MINISTERIO DE COMERCIO INDUSTRIA Y TURISMO
SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIRECCIÓN DE NUEVAS CREACIONES
E. S. D.

EXPEDIENTE No. : NC2017/0004974
TÍTULO : FORMULACIONES QUE COMPRENDEN EXTRACTO DE CANNABIS
SOLICITANTE : UNITED CANNABIS CORP

FERNANDO TRIANA SOTO, mayor y vecino de esta ciudad, identificado como aparece al pie de mi firma en mi calidad de apoderado de la sociedad **UNITED CANNABIS CORP.** constituida de acuerdo con las leyes de los Estados Unidos de América, con domicilio en 1600 Broadway Suite 1600 Denver, Colorado 80202, Estados Unidos de América, como resultado del examen de fondo realizado con fundamento al artículo 45 de la Decisión 486 de la Comisión de la Comunidad Andina, y conforme con la prórroga presentada oportunamente ante esa entidad, me permito presentar respuesta al oficio No. 8389 del 17 de mayo de 2023, de acuerdo con las siguientes consideraciones:

1. SOBRE LA SOLICITUD

1.1 En relación con el capítulo reivindicatorio, la Oficina indica que la reivindicación 1 emplea el término: "al menos", que es impreciso, por lo cual, no permite distinguir la invención del estado de la técnica. Se sugiere sustituirlo por un término preciso o un rango concreto. Agrega que, las reivindicaciones 1 y 2, emplean la expresión: "y/o", que precediendo una característica no es limitativa, porque hace opcional la característica y no limita el alcance de la reivindicación y sugiere corregir.

1.2 Con base en lo anterior, simultáneamente con la presentación de esta respuesta, presentamos una modificación de reivindicaciones, pagando la tasa oficial requerida, en la que constan las correcciones solicitadas.

En consecuencia, adjunto a este memorial se presenta un archivo que contiene de forma visible las enmiendas al pliego reivindicatorio. Así como el archivo con el juego de reivindicaciones en limpio y numeradas, conforme a la modificación presentada.

1.3 Las reivindicaciones 1, 3 y 4 se modifican en la presente respuesta. La reivindicación 2 se ha eliminado y se ha sustituido por la nueva reivindicación 2. El sustento de las enmiendas a las reivindicaciones y a la nueva reivindicación 2 puede

encontrarse en toda la solicitud, tal como se presentó originalmente, y al menos en los párrafos [0027], [0044]-[0054] y [0056]. No se añade ninguna materia nueva.

1.4 Respecto al requisito de claridad, la reivindicación 1 fue objetada por el término "al menos", que el Examinador considera impreciso. El solicitante respetuosamente no está de acuerdo. Sin aceptar la objeción y únicamente para acelerar el trámite, la reivindicación 1 se modifica en la presente respuesta para recitar "uno o más terpenos seleccionados del grupo que consiste en borneol, β-cariofileno, 1,8-cineol (eucaliptol), Δ-3-careno, d-limoneno, linalol, β-mirceno, α-pineno, pulegona, p-cimeno y terpineol-4-ol". De manera similar, la reivindicación 2 se modifica aquí para recitar "uno o más flavonoides seleccionados del grupo que consiste en β-sitosterol, cannflavina A, apigenina y quercetina".

1.5 El solicitante señala respetuosamente que las reivindicaciones 1 y 2 modificadas identifican los terpenos y flavonoides con precisión. Las reivindicaciones 1 y 2 se objetaron por carecer de claridad para la expresión "terpeno y/o flavonoide", solicitando el Examinador que se proporcionen las diferentes opciones en las reivindicaciones dependientes. El solicitante considera que esto podría ser un problema de traducción, ya que se entiende que la reivindicación 1 se refiere a un "terpeno o flavonoide" no "terpeno y/o flavonoide". Sin embargo, la reivindicación 1 se modifica para recitar "al menos un terpeno", mientras que la nueva reivindicación 2 recita "al menos un flavonoide". El solicitante sostiene respetuosamente que las enmiendas a las reivindicaciones superan este rechazo.

1.6 El Examinador ha objetado la reivindicación 1 sobre la base de que la descripción de la invención no sería lo suficientemente clara y completa para que una persona experta en la materia lleve a cabo la invención. Específicamente, el Examinador indica que no habría correspondencia suficiente entre la descripción y las reivindicaciones. El solicitante respetuosamente no está de acuerdo.

1.7 Respecto a la descripción, esa Oficina advierte que, en la memoria descriptiva no se encuentra descrita la forma como se obtiene la formulación reclamada, que la formulación reivindicada es completamente diferente a lo definido en la descripción. Adicionalmente, agrega que no se presentan pruebas técnicas, ni ejemplos, ni resultados concluyentes que permitan evidenciar que efectivamente la formulación líquida, presente eventuales efectos técnicos.

En respuesta, la Solicitante indica que la memoria descriptiva ilustra una formulación con la mezcla de cannabinoides reivindicada al menos en el párrafo [0064]. Que esta formulación puede contener uno o más terpenos que se describe al menos en el párrafo [0005], y el grupo específico de terpenos recitados por la reivindicación se divulga al menos en los párrafos [0045]-[0054] y [0058]. La

infusión en un triglicérido de cadena media se describe al menos en el párrafo [0007]. Por lo tanto, la formulación de la reivindicación 1 está completamente descrita en la descripción.

1.8 Con respecto al Ejemplo 3, el Examinador afirma que el Ejemplo no estaría de acuerdo con la formulación de la reivindicación 1 porque el Ejemplo discute la descarboxilación, mientras que la formulación reivindicada está dirigida a las formas ácidas de los cannabinoides. El solicitante respetuosamente no está de acuerdo con esta caracterización de los ejemplos.

