker-

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nel oil, coconut oil, tallow, lard, enriched concentrates of triglycerides having high levels of saturated fatty acids obtainable from these sources and sources such as highly saturated cottonseed oil fractions obtained by processes such as crystallization or directed rearrangement which yield the desired higher concentrations of the more saturated fatty acids in the resulting "hard-stock" fractions. Such materials are all available by well-known processes.

Partially hydrogenated oils, including all of the above, as well as partially hydrogenated soybean oil, safflower seed oil, rapeseed oil, or such materials which are hydrogenated and concentrated, for example by crystallization, to provide fractions which are enriched in sources of the longer-chain, substantially saturated fatty acids, are all useful as the AAL agent herein. (By "substantially hydrogenated" herein is meant oils having an iodine value of ca. 50, or lower.)

Of course, any of the foregoing unsaturated oils are useful herein after they have been substantially completely hydrogenated to convert the unsaturated fatty acid (ester) groups to the corresponding saturated fatty acids.

Synthetic materials, especially fatty acid esters made from the C₁₂-C₂₄, more preferably C₁₆-C₂₂, most preferably C₁₆-C₁₈, saturated fatty acids are useful herein. Such materials include the esters of tetrahydric alcohols such as erythritol, esters of pentahydric alcohols such as xylitol, and esters of hexahydric alcohols such as sorbitol, and the like.

The C₁₂-C₂₄ saturated fatty acid esters of monohydric alcohols such as methyl, ethyl and propyl alcohols (preferably ethyl alcohol) are also useful herein. Esters of dihydric alcohols such as 1,2-propanediol, 1,3-butanediol, and the like, can also be used.

Highly preferred AAL agents herein which yield the foregoing fatty acids on hydrolysis in the gut are those which, in combination with the liquid polyesters herein, provide compositions having aesthetically pleasing organoleptic qualities, i.e., better "mouth feel". Such aesthetically pleasing materials include naturally occurring cocoa butter and various synthetic cocoa and confectioners' butters. These preferred AAL agents include, for example, the so-called "position-specific" triglycerides such as 1-stearoyl diolein (SOO); 2-oleoyl-1,3-distearin (SOS); or the corresponding compounds wherein the stearoyl group is replaced by palmitoyl, arachidoyl or behenoyl groups. Another class of aesthetically preferred anti-laxative agents herein are 1-oleoyl distearin (OSS), 1-palmitoyl distearin (PSS), 1-arachidoyl distearin (ASS) and 1-behenoyl distearin (BSS).

These highly preferred, position-specific triglycerides which can be used as a fatty acid source-type of AAL agent herein can be prepared according to the methods described in U.S. Pat. No. 3,809,711, Yetter, issued May 7, 1974, the disclosures of which are incorporated herein by reference.

As noted hereinabove, the foregoing types of AAL agents appear to function by providing a saturated fatty acid in the gut, said fatty acid thereafter presumably forming an insoluble calcium or magnesium soap in situ. This soap then appears to provide the "stiffening" effect on the liquid polyester, thereby preventing the undesirable anal leakage effect. As noted hereinabove, the solid polyester materials of the present type (i.e., solid, edible, but non-digestible, non-absorbable polyesters) do not cause the undesirable anal leakage effect. It has been determined that these solid polyester materials can also

be used as an AAL agent and these represent a second class of AAL agents herein. Since these solid polyester materials do not hydrolyze in the gut to form free fatty acids, or calcium or magnesium fatty acid soaps, their anti-anal leakage effect must be the result of a different mechanism from that which operates with the hydrolyzable esters and fatty acid sources described immediately hereinabove. Presumably, the combination of the solid polyester with the liquid polyesters simply provides a stiffening effect due to some type of crystallization or phase change within the gut.

It will be appreciated that by combining liquid and solid non-absorbable, non-digestible polyesters to provide the desired anti-anal leakage effect, wholly edible, but non-digestible, non-absorbable, non-caloric compositions are secured. These compositions are quite effective in the treatment of hypercholesterolemia and in low calorie diets.

Typical examples of solid, non-absorbable, non-digestible polyester AAL agents herein include sucrose octastearate, sucrose octapalmitate, sucrose heptastearate, xylitol pentastearate, galactose pentapalmitate, and like, saturated polyol polyesters having at least four —OH groups esterified with C₁₀-C₂₂ saturated fatty acids.

Another type of AAL agent herein comprises fatty acid esters which are non-digestible by virtue of branching on the α -carbon atom of the fatty acid moiety. Such materials, which are well known in the chemical arts, include, for example, α -methyl and α,α -dimethyl C₁₀-C₁₈ fatty acid esters of lower alcohols such as ethanol and of polyols such as glycerol.

LIQUID POLYESTERS

The liquid polyol polyesters (or simply, polyesters) employed in this invention comprise certain polyols, especially sugars or sugar alcohols, esterified with at least four fatty acid groups. Accordingly, the polyol starting material must have at least four esterifiable hydroxyl groups. Examples of preferred polyols are sugars, including monosaccharides and disaccharides, and sugar alcohols. Examples of monosaccharides containing four hydroxyl groups are xylose and arabinose and the sugar alcohol derived from xylose, which has five hydroxyl groups, i.e., xylitol. (The monosaccharide, erythrose, is not suitable in the practice of this invention since it only contains three hydroxyl groups, but the sugar alcohol derived from erythrose, i.e., erythritol, contains four hydroxyl groups and accordingly can be used.) Suitable five hydroxyl group-containing monosaccharides are galactose, fructose, and sorbose. Sugar alcohols containing six —OH groups derived from the hydrolysis products of sucrose, as well as glucose and sorbose, e.g., sorbitol, are also suitable. Examples of disaccharide polyols which can be used include maltose, lactose, and sucrose, all of which contain eight hydroxyl groups.

Preferred polyols for preparing the polyesters for use in the present invention are selected from the group consisting of erythritol, xylitol, sorbitol, glucose and sucrose. Sucrose is especially preferred.

The polyol starting material having at least four hydroxyl groups must be esterified on at least four of the —OH groups with a fatty acid containing from about 8 to about 22 carbon atoms. Examples of such fatty acids include caprylic, capric, lauric, myristic, myristoleic, palmitic, palmitoleic, stearic, oleic, ricinoleic, linoleic, linolenic, eleostearic, arachidic, arachidonic, behenic,

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and erucic acid. The fatty acids can be derived from naturally occurring or synthetic fatty acids; they can be saturated or unsaturated, including positional and geometrical isomers. However, in order to provide liquid polyesters of the type used herein, at least about half of the fatty acid incorporated into the polyester molecule must be unsaturated. Oleic and linoleic acids, and mixtures thereof, are especially preferred.

The liquid polyol fatty acid polyesters useful in this invention must contain at least four fatty acid ester groups. Polyol fatty acid polyester compounds that contain three or less fatty acid ester groups are digested in and the products of digestion are absorbed from the intestinal tract much in the manner of ordinary triglyceride fats, whereas the polyol fatty acid polyester compounds that contain four or more fatty acid ester groups are substantially non-digestible and consequently non-absorbable by the human body. It is not necessary that all of the hydroxyl groups of the polyol be esterified with fatty acid, but it is preferable that the polyester contain no more than two unesterified hydroxyl groups. Most preferably, substantially all of the hydroxyl groups of the polyol are esterified with fatty acid, i.e., the compound is substantially completely esterified. The fatty acids esterified to the polyol molecule can be the same or mixed (but, as noted above, a substantial amount of the unsaturated acid ester groups must be present to provide liquidity).

To illustrate the above points, a sucrose fatty triester would not be suitable for use herein because it does not contain the required four fatty acid ester groups. A sucrose tetra-fatty acid ester would be suitable, but is not preferred because it has more than two unesterified hydroxyl groups. A sucrose hexa-fatty acid ester would be preferred because it has no more than two unesterified hydroxyl groups. Highly preferred compounds in which all the hydroxyl groups are esterified with fatty acid include the liquid sucrose octa-fatty acid esters.

The following are non-limiting examples of specific liquid polyol fatty acid polyesters containing at least four fatty acid ester groups suitable for use in the present invention: glucose tetraoleate, the glucose tetraesters of soybean oil fatty acids (unsaturated), the mannose tetraesters of mixed soybean oil fatty acids, the galactose tetraesters of oleic acid, the arabinose tetraesters of linoleic acid, xylose tetralinoleate, galactose pentaoleate, sorbitol tetraoleate, the sorbitol hexaesters of unsaturated soybean oil fatty acids, xylitol pentaoleate, sucrose tetraoleate, sucrose pentaoleate, sucrose hexaoleate, sucrose heptaoleate, sucrose octaoleate, and mixtures thereof.