En primer lugar, los ejemplos están destinados a demostrar realizaciones representativas de la invención, y no pretenden ser limitantes de la misma. En segundo lugar, el solicitante, en los párrafos [0094]-[0099], describe los métodos de extracción de cannabinoides ácidos, tal como se citan en la reivindicación. Además, los ejemplos del solicitante en el párrafo [0108] y la descripción detallada en los párrafos [0069]-[0072] discuten cómo se pueden extraer los cannabinoides en formas inactivas (carboxiladas, ácidas), seguidas de calentamiento para descarboxilar los cannabinoides. Así, una persona experta en la materia entendería fácilmente que los métodos de extracción incluidos en los Ejemplos, al menos en los párrafos [0101]-[0106] podrían modificarse para omitir el paso de calentamiento y producir extractos de cannabinoides que comprenden cannabinoides ácidos, como se reivindica.

1.9 En conclusión, se ha dado respuesta a cada uno de requerimientos de la primera parte del oficio de fondo.

Es de aclarar que las nuevas reivindicaciones corregidas con base en lo solicitado no amplían la materia inicialmente presentada, sino que hacen referencia a aclarar la presente invención conforme lo recomendado por el señor examinador. Con lo anterior, esperamos haber cumplido con los requerimientos de forma exigidos por este Despacho.

2 ESTADO DE LA TECNICA

2.1. El señor examinador, procede a determinar el examen del estado de la técnica con base en:

Ítem	Documento	Título	Fecha de publicación
D2	US20130059018	"PHYTOCANNABINOIDS IN THE TREATMENT OF CANCER"	07 de marzo de 2013
D6	WO2012144892	"MEDICAL USE FOR ACIDIC CANNABINOIDS"	26 de octubre de 2012

2.2 De acuerdo con el arte anterior, el examinador concluye que las reivindicaciones no comprenden actividad inventiva donde:

Ítem	Documento	Reivindicaciones afectadas	Requisito que afecta
D2	US20130059018	1 a 9	Nivel inventivo
D6	WO2012144892	1 a 9	Nivel inventivo

2.3 El Examinador cita de nuevo los mismos documentos D2 (US20130059018) y D6 (WO2012144892) donde las reivindicaciones han sido objetadas supuestamente por carecer de actividad inventiva. El solicitante respetuosamente no está de acuerdo.

2.4 La reivindicación 1 se dirige a:

> *"una formulación de cannabinoides líquidos, caracterizada porque la proporción mayor o igual al 95% (p/p) del total de cannabinoides es ácido tetrahidrocannabinólico (THCa), donde el ácido cannabidiólico (CBDa) es menor o igual al 1% (p/p) del total de cannabinoides, donde el ácido cannabinólico (CBNa) es menor o igual al 3% (p/p) del total de cannabinoides, donde el ácido cannabicroménico (CBCa) es menor o igual al 1% (p/p) del total de cannabinoides, donde la formulación comprende uno o más terpenos seleccionados del grupo que consiste en borneol, β-cariofileno, 1,8-cineol (eucaliptol), Δ-3-careno, d-limoneno, linalol, β-mirceno, α-pineno, pulegona, p-cimeno y terpineol-4-ol; y en donde la formulación cannabinoide se infunde en un triglicérido de cadena media (MCT)".*

2.5 Todas las demás reivindicaciones objetadas dependen adecuadamente de la reivindicación 1 y, por lo tanto, citan todos los elementos de la reivindicación 1.

2.6 Como se argumentó en la respuesta anterior del solicitante, la formulación reivindicada es adecuada para la administración a un sujeto como parte de un régimen de dosificación personalizado que proporciona un control y personalización superiores, como se describe en los Ejemplos 7 a 9. Además, la infusión en MCT resulta en una idoneidad superior para el consumo humano (véase la memoria descriptiva, párrafo [0063], y el Anexo 2 presentado con la respuesta anterior del solicitante). Además, la formulación líquida MCT resultante citada por las reivindicaciones proporciona una facilidad de uso y control superiores del tamaño de la dosis, en comparación con otras formas de dosificación de formulaciones de cannabinoides. Por consiguiente, *discrepamos de la formulación del problema técnico objetivo por el Examinador como la provisión de una formulación alternativa a la de D2*. La reivindicación del solicitante está dirigida a una

formulación mejorada de cannabinoides, con mayor flexibilidad durante la administración, idoneidad para la administración oral y facilidad de uso.

2.7 D2 no enseña ni sugiere la formulación líquida de la reivindicación 1, en la que:

> "la proporción mayor o igual al 95% (p/p) del total de cannabinoides es ácido tetrahidrocannabinólico (THCa)".

En el mejor de los casos, D2 enseña que:

> *"[t]he amount of the principle phytocannabinoid in the THCA BDS as a percentage of the phytocannabinoid containing fraction is approximately 71-86% (w/w)" (see D2, at paragraph [0152]) "la cantidad del fitocannabinoide principal en el BDS de THCA como porcentaje de la fracción que contiene fitocannabinoides es aproximadamente 71-86% (p/p)".*

2.8 De hecho, D2 en el Ejemplo 2 solo demostró una formulación de THCa en la que la cantidad de THCa es el 78% del total de cannabinoides (ver Tabla 2.81.). D2 también es silente con respecto a la infusión en un triglicérido de cadena media. En resumen, D2 no enseña ni sugiere todos los elementos de la reivindicación 1. D2 tampoco proporciona ninguna enseñanza, sugerencia o motivación que permita a un experto en la materia llegar a las reivindicaciones presentes con una expectativa razonable de resultados predecibles o éxito. Por lo tanto, **las reivindicaciones pendientes son inventivas sobre D2**.

2.9 El Examinador se basa en D6 para supuestamente subsanar las deficiencias de D2. Específicamente, el Examinador indica que si bien D2 no enseña una formulación líquida de cannabinoides que comprenda más o igual al 95% de ácido tetrahidrocannabinólico (THCa), esta deficiencia se remediaría con D6 en la página 11, líneas 9 a 19, lo que indica que la cantidad de al menos un cannabinoide ácido, por ejemplo THCa, es de 1 a 100%. El solicitante respetuosamente no está de acuerdo.

2.10 En su conjunto, la pág. 11, líneas 9-19 de D6 señalan que:

> *"Preferably, a composition according to the invention, such as a (cannabis) extract, comprises at least one compound selected from the group consisting of Δ9-tetrahydrocannabinolic acid (THCA), cannabidiolic acid (CBDA), cannabidiol (CBD), cannabigerolic acid (CBGA), cannabigerol (CBG), cannabinolic acid (CBN-A) and cannabinol (CBN), cannabichromenic acid(CBC-A) and*

cannabichromene (CBC). The amount of the compounds of this group may be chosen within wide limits. Good results have inter alia been achieved with a composition, in particular an extract, wherein the total amount is in the range of about 0.01-200 %, more in particular about 1-100 wt. % based upon the amount of the at least one acidic cannabinoid. In particular in this range indications exist that synergy occurs."

"Preferentemente, una composición de acuerdo con la invención, como un extracto (de cannabis), comprende al menos un compuesto seleccionado del grupo que consiste en ácido Δ9-tetrahidrocannabinólico (THCA), ácido cannabidiólico (CBD-A), cannabidiol (CBD), ácido cannabigerólico (CBGA), cannabigerol (CBG), ácido cannabinólico (CBN-A) y cannabinol (CBN), ácido cannabicroménico (CBC-A) y cannabicromeno (CBC). La cantidad de los compuestos de este grupo puede elegirse dentro de límites amplios. Se han logrado buenos resultados, entre otras cosas, con una composición, en particular un extracto, en la que la cantidad total está en el rango de aproximadamente 0.01-200%, más en particular alrededor de 1-100 % en peso basado en la cantidad de al menos un cannabinoide ácido. En particular, en este rango existen indicios de que se produce sinergia."

2.11 Por lo tanto, este pasaje de D6 indica que cualquiera de los 8 cannabinoides puede estar presente en la composición de D6, en una concentración de 1 a 100% en peso. Como tal, la divulgación en la que se basa el Examinador no es más que un ejercicio de redacción de patentes, y no una divulgación que proporcionaría a una persona experta cualquier expectativa razonable de éxito en la formulación reivindicada por el solicitante. Por lo tanto, *una persona experta recurriría a los Ejemplos de D6 para obtener orientación adicional sobre las formulaciones de cannabinoides*. Sin embargo, los ejemplos de D6 son silentes, señalando solamente que "al día siguiente se agregaron arsenito y THCA a [células] a las concentraciones indicadas" (D6, pp. 15-16). Por lo tanto, una persona experta, proporcionado las enseñanzas de D2 y D6, no aplicaría las enseñanzas de D6 a D2 para llegar a las reivindicaciones pendientes con ninguna expectativa razonable de resultados predecibles o éxito. **En consecuencia, las reivindicaciones pendientes son inventivas sobre D2 y D6**. Se solicita respetuosamente la reconsideración y la retirada del rechazo.

2.12 Finalmente, hacemos notar que el presente caso cuenta con patentes equivalentes concedidas en el extranjero, tales como:

- US11291650 (B2). https://lp.espacenet.com/searchResults?submitted=true&locale=es_LP&DB=EPODOC&ST=advanced&TI=&AB=&PN=US11291650+&AP=&PR=&PD=&PA=&IN=&CPC=&IC=

y

- AU2015335997(B2). https://lp.espacenet.com/publicationDetails/biblio?DB=EPODOC&II=0&ND=3&adjacent=true&locale=es_LP&FT=D&date=20170518&CC=AU&NR=2015335997A1&KC=A1

En todo caso acompañamos las copias de las respectivas patentes, donde se han reconocido los méritos de patentabilidad para la presente invención, inclusive con un alcance más amplio que aquel solicitado en Colombia.

2.13 En conclusión, se adjunta un nuevo capítulo reivindicatorio con pago por modificación voluntaria que ha sido modificado para superar los requerimientos de forma y fondo.

2.14 Por tanto, se ha probado que los documentos citados no son perjudiciales respecto al requisito de NIVEL INVENTIVO de la invención, ni contradice cualquier disposición legal o reglamentaria. En consecuencia, a la luz de todo lo anterior, me permito solicitar a ese despacho, que esta solicitud sea concedida bajo el tenor de las nuevas reivindicaciones, conforme el artículo 45 de la Decisión 486 de la Comisión de la Comunidad Andina. Sin embargo, incluso si el examinador lo considera insuficiente en conjunto con las nuevas reivindicaciones que aquí se presenta, la solicitante ruega respetuosamente que se le ofrezca una nueva oportunidad, a través un nuevo Oficio para expresarse sobre cualquier tema en controversia.

3 FUNDAMENTO DE DERECHO

Fundamento esta remisión en las normas legales siguientes:

3.1 Artículo 45 de la Decisión 486 de la Comisión de la Comunidad Andina.

3.2 En las demás normas concordantes.

4 ANEXOS

4.1 Un nuevo capítulo reivindicatorio, con enmiendas visibles, así como el archivo en limpio con las reivindicaciones modificadas, de acuerdo con el trámite presentado

simultáneamente con esta respuesta, en que se pagan las respectivas tasas oficiales de modificación.