As noted above, highly preferred polyol fatty acid esters are those wherein the fatty acids contain from about 14 to about 18 carbon atoms.

The polyol fatty acid polyesters suitable for use herein can be prepared by a variety of methods well known to those skilled in the art. These methods include: transesterification of the polyol with methyl, ethyl or glycerol fatty acid esters using a variety of catalysts; acylation of the polyol with a fatty acid chloride; acylation of the polyol with a fatty acid anhydride; and acylation of the polyol with a fatty acid, per se. As an example, the preparation of polyol fatty acid esters is described in U.S. Pat. No. 2,831,854, incorporated herein by reference.

Specific, but non-limiting, examples of the preparation of polyol fatty acid esters suitable for use in the practice of this invention are as follows.

Erythritol tetraoleate — Erythritol and a five-fold molar excess of methyl oleate are heated at 180° C., under vacuum, with agitation, in the presence of sodium methoxide catalyst over two reaction periods of several hours each. The reaction product (predominately erythritol tetraoleate) is refined in petroleum ether and crystallized three times from several volumes of acetone at 1° C. acetone

Xylitol pentaoleate — Xylitol and a five-fold molar excess of methyl oleate in dimethylacetamide (DMAC) solution are heated at 180° C. for five hours in the presence of sodium methoxide catalyst, under vacuum. During this time the DMAC is removed by distillation. The product (predominately xylitol pentaoleate) is refined in petroleum ether solution and, after being freed of petroleum ether, is separated as a liquid layer four times from acetone at ca. 1° C. and twice from alcohol at ca. 10° C.

Sorbitol hexaoleate is prepared by essentially the same procedure used to prepare xylitol pentaoleate except that sorbitol is substituted for xylitol.

Sucrose octaoleate is prepared by substantially the same procedure as that used to prepare erythritol tetraoleate except that sucrose is substituted for erythritol.

In therapeutic regimens the dosage of the compositions herein can vary with the severity of the hypercholesterolemic condition and the duration of the treatment. Individual dosages can range from about 0.01 mg./kg. to about 500 mg./kg., and greater (unless otherwise specified, the unit designated "mg./kg." as used herein refers to mg. of liquid polyester per kilogram of body weight), preferably from about 0.1 mg./kg. to about 125 mg./kg. per dosage, with up to six dosages, preferably three dosages, being given daily, most preferably at meal times. Because of the AAL agent, such high dosages can be administered without fear of producing anal leakage effects. Dosages of less than about 0.1 mg./kg. do not materially inhibit the absorption of cholesterol in most patients. The dosages can be administered orally in any suitable unit dosage form such as pills, tablets, and capsules. Preferred are capsules made from gelatin. The dosages can also be administered as part of a controlled dietary regimen, e.g., as a synthetic salad oil or cooking oil or fat.

The pharmaceutical compositions herein can comprise the polyester/AAL agent alone, or in combination with any desired, non-interfering pharmaceutical carrier. As used herein, the term "pharmaceutical carrier" means a solid or liquid filler, diluent or encapsulating substance. Some examples of the substances which can serve as pharmaceutical carriers are sugars such as lactose, glucose and sucrose; starches such as corn starch and potato starch; cellulose and its derivatives such as sodium carboxymethylcellulose, ethylcellulose, cellulose acetate; powdered tragacanth; malt; gelatin; talc; oils such as peanut oil, cottonseed oil, sesame oil, olive oil, corn oil and soybean oil; polyols such as propylene glycol, glycerin, sorbitol, mannitol, and polyethylene glycol; agar; alginic acid; pyrogen-free water; isotonic saline; ethyl alcohol and phosphate buffer solutions, as well as other non-toxic compatible substances used in pharmaceutical formulations. Wetting agents and lubricants such as sodium lauryl sulfate, as well as coloring agents, flavoring agents and preservatives can also be present in the compositions, according to the desires of the formulator.

The pharmaceutical carriers of the foregoing type can optionally be employed in conjunction with the liquid polyesters herein to provide a practical size to

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dosage relationship, composition forms which can be easily ingested, and means for providing accurate unit dosages in a convenient form. The pharmaceutical carrier usually will comprise from about 5% to about 50% by weight of the total pharmaceutical composition.

Since the liquid polyesters of the present compositions are not unlike cooking and salad oils and fats in their physical properties, the present compositions can be used as a partial or total replacement for normal triglyceride fats in any fat-containing food composition to provide anti-hypercholesterolemic and low calorie benefits. In order to achieve these benefits in a reasonable time, it is necessary that at least about 10% of the fat in the food composition comprises the polyesters herein. Highly desirable food compositions are those wherein the fatty component comprises up to about 100% of the polyester/anti-anal leakage compositions herein. Accordingly, the compositions of this invention can be used as a partial or complete replacement for normal triglyceride fats in a salad or cooking oil, or in plastic shortenings for use in frying, cake making, bread making, and the like. The compositions can also be used as partial or complete replacements for normal triglyceride fats in fat-containing food products such as mayonnaise, margarine, and dairy products.

Preferred fat-containing food compositions of the present type comprise non-fat ingredients and fat ingredients wherein from about 10% to about 95% of the total fat consists essentially of a liquid sugar fatty acid polyester having at least four fatty acid ester groups, each fatty acid having from about 8 to about 22 carbon atoms, said sugar fatty acid polyester and/or food composition made therefrom also comprising an AAL agent of the type disclosed herein. Such food compositions will most often contain at least about 10%, generally 15% to 25% (by weight of liquid polyester) of a fatty acid source which provides the anti-anal leakage effect. Highly preferred are food compositions wherein the sugar fatty acid ester contains no more than two unsaturated hydroxyl groups. Liquid sucrose polyesters, especially those wherein the ester groups are mainly of the unsaturated type and contain 14 to 18 carbon atoms, when used in the manner of this invention, are especially preferred for use in such anti-hypercholesterolemic and low calorie food compositions.

The total AAL agent employed in any of the compositions and methods herein will depend, somewhat on the total amount of liquid polyester being ingested per day. The anti-anal leakage agent should be present in an amount equaling at least about 10% by weight of the liquid polyester. It is more preferred that the AAL agent comprises at least about 20% by weight of the liquid polyester to ensure that anal leakage does not, even at high ingestion rates. Compositions wherein the weight of AAL agent comprises from about 20% to about 50% of the weight of liquid polyester provide excellent control of serum cholesterol without anal leakage of the polyester.

Compositions comprising edible fatty acids, their edible salts or their edible, digestible esters as the AAL agent preferably comprise about 10% to about 50% by weight of these materials by weight of liquid polyester. Compositions using the palatable position-specific triglycerides as the AAL agent preferably comprise about 20% to about 40% (by weight of liquid polyester) of these AAL agents. When the edible, non-absorbable, non-digestible solid polyesters are used as the AAL

agent, they are preferably used at a rate of from about 20% to about 50% by weight of the liquid polyester.

The following, non-limiting examples illustrate the compositions and processes of this invention. It will be appreciated that sugars and sugar alcohols, appropriately esterified, are encompassed by the term "sugar" as used herein and such materials can be interchanged in the compositions.

EXAMPLE I

Gelatin capsules for use by the hypercholesterolemic patient are prepared by conventional methods, as follows:

Ingredient	Amount per Capsule
Sucrose polyester*	2000 mg.
Stearic Acid	250 mg.

*Liquid mixed hexa-, hepta- and octa-sucrose esters, predominately the octa-ester, esterified with mixed soybean oil fatty acids, predominately in the C₁₆-C₁₈ chain length.

The capsules of the foregoing type are prepared by simply mixing the ingredients and filling the standard gelatin capsules. The capsules are administered orally three times daily (three with each meal). This treatment regimen inhibits cholesterol uptake significantly and decreases the serum cholesterol levels in the circulatory systems of humans with, or disposed towards, hypercholesterolemia. The patients are not troubled by undesired anal leakage with this regimen.

Similar results are obtained when the sucrose polyester in the capsules of Example I is replaced with an equivalent quantity of a fatty acid polyester selected from the group consisting of glucose tetraoleate; glucose tetraoleate; mixed glucose tetraesters of unsaturated soybean oil fatty acids; mixed mannose tetraesters of oleic acid; mixed galactose tetraesters of linoleic acid; mixed arabinose tetraesters of oleic acid; xylose tetralinoleate; galactose pentaoleate; sorbitol tetraoleate; sucrose tetraoleate; sucrose pentaoleate; sucrose hexaoleate; sucrose heptaoleate; and sucrose octaoleate, respectively.

In the composition of Example I, the stearic acid anti-anal leakage ingredient is replaced by an equivalent amount of methyl stearate, propyl stearate, methyl behenate, ethyl behenate, substantially completely hydrogenated palm oil, hydrogenated rapeseed oil, and mixed hydrogenated tallow triglycerides, respectively, and equivalent results are secured.

Preferred pharmaceutical compositions of the type of Example I for inhibiting the absorption of cholesterol, especially in the human body, preferably comprise from about 0.1 gram to about 5 grams of the liquid polyester and an effective amount (as disclosed hereinabove) of the AAL agent.

EXAMPLE II

Gelatin capsules comprising a unit dose of an AAL agent and a liquid polyester are prepared by conventional means, as follows:

Ingredient	Amount per Capsule
Sucrose octaoleate	3500 mg.
Hydrogenated palm oil	750 mg.

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The above capsules are administered orally three times daily (three per meal/70 kg. man) over a one-month period. This treatment regimen substantially inhibits cholesterol uptake in the patient and decreases the serum level of cholesterol. No anal leakage from use of the capsules is noted.

The hydrogenated palm oil in Example II is replaced by an equivalent amount of tristearin and equivalent anti-anal leakage results are secured.

When oleic acid is used to replace the hydrogenated palm oil, no substantial anti-anal leakage effect is noted.

EXAMPLE III

Gelatin capsules comprising an AAL agent and a liquid polyester are as follows:

Ingredient	Mg. per Capsule
Sucrose octoate	2000
Ethyl stearate	250

Three capsules of the type prepared in Example III are administered orally five times daily (three capsules per occurrence) to inhibit cholesterol uptake and decrease the level of cholesterol in the circulatory system of a 70 kg. patient afflicted with hypercholesterolemia. At these dosage levels, no anal leakage is noted. Similar dosages of the foregoing capsules without ethyl stearate cause an undesired leakage of sucrose octanoate through the anal sphincter.

EXAMPLE IV

A highly palatable, low calorie composition suitable for use by patients on anti-hypercholesterolemic therapeutic regimens and/or as a cooking fat substitute by individuals on an anti-hyperlipidemic diet is as follows:

Ingredient	% by Weight
Liquid sucrose polyester*	50
Cocoa butter	50

*Avg. 7.5 ester of sucrose and oleic acid.

The composition of the foregoing type is suitable for use in standard fashion as a low calorie cooking fat. No anal leakage of the liquid polyester is noted.

The composition of Example IV is ingested at a rate of 50 g./day (150 lb. patient) and reduces serum cholesterol without anal leakage of the liquid polyester.

In the composition of Example IV the natural cocoa butter is replaced by an equivalent amount of the position-specific triglycerides SOO, SOS, OSS, PSS, ASS and BSS, respectively, and equivalent compositions are secured.

EXAMPLE V

A plastic shortening is prepared from the following ingredients.

Ingredient	% by Weight
Cocoa butter	40
Liquid xylitol pentaoleate	50
OSS	10

The composition of Example V is prepared by thoroughly mixing the indicated ingredients. The composition is suitable for use in frying and other types of cook-

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ing where a plastic fat is employed. The fat composition of Example V can also be employed in the preparation of baking doughs suitable for use by the hypercholesterolemic patient. Continued ingestion of the plastic shortening of Example V, or foods made therefrom, reduces the body's serum cholesterol level without anal leakage of the xylitol pentaoleate.

The shortening of Example V can be used by the normal or hyperlipidemic patient to control body weight.

EXAMPLE VI

A non-anal leakage, low calorie, anti-hypercholesterolemic composition prepared with an edible, but non-absorbable, non-digestible, solid polyester AAL agent is as follows:

Ingredient	% by Weight
Sucrose octoate	70
Sucrose octastearate	30

The composition of Example VI is prepared by simply combining the ingredients. The composition is suitable for use by the hypercholesterolemic patient to reduce serum cholesterol levels; no anal leakage is noted.

The composition of Example VI can be used by the normal or hyperlipidemic patient to control serum cholesterol without increasing caloric intake.

In the composition of Example VI the sucrose octastearate is replaced by an equivalent amount of sucrose heptastearate, and sucrose octapalmitate, respectively, as the AAL agent and equivalent results are secured.

What is claimed is:

1. A composition of matter, comprising:

(a) an edible, non-absorbable, non-digestible liquid polyol fatty acid polyester having at least 4 fatty acid ester groups, wherein the polyol is selected from the group consisting of sugars and sugar alcohols containing from 4 to 8 hydroxyl groups and wherein each fatty acid group has from about 8 to about 22 carbon atoms; and

(b) sufficient anti-anal leakage agent to prevent leakage of said liquid polyester through the anal sphincter, wherein the anti-anal leakage agent is a member selected from the group consisting of: edible C_{12} and higher saturated fatty acids, and their edible salts; edible, digestible sources of C_{12} and higher saturated fatty acids, other than tristearin or C_{18} saturated fatty acid esters of 1,3-propanediol; edible, non-absorbable, non-digestible solid polyol fatty acid polyesters having at least 4 fatty acid ester groups, wherein the polyol is selected from the group consisting of sugars and sugar alcohols containing from 4 to 8 hydroxyl groups and wherein each fatty acid group is a saturated fatty acid group having from about 8 to about 22 carbon atoms; and edible, non-digestible esters of alpha-branched chain C_{10} - C_{18} fatty acids.

2. A composition according to claim 1 wherein the liquid polyol fatty acid polyester contains no more than about 2 free hydroxyl groups.

3. A composition according to claim 2 wherein the fatty acid ester groups contain from about 14 to about 18 carbon atoms.

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4. A composition according to claim 3 wherein the polyol is a member selected from the group consisting of erythritol, xylitol, sorbitol, glucose and sucrose.

[5. A composition according to claim 4 wherein the polyol is sucrose.]

[6. A composition according to claim 5 wherein the sucrose fatty acid polyester is a member selected from the group consisting of the hexaoleate, heptaoleate and octaoleate of sucrose, and mixtures thereof.]

[7. A composition according to claim 1 wherein the anti-anal leakage agent is a member selected from the group consisting of: edible C₁₂ and higher saturated fatty acids, and their edible salts; edible, digestible sources of C₁₂ and higher saturated fatty acids; edible, non-absorbable, non-digestible solid polyol fatty acid polyesters having at least 4 fatty acid ester groups, wherein the polyol is selected from the group consisting of sugars and sugar alcohols containing from 4 to 8 hydroxyl groups and wherein each fatty acid group has from about 8 to about 22 carbon atoms; and edible, non-digestible esters of alpha-branched chain C₁₀-C₁₈ fatty acids.]

8. A composition according to claim [7] / which comprises at least about 10% by weight of the anti-anal leakage agent.

9. A composition according to claim [7] / which comprises at least about 20% by weight of the anti-anal leakage agent.

10. A composition according to claim [7] / which comprises from about 20% to about 50% by weight of the anti-anal leakage agent.

11. A composition according to claim [7] / which comprises from about 10% to about 50% by weight of an anti-anal leakage agent selected from the group consisting of edible C₁₂-C₂₄ saturated fatty acids and edible salts of C₁₂-C₂₄ saturated fatty acids.

12. A composition according to claim [7] / which comprises from about 10% to about 50% by weight of an anti-anal leakage agent selected from the group consisting of edible, digestible sources of C₁₂-C₂₄ saturated fatty acids, and mixtures thereof, *other than tristearin or C₁₈ saturated fatty acid esters of 1,3-propanediol.*

13. A composition according to claim 12 wherein the anti-anal leakage agent is a lower alkyl ester of C₁₂-C₂₄ saturated fatty acids, or mixtures thereof.

14. A composition according to claim 12 wherein the anti-anal leakage agent comprises substantially saturated triglyceride esters of C₁₂-C₂₄ fatty acids, or mixtures thereof, *other than tristearin.*

15. A composition according to claim 14 wherein the anti-anal leakage agent is hydrogenated palm oil.

16. A composition according to claim 14 wherein the anti-anal leakage agent is natural or synthetic cocoa butter.

17. A composition according to claim 14 wherein the anti-anal leakage agent is an edible position-specific triglyceride selected from the group consisting of: the 1-stearoyl, 1-palmitoyl, 1-arachidoyl and 1-behenoyl 2,3-dioleins; the 2-oleoyl 1,3-distearins, 1,3-dipalmitins, 1,3-diarachidins and 1,3-dibehenins; 1-oleoyl distearin; 1-palmitoyl distearin; 1-arachidoyl distearin; and 1-behenoyl distearin; and mixtures thereof.

18. A composition according to claim 17 which comprises from about 20% to about 40% by weight of the position-specific triglyceride.