5 PETICIÓN

Teniendo en cuenta las anteriores aclaraciones y a la modificación realizada al capítulo reivindicatorio, solicito continuar con el trámite de rigor.

De la Señora Directora,

FERNANDO TRIANA SOTO
C.C. No. 79.154.036
T.P.A. 45.265 del C.S. de la J.

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COLO 7804 0301 76755

REIVINDICACIONES

1. Una formulación líquida de cannabinoides, caracterizada porque la proporción mayor o igual que el 95% (p/p) del total de cannabinoides es ácido tetrahidrocannabinólico (THCa),
donde el ácido cannabidiólico (CBDa) es menos o igual que el 1% (p/p) del total de cannabinoides;
donde el ácido cannabinólico (CBNa) es menos o igual que el 3% (p/p) del total de cannabinoides;
donde el ácido cannabicroménico (CBCa) es menos o igual que el 1% (p/p) del total de cannabinoides;
donde la formulación comprende ~~al menos un terpeno y/o~~ uno o más terpenos seleccionados del grupo que consiste en borneol, β-cariofileno, 1,8-cineol (eucaliptol), Δ-3-careno, d-limoneno, linalol, β-mirceno, α-pineno, pulegona, p-cimeno y terpineol-4-ol~~flavonoide~~; y, en el que la formulación de cannabinoides se infunde en un triglicérido de cadena media (MCT).

2. La formulación de la reivindicación 1, caracterizada porque la formulación comprende uno o más flavonoides seleccionados del grupo que consiste en β-sitosterol, canflavina A, apigenina y quercetina.

~~2. La formulación de la reivindicación 1, caracterizada porque el terpeno y/o flavonoide es d-limoneno linalol, 1,8-cineol (eucaliptol), α-pineno, terpineol-4-ol, p-cimeno, borneol, Δ-3-careno, β-sitosterol, β-mirceno, β-cariofileno, canflavina A , apigenina, quercetina o pulegona.~~

3. La formulación de la reivindicación 1, caracterizada porque dicho uno o más terpenos comprende mirceno, cariofileno y d-limoneno.

4. La formulación de la reivindicación 1, caracterizada porque dicho uno o más terpenos comprende mirceno, limoneno, pineno y cariofileno.

5. La formulación de la reivindicación 1, caracterizada porque el MCT está compuesto por 97%:3% de ácidos grasos C-8:C10;C12.

6. La formulación de cualquiera de las reivindicaciones 1 a 5, caracterizada porque está formulada para administración oral, sublingual, bucal o tópica.

7. La formulación de la reivindicación 6, caracterizada porque la formulación sublingual comprende además un edulcorante.

8. La formulación de la reivindicación 7, caracterizada porque ~~donde~~ el edulcorante es un extracto de estevia.

9. La formulación de la reivindicación 7 o la reivindicación 8, caracterizada porque comprende además aceite de limón, aceite de naranja o ambos.

REIVINDICACIONES

1. Una formulación líquida de cannabinoides, caracterizada porque la proporción mayor o igual que el 95% (p/p) del total de cannabinoides es ácido tetrahidrocannabinólico (THCa),

donde el ácido cannabidiólico (CBDa) es menos o igual que el 1% (p/p) del total de cannabinoides;

donde el ácido cannabinólico (CBNa) es menos o igual que el 3% (p/p) del total de cannabinoides;

donde el ácido cannabicroménico (CBCa) es menos o igual que el 1% (p/p) del total de cannabinoides;

donde la formulación comprende uno o más terpenos seleccionados del grupo que consiste en borneol, β-cariofileno, 1,8-cineol (eucaliptol), Δ-3-careno, d-limoneno, linalol, β-mirceno, α-pineno, pulegona, p-cimeno y terpineol-4-ol; y,
en el que la formulación de cannabinoides se infunde en un triglicérido de cadena media (MCT).

2. La formulación de la reivindicación 1, caracterizada porque la formulación comprende uno o más flavonoides seleccionados del grupo que consiste en β-sitosterol, canflavina A, apigenina y quercetina.

3. La formulación de la reivindicación 1, caracterizada porque dicho uno o más terpenos comprende mirceno, cariofileno y d-limoneno.

4. La formulación de la reivindicación 1, caracterizada porque dicho uno o más terpenos comprende mirceno, limoneno, pineno y cariofileno.

5. La formulación de la reivindicación 1, caracterizada porque el MCT está compuesto por 97%:3% de ácidos grasos C-8:C10;C12.

6. La formulación de cualquiera de las reivindicaciones 1 a 5, caracterizada porque está formulada para administración oral, sublingual, bucal o tópica.

7. La formulación de la reivindicación 6, caracterizada porque la formulación sublingual comprende además un edulcorante.

8. La formulación de la reivindicación 7, caracterizada porque el edulcorante es un extracto de estevia.

9. La formulación de la reivindicación 7 o la reivindicación 8, caracterizada porque comprende además aceite de limón, aceite de naranja o ambos.

US011291650B2

(12) **United States Patent**
Blackmon et al.

(10) **Patent No.: US 11,291,650 B2**
(45) **Date of Patent: *Apr. 5, 2022**

(54) **CANNABIS EXTRACTS AND METHODS OF PREPARING AND USING SAME**

(71) Applicant: **United Cannabis Corp.**, Golden, CO (US)

(72) Inventors: **Earnie Blackmon**, Denver, CO (US); **Tony Verzura**, Denver, CO (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **16/717,914**

(22) Filed: **Dec. 17, 2019**

(65) **Prior Publication Data**

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Related U.S. Application Data

(60) Continuation of application No. 15/676,407, filed on Aug. 14, 2017, now Pat. No. 10,555,928, which is a division of application No. 14/919,245, filed on Oct. 21, 2015, now Pat. No. 9,730,911.