19. A composition according to claim [7] / which comprises from about 20% to about 50% by weight of an anti-anal leakage agent selected from the group con-

sisting of edible, non-absorbable, non-digestible solid polyol fatty acid polyesters having at least 4 fatty acid ester groups, wherein the polyol is selected from the group consisting of sugars and sugar alcohols containing from 4 to 8 hydroxyl groups and wherein each fatty acid group [has] *is a saturated fatty acid group having from about [8] 10 to about 22 carbon atoms.*

20. A composition according to claim 19 wherein the anti-anal leakage agent is selected from the group consisting of [C₁₀-C₂₂ saturated fatty acid polyol esters] *sucrose octastearate, sucrose octapalmitate, sucrose heptastearate, xylitol pentastearate and galactose pentapalmitate.*

21. A method for inhibiting the absorption of cholesterol in animals without causing an anal leakage effect comprising systemically administering to an animal susceptible to or afflicted with hypercholesterolemia successive therapeutically effective doses of a composition comprising: a non-absorbable, non-digestible liquid polyol fatty acid polyester having at least 4 fatty acid ester groups, wherein the polyol is selected from the group consisting of sugars and sugar alcohols containing from 4 to 8 hydroxyl groups and wherein each fatty acid group has from about 8 to about 22 carbon atoms and sufficient anti-anal leakage agent to prevent leakage of said liquid polyester through the anal sphincter.

22. A method according to claim 21 wherein the anti-anal leakage agent is a member selected from the group consisting of: edible C₁₂-C₂₄ saturated fatty acids, and their edible salts; edible, digestible sources of C₁₂-C₂₄ saturated fatty acids; edible, non-absorbable, non-digestible solid polyol fatty acid polyesters having at least 4 fatty acid ester groups, wherein the polyol is selected from the group consisting of sugars and sugar alcohols containing from 4 to 8 hydroxyl groups and wherein each fatty acid group has from about 8 to about 22 carbon atoms; and edible, non-digestible esters of alpha-branched chain C₁₀-C₁₈ fatty acids.

23. A method according to claim 22 wherein the composition comprises at least about 10% by weight of the anti-anal leakage agent.

24. A method according to claim 23 wherein the composition comprises at least about 20% by weight of the anti-anal leakage agent.

25. A low calorie fat-containing food composition comprising non-fat ingredients and fat ingredients, wherein from about 10% to about 100% of the total fat ingredients comprise:

(a) a portion comprising an edible, non-absorbable, non-digestible liquid polyol fatty acid polyester having at least 4 fatty acid ester groups, wherein the polyol is selected from the group consisting of sugars and sugar alcohols containing from 4 to 8 hydroxyl groups and wherein each fatty acid group has from about 8 to about 22 carbon atoms; and

(b) sufficient anti-anal leakage agent, *other than tristearin or C₁₈ saturated fatty acid esters of 1,3-propanediol*, to prevent leakage of said liquid polyester through the anal sphincter.

26. A composition according to claim 25 wherein the liquid polyol fatty acid polyester contains no more than about 2 free hydroxyl groups.

27. A composition according to claim 26 wherein the fatty acid ester groups contain from about 14 to about 18 carbon atoms.

28. A composition according to claim 27 wherein the polyol is a member selected from the group consisting of erythritol, xylitol, sorbitol, glucose and sucrose.

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55. A composition according to claim 51 which comprises from about 10% to about 50% by weight of an anti-anal leakage agent selected from the group consisting of edible C_{12} - C_{24} saturated fatty acids and edible salts of C_{12} - C_{24} fatty acids.

56. A composition according to claim 51 which comprises from about 10% to about 50% by weight of an anti-anal leakage agent selected from the group consisting of edible, digestible sources of C_{12} - C_{24} saturated fatty acids, and mixtures thereof.

57. A composition according to claim 56 wherein the anti-anal leakage agent is a lower alkyl ester of C_{12} - C_{24} saturated fatty acids, or mixtures thereof.

58. A composition according to claim 56 wherein the anti-anal leakage agent comprises substantially saturated triglyceride esters of C_{12} - C_{24} fatty acids, or mixtures thereof.

59. A composition according to claim 58 wherein the anti-anal leakage agent is hydrogenated palm oil.

60. A composition according to claim 58 wherein the anti-anal leakage agent is natural or synthetic cocoa butter.

61. A composition according to claim 58 wherein the anti-anal leakage agent is an edible position-specific triglyceride selected from the group consisting of: the 1-stearoyl, 1-palmitoyl, 1-arachidoyl and 1-behenoyl 2,3-dioleins; the 2-oleoyl 1,3-distearins, 1,3-dipalmitins, 1,3-diarachidins and 1,3-dibehenins; 1-oleoyl distearin; 1-palmitoyl distearin; 1-arachidoyl distearin; and 1-behenoyl distearin; and mixtures thereof.

62. A composition according to claim 61 which comprises from about 20% to about 40% by weight of the position-specific triglyceride.

63. A composition according to claim 51 which comprises from about 20% to about 50% by weight of an anti-anal leakage agent selected from the group consisting of edible, non-absorbable, non-digestible solid polyol fatty acid polyesters having at least 4 fatty acid ester groups, wherein the polyol is selected from the group consisting of sugars and sugar alcohols containing from 4 to 8 hydroxyl groups and wherein each fatty acid group has from about 8 to about 22 carbon atoms.

64. A composition according to claim 63 wherein the anti-anal leakage agent is selected from the group consisting of C_{10} - C_{22} saturated fatty acid polyol esters.

65. A composition according to claim 12 wherein said edible sources of saturated fatty acids have an iodine value of from about 9.8 to about 50.

66. A composition according to claim 36 wherein said edible sources of saturated fatty acids have an iodine value of from about 9.8 to about 50.

67. A composition of matter, comprising:

(a) an edible, non-absorbable, non-digestible liquid polyol fatty acid polyester having at least 4 fatty acid ester groups, wherein the polyol is sucrose and wherein each fatty acid group has from about 8 to about 22 carbon atoms; and

(b) sufficient anti-anal leakage agent to prevent leakage of said liquid polyester through the anal sphincter, wherein the anti-anal leakage agent is a member selected from the group consisting of: edible C_{12} and higher saturated fatty acids, and their edible salts; edible, digestible sources of C_{12} and higher saturated fatty acids; edible, non-absorbable, non-digestible solid polyol fatty acid polyesters having at least 4 fatty acid ester groups, wherein the polyol is selected from the group consisting of sugars and sugar alcohols containing from 4 to 8 hydroxyl groups and wherein

each fatty acid group is a saturated fatty acid group having from about 8 to about 22 carbon atoms; and edible, non-digestible esters of alpha-branched chain C_{10} - C_{18} fatty acids.

68. A composition according to claim 67 wherein the sucrose fatty acid polyester is a member selected from the group consisting of the hexaoleate, heptaoleate and octaoleate of sucrose, and mixtures thereof.

69. A composition according to claim 67 which comprises from about 20% to about 50% by weight of an anti-anal leakage agent selected from the group consisting of edible, non-absorbable, non-digestible solid polyol fatty acid polyesters having at least 4 fatty acid ester groups, wherein the polyol is sucrose and wherein each fatty acid group is a saturated fatty acid group having from about 10 to about 22 carbon atoms.

70. A composition according to claim 69 wherein the anti-anal leakage agent is selected from the group consisting of sucrose octastearate, sucrose octapalmitate, and sucrose heptastearate.

71. A low calorie fat-containing food composition comprising non-fat ingredients and fat ingredients, wherein from about 10% to about 100% of the total fat ingredients comprise:

(a) a portion comprising an edible, non-absorbable, non-digestible liquid polyol fatty acid polyester having at least 4 fatty acid ester groups, wherein the polyol is sucrose and wherein each fatty acid group has from about 8 to about 22 carbon atoms; and

(b) sufficient anti-anal leakage agent to prevent leakage of said liquid polyester through the anal sphincter.

72. A composition according to claim 71 wherein the sucrose fatty acid polyester is a member selected from the group consisting of the hexaoleate, heptaoleate and octaoleate of sucrose, and mixtures thereof.

73. A composition according to claim 71 wherein the liquid polyester portion of the fat ingredients comprises from about 20% to about 50% by weight of an anti-anal leakage agent selected from the group consisting of edible, non-absorbable, non-digestible solid polyol fatty acid polyesters having at least 4 fatty acid ester groups, wherein the polyol is selected from the group consisting of sugars and sugar alcohols containing from 4 to 8 hydroxyl groups and wherein each fatty acid group has from about 8 to about 22 carbon atoms.

74. A composition according to claim 73 wherein the anti-anal leakage agent is selected from the group consisting of C_{10} - C_{22} saturated fatty acid polyol esters of sucrose.

75. A composition according to claim 74 wherein the anti-anal leakage agent is selected from the group consisting of sucrose octastearate, sucrose octapalmitate and sucrose heptastearate.

76. A composition of matter, comprising fat ingredients and nonfat ingredients in which at least a portion of the fat ingredients comprise:

(a) an edible, non-absorbable, non-digestible liquid polyol fatty acid polyester having at least 4 fatty acid ester groups, wherein the polyol is selected from the group consisting of sugars and sugar alcohols containing from 4 to 8 hydroxyl groups and wherein each fatty acid group has from about 8 to about 22 carbon atoms; and

(b) sufficient anti-anal leakage agent, other than tristearin or C_{18} saturated fatty acid esters of 1,3-propanediol, to prevent leakage of said liquid polyester through the anal sphincter.

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REYES & REYES

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Señor

SUPERINTENDENTE DE INDUSTRIA Y COMERCIO

E. S. D.

REF: Expediente 00-68859

TÍTULO SOLICITADO: "Formulaciones en dispersión que contienen orlistat con eficacia mejorada y disminución de efectos secundarios"

SOLICITANTE: F. Hoffmann - La Roche AG

APODERADO: José Antonio Lloreda

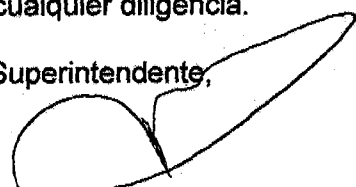
TRÁMITE: Sustitución de Poder

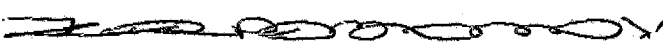
JOSÉ LUIS REYES VILLAMIZAR, mayor de edad y vecino de Bogotá, conocido apoderado de la sociedad opositora **TECNOQUÍMICAS S.A.** en el asunto de la referencia, de manera respetuosa manifiesto que, debidamente facultado para actuar, sustituyo el poder a mí conferido, con idénticas facultades, al Doctor **JUAN PABLO REYES VILLAMIZAR**, mayor de edad y vecino de Bogotá, identificado como aparece al pie de su firma, para que asuma en su estado actual y lleve a su culminación la defensa de los intereses de mi representada en el asunto de la referencia.

En ejercicio de su encargo, el apoderado queda ampliamente facultado para realizar todas las gestiones necesarias para la oportuna atención y defensa de los intereses de la empresa que represento, y queda investido de las facultades mencionadas en el artículo 70 del Código de Procedimiento Civil, en especial para notificarse de los autos y providencias de toda índole que se emitan en desarrollo del proceso, aportar, presentar y solicitar pruebas, peticiones y recursos de cualquier índole, presentar demandas, constituir y prestar cauciones, recibir, desistir, conciliar, transigir, sustituir, reasumir, recibir y cobrar depósitos judiciales, así como ejercer todas las demás atribuciones requeridas para el cabal desarrollo de este mandato. El suscrito se reserva la facultad de reasumir la representación de los intereses de la aludida compañía en cualquier momento y para cualquier diligencia.

Señor Superintendente,

Acepto,


JOSE LUIS REYES VILLAMIZAR
C.C. 79.152.473 de Usaquén
T.P.A. 44.655 del C.S.J.


JUAN PABLO REYES VILLAMIZAR
C.C. 80.419.709 de Usaquén
T.P.A. 92.189 del C.S.J.

[Handwritten signature]

NOTARIA TREINTA DE BOGOTÁ, D.C.

Este memorial dirigido a SUPERINTENDENTE DE INDUSTRIA Y COMERCIO.

Ha presentado personalmente ante el suscrito Notario por

JOSE LUIS REYES VILLAMAZAR

Identificado (s) con Cds. Nos. 79.152.473 USARVEN

T. P. de Abogado No. 44.655. C-3-5 ABR 2007

Bogotá, D.C. de

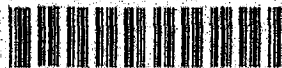
Diligenció [Handwritten signature]

EL NOTARIO





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CERTIFICADO NACIONAL

CAMARA DE COMERCIO DE CALI

Fecha: 20070430 Hora Certificado: 122802

Operacion: 02NA80430028 PAGINA NO 1

null

CERTIFICA:

NOMBRE: LABORATORIO FRANCO COLOMBIANO LAFRANCO S.A.
DOMICILIO: CALI VALLE
DIRECCION COMERCIAL: ---K 1 46 84
DIRECCION NOTIFICACION JUDICIAL: ---K 1 46 84
CIUDAD: CALI
MATRICULA MERCANTIL NRO. 5233-4 FECHA MATRICULA: 02 DE OCTUBRE DE 1958
DIRECCION ELECTRONICA: esperanzacortes@lafranco.net

AFILIADO

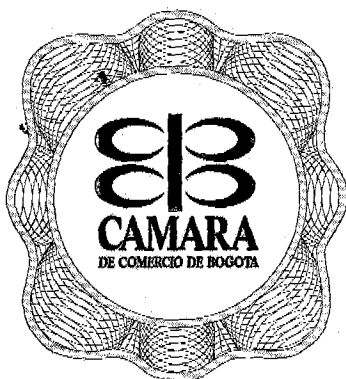
CERTIFICA:

NIT: 890301463-8
QUE POR ESCRITURA NRO. 1434 DEL 29 DE SEPTIEMBRE DE 1958 NOTARIA CUARTA DE CALI INSCRITA EN LA CAMARA DE COMERCIO EL 02 DE OCTUBRE DE 1958 BAJO EL NRO. 18319 DEL LIBRO IX SE CONSTITUYO LA SOCIEDAD DENOMINADA LABORATORIO FRANCO COLOMBIANO LAFRANCO S.A.

CERTIFICA:

REFORMAS	DOCUMENTO	FECHA DOC	ORIGEN	FECHA INS	NRO
INS LIBRO	E.P. 1104	30/06/1959	NOTARIA CUARTA DE CALI	07/07/1959	19467
	E.P. 2309	26/12/1959	NOTARIA CUARTA DE CALI	29/12/1959	20089
	E.P. 1725	24/07/1962	NOTARIA CUARTA DE CALI	26/07/1962	24528
	E.P. 1824	31/07/1963	NOTARIA CUARTA DE CALI	14/08/1963	

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CERTIFICADO NACIONAL

CAMARA DE COMERCIO DE CALI

Fecha : 20070430

Hora Certificado : 122802

Operacion: 02NAB0430028

PAGINA No. 3

625 IX-

CERTIFICA:

VIGENCIA: 29 DE SEPTIEMBRE DEL AÑO 2057

CERTIFICA:

OBJETO SOCIAL. SE OCUPA EN: A) FABRICACION, DISTRIBUCION Y VENTA EN EL TERRITORIO DE LA REPUBLICA DE COLOMBIA O EN EL EXTRANJERO DE CUALESQUIERA TIPOS DE VACUNAS, PRODUCTOS QUIMICOS, FARMACEUTICOS ALIMENTICIOS FUNCIONALES, COSMETICOS Y FISIOLOGICOS, REACTIVOS, ANTIBIOTICOS PARA USO HUMANO Y VETERINARIO, PRODUCTOS DIETETICOS, COLORANTES DE PERFUMERIA Y AFINES. B) LA REPRESENTACION DE CASAS FABRICANTES NACIONALES O EXTRANJERAS DE ESTOS MISMOS PRODUCTOS. C) FABRICACION, IMPORTACION, DISTRIBUCION Y VENTA DE CUALESQUIERA TIPOS DE PRODUCTOS VETERINARIOS. D) LA REALIZACION DE TODOS LOS ACTOS, CONTRATOS, CONVENIOS, DIRECTAMENTE RELACIONADOS CON LOS FINES ANTES INDICADOS. EN DESARROLLO DE SU OBJETO SOCIAL PODRA LA SOCIEDAD ADQUIRIR Y VENDER BIENES RAICES Y MUEBLES, DARLOS Y TOMARLOS EN ARRENDAMIENTO, GARANTIZAR CON HIPOTECA SOBRE LOS BIENES RAICES O CON PRENDA SOBRE LOS BIENES MUEBLES, OBLIGACIONES A CARGO DE LA SOCIEDAD, DAR Y RECIBIR A MUTUO COMERCIAL DINERO Y CELEBRAR LOS CONTRATOS COMERCIALES DE CAMBIO EN TODAS SUS MANIFESTACIONES, FUNDAR EMPRESAS QUE TENGAN LA MISMA FINALIDAD SOCIAL O ASOCIARSE CON ELLAS.

CERTIFICA:

ORGANOS DE DIRECCION Y ADMINISTRACION: 1) ASAMBLEA GENERAL DE ACCIONISTAS; 2) JUNTA DIRECTIVA; 3) GERENCIA GENERAL. TAMBIEN TENDRA UN REVISOR FISCAL.