(60) Provisional application No. 62/068,278, filed on Oct. 24, 2014, provisional application No. 62/066,795, filed on Oct. 21, 2014.

(51) **Int. Cl.**

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A61K 31/192	(2006.01)
A61K 31/352	(2006.01)
A61K 31/05	(2006.01)
A61K 36/185	(2006.01)

(52) **U.S. Cl.**

CPC ***A61K 31/353*** (2013.01); ***A61K 31/05*** (2013.01); ***A61K 31/192*** (2013.01); ***A61K 31/352*** (2013.01); ***A61K 36/185*** (2013.01)

(58) **Field of Classification Search**

CPC A61K 31/353

See application file for complete search history.

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(57) **ABSTRACT**

The invention relates to the extraction of pharmaceutically active components from plant materials, and more particularly to the preparation of a botanical drug substance (BDS) for incorporation in to a medicament. It also relates to a BDS, for use in pharmaceutical formulations. In particular it relates to BDS comprising cannabinoids obtained by extraction from cannabis.

13 Claims, No Drawings

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CANNABIS EXTRACTS AND METHODS OF PREPARING AND USING SAME

RELATED APPLICATIONS

This application is a continuation of U.S. patent application Ser. No. 15/676,407, filed on Aug. 14, 2017, which is a divisional of U.S. patent application Ser. No. 14/919,245, filed Oct. 21, 2015, now U.S. Pat. No. 9,730,911, and claims priority to and the benefit of U.S. Provisional Application No. 62/066,795 filed on Oct. 21, 2014 and U.S. Provisional Application No. 62/068,278 filed on Oct. 24, 2014, the contents of each of which are incorporated by reference in their entireties.

FIELD OF THE INVENTION

This invention relates to the extraction of pharmaceutically active components from plant materials, and more particularly to botanical drug substance (BDS) comprising cannabinoids obtained by extraction from *cannabis*. Methods of using the extracts to treat chronic pain, paralysis, neuropathy, Crohn's Disease, IBS, glaucoma, PTSD, anxiety, seizures, epilepsy, autoimmune disorders autism, tumors, and cancer are also included.

BACKGROUND OF THE INVENTION

Cannabis products have been consumed in various forms for thousands of years. The first descriptions of the medical uses date from Chinese herbal texts in the first century A.D. *Cannabis* products were taken orally in an herbal tea concoction and were used for their pain-relieving and sleep-inducing properties.

There presently exists the need to provide more effective and safer *cannabis* extracts for various medical uses, extraction methods that provide unique active compounds that are useful to treat pain and various medical conditions. Additionally, presently known extraction procedures do not provide the desired active ingredient(s) for the particular medical purpose. The present invention overcomes these limitations and provides other related advantages.

SUMMARY OF THE INVENTION

The invention provides an extract comprising a mixture of at least 95% total cannabinoids, and at least one terpene/flavonoid. The extract contains at least 4, 5, 6, 7 or more cannabinoids. The cannabinoids are selected from tetrahydrocannabinolic acid (THCa), cannabidiolic acid (CBDa), cannabinolic acid (CBNa) cannabichromenic acid (CBCa), tetrahydrocannabinol (THC), cannabinol (CBN), cannabidiol (CBD) or cannabichromene (CBC). In some aspect the cannabinoids are THCa and CBDa and at least two cannabinoids selected from CBNa, CBCa, THC, CBN and CBC. In a preferred embodiment the cannabinoids are THC, CBN, CBC and CBD. In another preferred embodiment the cannabinoids are THCa, CBDa, CBNa and CBCa. In yet another preferred embodiment the cannabinoids are THCa, CBDa, THC, CBN, and CBC.

The terpene/flavonoid is for example, d-limonene linalool, 1,8-cineole (eucalyptol), α-pinene, terpineol-4-ol, p-cymene, borneol, Δ-3-carene, β-sitosterol, β-myrcene, or β-caryophyllene.cannflavin A, apigenin, quercetin or pulegone.

Also provided by the invention are formulations containing the extracts according to the invention. For example the formulation contains any of the extracts according to the invention infused with a medium chain triglyceride (MCT). The MCT is for example, NEOBEE 895.

Preferably, the pH of the formulation is at least pH 8.0.

In some formulations the concentration of THCa is greater than or equal to 95%; CBDa is less than 1%; CBNa is less than 3%; and CBCa is less than 1%. Optionally the formulation further contains d-limonene, linalool, 1,8-cineole (eucalyptol), α-pinene, terpineol-4-ol, p-cymene, borneol, Δ-3-carene, β-sitosterol, cannflavin A, apigenin, quercetin

In other formulations the concentration of THCa is less than or equal to 35%; CBDa is greater than or equal to 60%; THC is less than 1%; CBN is less than 1%; and CBC is less than 1%. Optionally, the formulation further contains d-limonene, linalool, 1,8-cineole (eucalyptol), α-pinene, terpineol-4-ol, p-cymene, borneol, Δ-3-carene, β-sitosterol, cannflavin A, apigenin, quercetin

In another formulation the concentration of THCa is greater than or equal to 40%; CBDa is greater than or equal to 40%; THC is less than 1%; CBN is less than 1%; and CBC is less than 1%. Optionally, the formulation further conatains β-myrcene, β-caryophyllene, pulegone, α-terpineol, β-sitosterol, cannflavin A, apigenin, quercetin

In yet another formulation the concentration of THC is less than or equal to 9%; CBD is greater than or equal to 40%; CBN is greater than or equal to 40%; and CBS is less than 1%. Optionally, the formulation further contains β-myrcene, β-caryophyllene, pulegone, α-terpineol, β-sitosterol, cannflavin A, apigenin, quercetin.

In various aspects the formulation of the invention are formulated for r oral, sublingual, buccal, or topical administration. The sublingual formulation further contains a sweetener such as a *stevia* extract. Optionally, the sublingual formulation further contains lemon oil, orange oil or both.

In other aspects the invention provides a method of preparing a *cannabis* extract providing fresh or live *cannabis* plant material; extracting the cannabinoids from the plant material to produce a first extract; winterizing and purging the winterized extract. Optionally, the method further incudes decarboxylating the phytocannabinoids prior to extraction. The decarboxylation is accomplished for example, by heating the dried plant material at a temperature of about 221° F. for at least 15 minutes followed by heating at about 284° F. for at least 45 minutes. In some aspects the winterized extract is heated at 284° F. for at about 45-74 minutes followed by heating at about 293° F. for at least about 55-90 minutes.

Extraction is for example by hydrocarbon extraction. Winterizing includes adding cold ethanol to the first extract or storing the first extract at a temperature of about −20° to about −75° F. for about 48 hours to produce a waxy precipitate and removing the waxy precipitate by filtration. Optionally, the winterized extract is filtered through activated charcoal.

The *cannabis* plant material consists of flowers or flowers and leaves. In some aspects the *cannabis* plant material is frozen at a temperature between at least −10° F. to −50° F. for at least 36 hours prior to being extracted. Preferably, the *cannabis* plant material has been propagated from a single seed source or a tissue culture with specific ratios of cannabinoids. In some aspects the *cannabis* plant material is derived from a *cannabis* strain having a minimum of 15% THC and less that 1% CBD. In others aspect the *cannabis* plant material is derived from Sour Tsunami×Catatonic Sour Tsunami×Sour Tsunami, Sour Tsunami, Harlequin, R4 ACDC strains. In yet other as aspects the *cannabis* plant

material is derived from CBD1, Sour Pineapple, CBD Diesel, Harlequin, ACDC or R4. In yet a further aspect the *cannabis* plant material is derived from Sour Tsunami× Catatonic, Sour Tsunami×Sour Tsunami, Sour Tsunami, Harlequin, R4, Swiss Gold, ACDC, CBD1, Sour Pineapple, or CBD Diesel.

The invention further provides a method for preparing *cannabis* juice by blanching fresh *cannabis* leaves obtained from a *cannabis* plant in the vegetative stage in cold water; juicing the leaves in a cold press juicer or masticating juicer; and filtering the juice through a filter to remove particulates. Optionally, filter juice is freeze dried.

The juicer is for example, a cold press juicer or a masticating juicer. Also included in the invention is juice produced according to the method of the invention. In some embodiments the *cannabis* juice is obtained from *cannabis* flowers, *cannabis* roots or both.

The invention also provides method of relieving symptoms associated with anxiety, post traumatic stress disorder, chronic pain, or opiate dependency, paralysis, neuropathy, Crohns disease, inflammatory bowel disorders, glaucoma, seizures, epilepsy, autism, or cancer comprising administering to a subject in need thereof one or more of the formulations or juice according to the invention. The formulations are administered four times daily. For example the formulation is administered in the morning; afternoon, evening and at bedtime.

In specific embodiments the invention provides a method of treating cancer by administering to a subject a total daily doses of: 20 mg of cannabinoid extract and 50 mg of raw *cannabis* juice for seven days; 40 mg of cannabinoid extract and 50 mg of raw *cannabis* juice for seven days; 80 mg of cannabinoid extract and 50 mg of raw *cannabis* juice for seven days; 120 mg of cannabinoid extract and 50 mg of raw *cannabis* juice for seven days; and 160 mg of cannabinoid extract and 100 mg of raw *cannabis* juice for seven days. In some aspects the method further includes administering a total daily dose of 200 mg cannabinoid extract and 100 mg of raw *cannabis* juice every day thereafter or administering 200 mg of cannabinoid extract and 100 mg of raw *cannabis* juice for seven days; and 400 mg of cannabinoid extract and 100 mg of raw *cannabis* juice every day thereafter.

In another embodiment the invention provides method of treating opioid dependency by reducing the amount of opiates used per day by at least 10% and administering to a subject a total daily doses of: 31 mg of cannabinoid extract and 50 mg of raw *cannabis* for fourteen days; 56 mg of cannabinoid extract and 50 mg of raw *cannabis* for fourteen days; 84 mg of cannabinoid extract and 50 mg of raw *cannabis* juice for fourteen days; 104 mg of cannabinoid extract and 50 mg of raw *cannabis* for fourteen days; 89 mg of cannabinoid extract and 50 mg of raw *cannabis* for fourteen days; 69 mg of cannabinoid extract and 50 mg of raw *cannabis* for fourteen days; 49 mg of cannabinoid extract and 50 mg of raw *cannabis* for fourteen days; and 41 mg of cannabinoid extract and 50 mg of raw *cannabis* for fourteen days.

Optionally, the method further includes administering a total daily dose of 36 mg cannabinoid extract and 25 mg of raw *cannabis* every day thereafter and a single dose of 50 mg raw *cannabis* every three days.

In another embodiment, the invention provides a method of treating anxiety/PTSD by administering to a subject a total daily doses of about 28 mg to 42 mg of cannabinoid extract.

In a further embodiment, the invention includes a method of treating chronic pain by administering to a subject a total daily doses of about 36 mg to 48 mg of cannabinoid extract.

The formulations are administered four times daily. For example, the formulation is administered in the morning; afternoon, evening and at bedtime.

Other features and advantages of the invention will be apparent from and are encompassed by the following detailed description and claims.