ADMINISTRACION: LA ADMINISTRACION INMEDIATA DE LA SOCIEDAD, SU REPRESENTACION LEGAL Y LA GESTION DE LOS NEGOCIOS SOCIALES ESTARAN A CARGO DE UN GERENTE, DESIGNADO POR LA ASAMBLEA GENERAL DE ACCIONISTAS, PARA PERIODOS DE DE DOS (2) AÑOS REELEGIBLE INDEFINIDAMENTE Y REMOVIBLE LIBREMENTE POR ELLA EN CUALQUIER TIEMPO.

PARAGRAFO PRIMERO. SUPLENTES: EL GERENTE Y REPRESENTANTE LEGAL TENDRA LOS SIGUIENTES SUPLENTES: PRIMERO, SEGUNDO Y TERCERO QUE LO REEMPLAZARAN EN LOS CASOS DE AUSENCIAS ACCIDENTAL, TEMPORAL Y ABSOLUTA CON LAS LIMITACIONES QUE MAS ADELANTE SE ESTABLECEN.

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CERTIFICADO NACIONAL

CAMARA DE COMERCIO DE CALI

Fecha : 20070430

Hora Certificado : 122802

Operacion: 02NA80430028

PAGINA No. 4

PARAGRAFO SEGUNDO. EL TERCER SUPLENTE DEL GERENTE GENERAL Y REPRESENTANTE LEGAL ESTARA LIMITADO EN SUS FUNCIONES A: COMPROMETER LOS NEGOCIOS SOCIALES EN CUANTIA NO SUPERIOR A CUATRO MIL DOSCIENTOS SALARIOS MINIMOS MENSUALES LEGALES VIGENTES (4.200 SMLV); CELEBRAR CONTRATOS COMERCIALES DE COMPRAVENTA EN GENERAL YA SEA CON LA NACION (MINISTERIOS Y DEPARTAMENTOS ADMINISTRATIVOS), ENTIDADES DESCENTRALIZADAS (ESTABLECIMIENTOS PUBLICOS, EMPRESAS INDUSTRIALES Y COMERCIALES DEL ESTADO, SOCIEDADES DE ECONOMIA MIXTA), EMPRESAS SOCIALES CIVILES Y COMERCIALES, CUALQUIERA QUE SEA SU NATURALEZA CON FACULTADES PARA EXIGIR O SUSCRIBIR LOS DOCUMENTOS Y GARANTIAS NECESARIOS HASTA LA CUANTIA ANTES MENCIONADA.

FUNCIONES DEL GERENTE: A) ... B) EJECUTAR Y HACER CUMPLIR LOS ACUERDOS Y DECISIONES DE LA ASAMBLEA GENERAL DE ACCIONISTAS Y DE LA JUNTA DIRECTIVA Y HACER USO DE LA RAZON SOCIAL. C) REPRESENTAR LEGALMENTE A LA SOCIEDAD CONFORME A LA LEY ANTE TODAS LAS AUTORIDADES CIVILES, JUDICIALES, MILITARES, SANITARIAS, DE POLICIA, ADUANALES, POSTALES, ETC. G) LLEVAR A CABO LA GESTION COMERCIAL Y FINANCIERA. H) TENDRA LA PLENA RESPONSABILIDAD DE LA ACCION ADMINISTRATIVA, LA COORDINACION Y LA SUPERVISION GENERAL DE LA SOCIEDAD, LAS CUALES CUMPLIRA CON ARREGLO A LAS NORMAS DE LOS ESTATUTOS.

EN EL EJERCICIO DE SUS FUNCIONES, EL GERENTE PUEDE: 1.- COMPARECER EN LOS JUICIOS, TRANSIGIR Y COMPROMETER LOS NEGOCIOS SOCIALES DE CUALQUIERA NATURALEZA QUE FUEREN, INTERPONER TODO GENERO DE RECURSOS Y CONSTITUIR APODERADOS QUE LO REPRESENTEN JUDICIAL O EXTRAJUDICIALMENTE. 2.- ENAJENAR A CUALQUIER TITULO Y COMPRAR BIENES MUEBLES, CELEBRAR CONTRATOS COMERCIALES DE COMPRA Y VENTA EN GENERAL YA SEA CON LA NACION (MINISTERIOS Y DEPARTAMENTOS ADMINISTRATIVOS), ENTIDADES DESCENTRALIZADAS (ESTABLECIMIENTOS PUBLICOS), EMPRESAS INDUSTRIALES Y COMERCIALES DEL ESTADO, SOCIEDADES DE ECONOMIA MIXTA), EMPRESAS O SOCIEDADES CIVILES Y COMERCIALES CUALQUIERA QUE SEA SU NATURALEZA Y SU CUANTIA, CON AMPLIAS FACULTADES QUE EXIGIR O SUSCRIBIR LOS DOCUMENTOS, Y GARANTIAS NECESARIAS. CONTRATAR PRESTAMOS CUALQUIERA QUE SEA SU CUANTIA, CELEBRAR EL CONTRATO COMERCIAL DE MUTUO EN TODAS SUS MANIFESTACIONES Y SUSCRIBIR LOS DOCUMENTOS Y COMPROMISOS RESPECTIVOS. HACER DEPOSITOS EN BANCOS Y AGENCIAS BANCARIAS, FIRMAR CHEQUES, LETRAS, PAGARES, GIROS, LIBRANZAS Y CUALQUIER OTRO DOCUMENTO, ASI COMO NEGOCIAR ESTOS INSTRUMENTOS, TENERLOS, COBRARLOS, PAGARLOS, DESCARGARLOS, ETC.

CERTIFICA:

DOCUMENTO: ACTA No. 99 DEL 14 DE MARZO DE 2002

ORIGEN: ASAMBLEA GENERAL DE ACCIONISTAS

INSCRIPCION: 09 DE SEPTIEMBRE DE 2002 No. 14675 DEL LIBRO IX

FUE(RON) NOMBRADO(S):

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CERTIFICADO NACIONAL

CAMARA DE COMERCIO DE CALI

Fecha: 20070430

Hora Certificado: 122802

Operacion: 02NA80430028

PAGINA No 5

VICEPRESIDENTE

ROBERTO S. VENTURA PAULY

C.C. 16697614

GERENTE GENERAL Y REPRESENTANTE LEGAL

JUAN MARIA RENDON GUTIERREZ

C.C. 17125100

PRIMER SUPLENTE DEL GERENTE

ESTHER ISABEL VENTURA DE RENDON

C.C. 38979831

SEGUNDO SUPLENTE DEL GERENTE

ROBERTO M. VENTURA CRISPINO

C.C. 9086003

PRESIDENTE

ESTHER ISABEL VENTURA DE RENDON

C.C. 38979831

CERTIFICA:

DOCUMENTO: ACTA No. 105 DEL 09 DE NOVIEMBRE DE 2004

ORIGEN: ASAMBLEA DE ACCIONISTAS

INSCRIPCION: 17 DE FEBRERO DE 2005 No. 2032 DEL LIBRO IX

FUE (RON) NOMBRADO(S):

TERCER SUPLENTE DEL GERENTE

JUAN PABLO REYES VILLAMIZAR

C.C. 80419709

CERTIFICA:

CONTINUA

CERTIFICADO NACIONAL

CAMARA DE COMERCIO DE CALI

Fecha : 20070430

Hora Certificado : 122802

Operacion: 02NA80430028

PAGINA No. 6

DOCUMENTO: ACTA No. 99 DEL 14 DE MARZO DE 2002

ORIGEN: ASAMBLEA GENERAL DE ACCIONISTAS

INSCRIPCION: 09 DE SEPTIEMBRE DE 2002 No. 14675 DEL LIBRO IX

DOCUMENTO: ACTA No. 105 DEL 09 DE NOVIEMBRE DE 2004

ORIGEN: ASAMBLEA DE ACCIONISTAS

INSCRIPCION: 17 DE FEBRERO DE 2005 No. 2031 DEL LIBRO IX

FUE (RON) NOMBRADO (S)

JUNTA DIRECTIVA

PRINCIPALES

PRIMER RENGLON

ESTHER ISABEL VENTURA DE RENDON

C.C.38979831

SEGUNDO RENGLON

ROSA VICTORIA VENTURA DE VISBAL

C.C.38992048

TERCER RENGLON

JUAN PABLO REYES VILLAMIZAR

C.C.80419709

SUPLENTES

PRIMER RENGLON

JUAN MARIA RENDON GUTIERREZ

C.C.17125100

SEGUNDO RENGLON

ROBERTO M. VENTURA CRISPINO

C.C.9086003

TERCER RENGLON

ROBERTO S. VENTURA PAULY

C.C.16697614

CERTIFICA:

***** CONTINUA *****



CERTIFICADO NACIONAL

CAMARA DE COMERCIO DE CALI

Fecha : 20070430

Hora Certificado : 122802

Operation: 02NA80430028

PAGINA=NO ME

DOCUMENTO: ACTA No. 99 DEL 14 DE MARZO DE 2002

ORIGEN: ASAMBLEA GENERAL DE ACCIONISTAS

INSCRIPCION: 09 DE SEPTIEMBRE DE 2002 No. 14675 DEL LIBRO IX

FUE (RON) NOMBRADO (S) :

REVISOR FISCAL

ALFREDO LOPEZ & CIA. LTDA

NIT. 800026893-5

DOCUMENTO: DOCUMENTO PRIVADO DEL 20 DE OCTUBRE DE 2006

ORIGEN: ALFREDO LOPEZ & CIA LTDA

INSCRIPCION: 07 DE NOVIEMBRE DE 2006 No. 12672 DEL LIBRO IX

FUE (RON) NOMERADO (S)

REVISOR FISCAL PRINCIPAL

ALFREDO LÓPEZ CAMPO

C. C. 8241912

REVISOR FISCAL SUPLENTE

GEOVANA GONZALEZ GALINDO

C. C. 66959852

CAPITAL AUTORIZADO: \$7.500.000.000

NUMERO DE ACCIONES: 750.000.000

VALOR NOMINAL: \$10

CAPITAL SUSCRITO: \$6,000,000,000

NUMERO DE ACCIONES: 600,000,000

VALOR NOMINAL: \$10

CAPITAL PAGADO: \$6,000,000,000

NUMERO DE ACCIONES: 600,000,000

CERTIFICA:

*** CONTINUA

CERTIFICADO NACIONAL

CAMARA DE COMERCIO DE CALI

Fecha: 20070430

Hora Certificado: 122802

Operacion: 02NA80430028

PAGINA No. 18

VALOR NOMINAL: \$10

CERTIFICA:

QUE A NOMBRE DE LA SOCIEDAD FIGURA MATRICULADO EN LA CAMARA DE COMERCIO BAJO EL NRO 5234-2 ESTABLECIMIENTO DE COMERCIO: LABORATORIO FRANCO COLOMBIANO

LAFRANCOL

UBICADO EN: K 146 84 DE CALI

RENOVO POR EL AÑO 2007

CERTIFICA:

QUE A NOMBRE DE LA SOCIEDAD FIGURA MATRICULADO EN LA CAMARA DE COMERCIO BAJO EL NRO 369810-2 ESTABLECIMIENTO DE COMERCIO: LABORATORIO FRANCO COLOMBIANO

LAFRANCOL S A

UBICADO EN: K 146 A 32 DE CALI

FECHA MATRICULA: 29 DE ABRIL DE 1994

RENOVO POR EL AÑO 2007

CERTIFICA:

QUE A NOMBRE DE LA SOCIEDAD FIGURA MATRICULADO EN LA CAMARA DE COMERCIO BAJO EL NRO 369809-2 ESTABLECIMIENTO DE COMERCIO: LABORATORIO FRANCO COLOMBIANO

LAFRANCOL S A

UBICADO EN: K 146 A 70 DE CALI

FECHA MATRICULA: 29 DE ABRIL DE 1994

RENOVO POR EL AÑO 2007

CERTIFICA:

QUE LA SOCIEDAD EFECTUO LA RENOVACION DE SU MATRICULA MERCANTIL EL 29 DE MARZO DE 2007

CERTIFICA:

CONTINUA

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CERTIFICADO NACIONAL

CAMARA DE COMERCIO DE CALI

Fecha: 20070430 Hora Certificado: 122802

Operacion: 02NA80430028 PAGINA No. 9

QUE NO FIGURAN OTRAS INSCRIPCIONES QUE MODIFIQUEN TOTAL O PARCIALMENTE EL PRESENTE CERTIFICADO.

LOS ACTOS Y DOCUMENTOS REGISTRADOS QUEDAN EN FIRME CINCO (5) DIAS HABILDES DESPUES DE LA FECHA DE SU INSCRIPCION, SIEMPRE Y CUANDO DENTRO DE DICHO TERMINO NO SEAN OBJETO DE RECURSOS EN LA VIA GUBERNATIVA.

DE CONFORMIDAD CON EL DECRETO 2150 DE 1.995 Y LA AUTORIZACION IMPARTIDA POR LA SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO LA FIRMA MECANICA QUE APARECE A CONTINUACION TIENE PLENA VALIDEZ PARA TODOS LOS EFECTOS LEGALES.

DADO EN CALI A LOS 30 DIAS DEL MES DE ABRIL DEL AÑO 2007 HORA: 12:24:29

ES



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62
08
09
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12

The image features a large, stylized graphic of the number '1' with a diagonal line through it, set against a background of repeating text. The text is a dense, repeating pattern of the words 'CAMARA DE COMERCIO DE BOGOTA' and 'BOGOTA' in a sans-serif font, arranged in a grid-like fashion. The overall effect is a high-contrast, graphic design.

**SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIVISIÓN DE NUEVAS CREACIONES**

Radicación N° 00068859

Una vez recibido y estudiado el recurso de reposición presentado por el interesado, contra lo que dicta la Resolución N° 7996 de 23 de marzo de 2007 donde se Concede el otorgamiento de Patente de Invención, se emite el siguiente concepto:

1. Documentos estudiados:

- 1.1. Descripción: Folios: 5 a 22.
- 1.2. Reivindicaciones: 1 a 28 (folios: 23 a 27) como se radicó inicialmente.
Modificadas: 1 a 24 (folios: 157 a 161);
Modificadas: 1 a 21 (folios: 218 a 221);
Modificadas: 1 a 19 (folios: 253 a 256);
Últimas modificadas: 1 a 10 (folios: 265 a 267).
- 1.3. Oposiciones: Tecnoquímicas y Lafrancol (folios: 63 a 71 y 99 a 118).
- 1.4. Rtas. Solicitante: Folios: 129 a 155 (a la oposición); folios: 202 a 215 (al requerimiento artículo 45); 225 a 230 (al 2° requerimiento art. 45); 242 a 251 (al 3° requerimiento art. 45); 260 a 263 (al 4° requerimiento art. 45).
- 1.5. Argumentos Recurso De Reposición: Interpuesto por los opositores: Tecnoquímicas y Lafrancol (folios: 297 a 317).
- 1.6. Prioridad: Folios: 36 a 48 (13-09-99, EPO 99118180.1).

2. Objeto de invención:

La presente solicitud se titula: "Composición farmacéutica de orlistat que contiene tensoactivos y dispersantes" (según lo sugerido en el concepto técnico de concesión).

El objeto de la presente solicitud se refiere a composiciones farmacéuticas que comprenden por lo menos un inhibidor de lipasa, de preferencia un inhibidor de lipasa gastrointestinal y pancreática, por ejemplo orlistat, por lo menos un tensoactivo y por lo menos un dispersante.

Según la descripción, ejemplos de inhibidores de lipasa son lipstatin y orlistat. El último se conoce también como tetrahidrolipstatin o THL y se deriva de un producto natural excretado por *Streptomyces toxytricini*. Esta clase de compuestos se encontró que exhibe in vitro así como in vivo actividad frente a varias lipasa, tal como lipasa lingual, lipasa pancreática, lipasa gástrica y lipasa carboxiléster. Su empleo para el control o prevención de obesidad e hiperlipidemia se describe por ejemplo, en la patente estadounidense 4598089.

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Orlistat se administra normalmente a dosis de 120 mg por comida y la dosificación es independiente de la masa corporal del sujeto humano. Orlistat actúa localmente en el tracto gastrointestinal e impide que la lipasa digiera triglicéridos y subsiguientemente inhibe la formación de productos de degradación de lípidos absorbibles. Por este motivo no se requiere la disponibilidad sistémica de inhibidores de lipasa, y en su lugar, se prefiere la residencia local en el tracto gastrointestinal. Las composiciones inhibidoras de lipasa administradas normalmente inhiben alrededor el 30% de la absorción de grasa después del consumo de una comida mixta; un aumento de la concentración de inhibidores de lipasa en la composición farmacéutica no aumenta su eficacia clínica mientras aumenta la intensidad de los efectos secundarios locales.

En el capítulo reivindicatorio se reclamó lo siguiente:

Reivindicaciones: 1 a 9 (folios: 265 y 266): una composición farmacéutica que comprende orlistat en una cantidad que varía entre 3 y 30% del peso total de la composición, uno o más tensioactivos en una cantidad que varía entre 1 y 20% del peso total de la composición, los cuales son seleccionados del grupo conformado por: vitamina E-(polietilenglicol 1000) succinato (TPGS), estearatos de poli(oxietileno); alquil éteres de poli(oxietileno), aceites de ricino de poli(oxietileno), glicéridos poliglicolizados, lecitinas y mezclas de los mismos, y uno o más dispersantes en una cantidad que varía entre 5 y 70% del peso total de la composición, los cuales son seleccionados del grupo compuesto por: glucosa, sorbitol, manitol, maltodextrina, lactosa, sacarosa, polietilenglicol, glicerol, triacetin, glicofurol, efervescentes y mezclas de los mismos y triglicéridos, diglicéridos, monoglicéridos, mezclas de di-, mono- y triglicéridos, vitamina E, acetato de tocoferol, terpenos, escualeno y mezclas de los mismos.