DETAILED DESCRIPTION

The present invention is based in part upon extraction procedures and delivery approaches that allow selective utilization of various cannabinoid molecules and terpenes from the whole *Cannabis sativa* plant. These various cannabinoid compounds are designed to selectively affect various cannabinoid receptors in the nervous system, immune system and other tissues. The extract is an oil-based whole plant product that contains inactive and active compounds contained in the *cannabis* plant such as cannabinoids, terpenes and/or flavonoids. Compositions of the invention and methods of extraction disclosed herein provide an extract with specific physiological properties that are mediated through separate pathways and receptors, which provide numerous benefits and advantages.

The extracts and/or delivery methods of the invention allows a wide range of prevention, treatment and management options for patients. In some aspects the delivery methods of the invention employs micro-dosing with a stacking method of cannabinoid administration week by week until a certain saturation point that is based on response, weight, and monthly-quarterly test results.

Surprisingly, it was discovered that the age or the *cannabis* plant material, the temperature in which it is stored and processed is critical and the ratio of the specific cannabinoids extract is critical to effectiveness of the final formulation. Importantly, for an extract to maintain non-psychoactive properties the *cannabis* plant material is never heated above 160° F. Preferably, the non-psychoactive extracts according to the invention are formulated at 110° F. or below.

Cannabis is a genus of flowering plants that includes three different species, *Cannabis sativa, Cannabis indica* and *Cannabis ruderalis*. The term "*Cannabis* plant(s)" encompasses wild type *Cannabis* and also variants thereof, including *cannabis* chemovars which naturally contain different amounts of the individual cannabinoids. For example, some *Cannabis* strains have been bred to produce minimal levels of THC, the principal psychoactive constituent responsible for the high associated with it and other strains have been selectively bred to produce high levels of THC and other psychoactive cannabinoids.

Cannabis plants produce a unique family of terpenophenolic compounds called cannabinoids, which produce the "high" one experiences from consuming marijuana. There are 483 identifiable chemical constituents known to exist in the *cannabis* plant, and at least 85 different cannabinoids have been isolated from the plant. The two cannabinoids usually produced in greatest abundance are cannabidiol (CBD) and/or Δ9-tetrahydrocannabinol (THC), but only THC is psychoactive. *Cannabis* plants are categorized by their chemical phenotype or "chemotype," based on the overall amount of THC produced, and on the ratio of THC to CBD. Although overall cannabinoid production is influenced by environmental factors, the THC/CBD ratio is genetically determined and remains fixed throughout the life

of a plant. Non-drug plants produce relatively low levels of THC and high levels of CBD, while drug plants produce high levels of THC and low levels of CBD.

The best studied cannabinoids include tetrahydrocannabinol (THC), cannabidiol (CBD) and cannabinol (CBN). Other cannabinoids include for example, cannabichromene (CBC), cannabigerol (CBG) cannabinidiol (CBND), Cannabicyclol (CBL), Cannabivarin (CBV), Tetrahydrocannabivarin (THCV), Cannabidivarin (CBDV), Cannabichromevarin (CBCV) Cannabigerovarin (CBGV), Cannabigerol Monomethyl Ether (CBGM).

Cannabinoids are derived from their respective 2-carboxylic acids (2-COOH) by decarboxylation (catalyzed by heat, light, or alkaline conditions). As a general rule, the carboxylic acids form of the cannabinoid have the function of a biosynthetic precursor.

As used herein THC, CBD, CBN, CBC, CBG, CBND, CBL, CBV, THCV, CBDV, CBCV, CBGV and CBGM refer to the decarboxylated form of the cannabinoid. Whereas, THCa, CBDa, CBNa, CBCa, CBGa, CBNDa, CBLa, CBVa, THCVa, CBDVa, CBCVa, CBGVa and CBGM refer to the acid form of the cannabinoid.

Tetrahydrocannabinol (THC) is the primary psychoactive component of the *Cannabis* plant. THC is only psychoactive in is decarboxylated state. The carboxylic acid form (THCa) is non-psychoactive.

Delta-9-tetrahydrocannabinol (Δ9-THC, THC) and delta-8-tetrahydrocannabinol (Δ8-THC), mimic the action of anandamide, a neurotransmitter produced naturally in the body. These two THCs produce the effects associated with *cannabis* by binding to the CB1 cannabinoid receptors in the brain. THC appears to ease moderate pain (analgesic) and to be neuroprotective, while also offering the potential to reduce neuroinflammation and to stimulate neurogenesis. THC has approximately equal affinity for the CB1 and CB2 receptors.

Cannabidiol (CBD) is not psychoactive, and was thought not to affect the psychoactivity of THC. However, recent evidence shows that smokers of *cannabis* with a higher CBD/THC ratio were less likely to experience schizophrenia-like symptoms.[15] This is supported by psychological tests, in which participants experience less intense psychotic-like effects when intravenous THC was co-administered with CBD (as measured with a PANSS test). Cannabidiol has little affinity for CB1 and CB2 receptors but acts as an indirect antagonist of cannabinoid agonists. Recently it was found to be an antagonist at the putative new cannabinoid receptor, GPR55, a GPCR expressed in the caudate nucleus and putamen. Cannabidiol has also been shown to act as a 5-HT1A receptor agonist, an action that is involved in its antidepressant, anxiolytic, and neuroprotective effects.

It appears to relieve convulsion, inflammation, anxiety, and nausea. CBD has a greater affinity for the CB2 receptor than for the CB1 receptor. CBD shares a precursor with THC and is the main cannabinoid in low-THC *Cannabis* strains. CBD apparently plays a role in preventing the short-term memory loss associated with THC in mammals.