Reivindicación 10 (folio: 267): un procedimiento para la preparación de una composición farmacéutica de las reivindicaciones 1 a 9.

El problema técnico planteado en esta solicitud es: proporcionar composiciones inhibidoras de lipasa que son aptas para mejorar la eficacia clínica y/o la potencia del propio inhibidor, y/o minimizar o suprimir la pérdida anal de aceite (manchado oleoso) que es un efecto adverso.

La solución propuesta por la presente solicitud consiste en: una composición farmacéutica que comprende orlistat, uno o más tensioactivos y uno o más dispersantes.

El objeto de la solicitud definido anteriormente se clasificó en la IPC A 61K 9/10, 31/365, 31/19; C07D 305/12.

3. Respuesta a los argumentos de los Opositores:

3.1. Fundamentos con respecto a la Resolución de Concesión de la Patente de Invención:

El señor recurrente afirma lo siguiente: "... es del caso reiterar lo expuesto en el complemento de información remitido el 15/03/2007, en el cual se llamaba la atención del Despacho en cuanto a que los tamaños de muestra que se utilizan para probar la efectividad en la supuesta reducción de efectos adversos (goteo de grasa anal), son totalmente inadecuados para el caso..." (Folios: 298 y 299).

Si se revisa la tabla 1 de la solicitud de patente (ver folio: 22) se encuentra que la

tabla muestra algunos ejemplos de resultados in vivo del estudio realizado donde se muestra el número de muestras de heces conteniendo aceite libre/número de voluntarios. Como puede observarse allí, se trata de algunos ejemplos de comparación frente a la referencia (Xenical 120 mg) y no se muestra todo el estudio realizado por el solicitante, no obstante, estos ejemplos revelan que la composición farmacéutica solicitada soluciona un problema técnico existente, que si bien no se presentaba en todos los pacientes, sí era un efecto adverso que el solicitante lo consideró un problema técnico y le dio solución por medio de la composición farmacéutica propuesta en la solicitud de patente concedida.

En cuanto a la relevancia estadística de los datos mostrados en dicha tabla 1, se puede anotar que si bien en la solicitud no se encuentra descrito todo el estudio realizado sino unos cuantos ejemplos del mismo, lo cual puede no revelar datos más adecuados para el caso, estadísticamente hablando, no obstante, en patentes habitualmente el solicitante no revela la totalidad de sus estudios y/o ensayos, sino los más representativos y que revelan un salto tecnológico o solución a un problema técnico existente.

De todas maneras, vale la pena decir que la materia reivindicada, una composición farmacéutica de orlistat en una cantidad que varía entre 3 y 30% del peso total de la composición, uno o más tensioactivos en una cantidad que varía entre 1 y 20% del peso total de la composición, los cuales son seleccionados del grupo conformado por: vitamina E-(polietilenglicol 1000) succinato (TPGS), estearatos de poli(oxietileno); alquil éteres de poli(oxietileno), aceites de ricino de poli(oxietileno), glicéridos poliglicolizados, lecitinas y mezclas de los mismos, y uno o más dispersantes en una cantidad que varía entre 5 y 70% del peso total de la composición, los cuales son seleccionados del grupo compuesto por: glucosa, sorbitol, manitol, maltodextrina, lactosa, sacarosa, polietilenglicol, glicerol, triacetin, glicofurol, efervescentes y mezclas de los mismos y triglicéridos, diglicéridos, monoglicéridos, mezclas de di-, mono- y triglicéridos, vitamina E, acetato de tocoferol, terpenos, escualeno y mezclas de los mismos, no se encontraba en las anterioridades WO 98/34607 y WO 98/34630, documentos aportados en su momento por los Opositores, así como tampoco dicha composición fue sugerida por "Remington Farmacia" ni por "Farmacotecnia Teórica y Práctica", documentos que también se habían adjuntado como anterioridades relevantes en estudios técnicos anteriores.

Esta composición farmacéutica por no encontrarse en el estado de la técnica, por no resultar obvia para una persona medianamente versada en la materia ni haber sido sugerida por las anterioridades adjuntadas por el opositor y tenidas en cuenta por esta Oficina por resultar relevantes antes de las últimas modificaciones realizadas por el solicitante, y por haber solucionado un problema técnico existente, se observó que cumplía con los requisitos de Novedad y Nivel Inventivo.

3.2. Fundamentos con respecto a los documentos WO 00/009122 y RE 33996:

Si bien estos documentos se presentan en forma extemporánea, se puede decir lo siguiente: el documento WO 00/009122, por se publicado en fecha posterior a la fecha de prioridad de la solicitud en cuestión, no se puede considerar como anterioridad relevante.

En cuanto al documento RE 33996 los opositores afirman lo siguiente: "... se refiere a una composición para el tratamiento de la hipercolesterolemia que comprende un poliol de éster de ácido graso líquido y un agente antigoteo anal como por ejemplo un ácido graso saturado..." (Folios: 301 y 302).

Este documento menciona una formulación de dos agentes: un poliéster de ácido graso, donde el poliol es seleccionado de azúcares o azúcares hidroxilados que contienen 4 a 8 hidroxilos y donde cada ácido graso tiene de 8 a 22 carbonos; el otro agente es un poliéster líquido que puede ser un triglicérido por ejemplo derivados de aceite de palma, aceite de coco, aceite de almendra, y es un agente antigoteo anal.

Se puede observar que esta formulación no contiene un principio activo; además, de acuerdo a lo revelado en la descripción, dichas formulaciones son nutricionales (comestibles) y se emplean en dietas para la hiperlipidemia e inhiben la absorción de colesterol.

La formulación de la solicitud de patente estudiada, sí contiene principio activo (orlistat) y el vehículo está conformado por: uno o más tensioactivos en una cantidad que varía entre 1 y 20% del peso total de la composición, los cuales son seleccionados del grupo conformado por: vitamina E-(polietilenglicol 1000) succinato (TPGS), estearatos de poli(oxietileno); alquil éteres de poli(oxietileno), aceites de ricino de poli(oxietileno), glicéridos poliglicolizados, lecitinas y mezclas de los mismos, y uno o más dispersantes en una cantidad que varía entre 5 y 70% del peso total de la composición, los cuales son seleccionados del grupo compuesto por: glucosa, sorbitol, manitol, maltodextrina, lactosa, sacarosa, polietilenglicol, glicerol, triacetin, glicofurol, efervescentes y mezclas de los mismos y triglicéridos, diglicéridos, monoglicéridos, mezclas de di-, mono- y triglicéridos, vitamina E, acetato de tocoferol, terpenos, escualeno y mezclas de los mismos. Esta formulación hace que se inhiba la formación de lípidos, porque contiene orlistat que es un inhibidor de lipasa.

Como se puede apreciar, estas dos formulaciones no contienen los mismos componentes, aun cuando se relacionan en su uso en tratamientos contra la hiperlipidemia. Además, actúan de diferente manera, la del documento RE 33996 inhibiendo la absorción de colesterol y la de la presente solicitud, por su absorción en sangre, actúa inhibiendo las enzimas lipasas para que no se formen lípidos, lo cual es adecuado en tratamientos contra la obesidad e hiperlipidemia. Por lo tanto, no es relevante para el requisito de Novedad.

De igual modo, este documento RE 33996 no le sugiere a una persona medianamente versada en la materia la formulación de la solicitud evaluada, por cuanto no tiene principio activo y su modo de actuar es distinta al de la solicitud estudiada, aun cuando su uso esté relacionado con tratamientos contra la hiperlipidemia. Por lo tanto, tampoco es relevante para el requisito de Nivel Inventivo.

Teniendo en cuenta lo anterior y debido a que los argumentos presentados en el Recurso de Reposición no desvirtúan lo que dicta la Resolución N° 7996 donde se Concede el otorgamiento de la Patente de Invención, se recomienda ratificar dicha Resolución donde se Concede el Privilegio solicitado para las reivindicaciones 1 a 10 (folios: 265 a 267).

Lo anterior para los efectos legales a que haya lugar.

Bogotá, D.C., 16 de noviembre de 2007

CONCEPTO TÉCNICO No. 2269

EXAMINADOR TÉCNICO
Código No. 202005