Cannabinol (CBN) is the primary product of THC degradation, and there is usually little of it in a fresh plant. CBN content increases as THC degrades in storage, and with exposure to light and air. It is only mildly psychoactive. Its affinity to the CB2 receptor is higher than for the CB1 receptor

Cannabigerol (CBG) is non-psychotomimetic but still affects the overall effects of *Cannabis*. It acts as an α2-adrenergic receptor agonist, 5-HT1A receptor antagonist, and CB1 receptor antagonist.[31] It also binds to the CB2 receptor.[31]

Tetrahydrocannabivarin (THCV) is prevalent in certain central Asian and southern African strains of *Cannabis*. It is an antagonist of THC at CB1 receptors and attenuates the psychoactive effects of THC.

Cannabidivarin (CBDV) is usually a minor constituent of the cannabinoid profile.

Cannabichromene (CBC) is non-psychoactive and does not affect the psychoactivity of THC. More common in tropical *cannabis* varieties. Effects include anti-inflammatory and analgesic.

In addition to cannabinoids, *cannabis* plants produce terpenes, a diverse group of organic hydrocarbons that are the building blocks of the cannabinoids.

Over 100 different terpenes have been identified in the *cannabis* plant, and every strain tends toward a unique terpene type and composition. The terpenes act synergistically with the cannabinoids to provide a therapeutic effect. Examples of some common terpenes found in *Cannabis* include:

Borneol—menthol, camphor, pine, woody. Can be easily converted into menthol. It is considered a "calming sedative" in Chinese medicine. It is directed for fatigue, recovery from illness and stress.

Caryophyllene—spicy, sweet, woody, clove, camphor, peppery. It binds weakly to CB2 receptor. As a topical it is one of the constituents of an anti-inflammatory and analgesic treatment for toothache. In high amounts, it's a calcium and potassium ion channel blocker. As a result, it impedes the pressure exerted by heart muscles.

Cineole/Eucalyptol—spicy, camphor, refreshing, minty. It is used to increase circulation, pain relief and easily crosses the blood-brain-barrier to trigger fast olfactory reaction.

Delta3Carene—sweet, pine, cedar, woodsy, pungent. In aroma therapy, cypress oil, high in D-3-carene, is used to dry excess fluids, tears, running noses, excess menstrual flow and perspiration.

Limonene—citrus (orange, tangerine, lemon, and grapefruit), rosemary, juniper, peppermint. Repulsive to predators. Found in the rinds of many fruits and flowers. With the presence of other certain terpenes, Limonene can be an anti-bacterial, anti-fungal, anti-depressant and anti-carcinogen. It can synergistically promote the absorption of other terpenes by quickly penetrating cell membranes. The result can be increased systolic blood pressure.

Linolool—floral (spring flowers), lily, citrus and candied spice. Possesses anti-anxiety and sedative properties.

Myrcene—clove like, earthy, green-vegetative, citrus, fruity with tropical mango and minty nuances. The most prevalent terpene found in most varieties of marijuana. It's a building block for menthol, citronella, and geraniol. It possesses antimicrobial, antiseptic, analgesic, antioxidant, anti-carcinogen, anti depressant, anti-inflammatory, and muscle relaxing effects. Myrcene affects the permeability of the cell membranes, allowing more THC to reach brain cells.

Pinene—Alpha: pine needles, rosemary Beta: dill, parsley, rosemary, basil, yarrow, rose, hops, the familiar odor associated with pine trees and their resins. Pinene can increase mental focus and energy, as well as act as an expectorant, bronchodilator, and topical antiseptic. It easily crosses the blood-brain barrier where it inhibits activity of acetylcholinesterase, which destroys acetylcholine, an information transfer molecule, resulting in better memory. It may counteract THC's activity, which leads to low acetylcholine levels.

Pulegone—mint, camphor, rosemary, candy. Pulegone is an acetylcholinesterase inhibitor. That is, it stops the action of the protein that destroys acetylcholine, which is used by the brain to store memories.

In various aspects the invention provides *cannabis* extracts with predefined ratios of cannabinoids. Standard conditions for cannabinoid assays, and methods of calculating cannabinoid content (as %) are well known in the art.

The extracts are mixture of at least 95% total cannabinoids and include terpenes and/or flavonoids. Preferably the extracts contains a mixture of at least cannabinoids four cannabinoid such as tetrahydrocannabinolic acid (THCa), cannabidiolic acid (CBDa), cannabinolic acid (CBNa) cannabichromenic acid (CBCa), tetrahydrocannabinol (THC), cannabinol (CBN), cannabidiol (CBD) and cannabichromene (CBC).

In some embodiments the extract contains THCa and CBDa and at least two cannabinoids selected from CBNa, CBCa, THC, CBN and CBC. In other embodiments the extract includes THC, CBN, CBC and CBD. In further embodiments the extract includes THCa, CBDa, CBNa and CBCa. In other embodiments the extract includes THCa, CBDa, THC, CBN, and CBC.

The terpene and/or flavonoids in the extract include for example, terpene is linalool, 1,8-cineole (eucalyptol), α-pinene, terpineol-4-ol, p-cymene, borneol, Δ-3-carene, β-sitosterol, β-myrcene, β-caryophyllene.d-limonene, cannflavin A, apigenin, quercetin or pulegone.

The extracts of the invention may be formulated with one or more pharmaceutically acceptable carriers, diluents or excipients or deposited on a pharmaceutically acceptable surface for vaporisation in order to produce pharmaceutical formulations containing cannabinoids as the pharmaceutically active agents.

Therefore, in a further aspect the invention provides a method of making a pharmaceutical composition comprising, as an active agent, a substance which is an extract from at least one *cannabis* plant variety.

Separate extracts may be prepared from single *cannabis* plant varieties having differing cannabinoid content (e.g. high THC and high CBD plants) and then mixed or blended together prior to formulation to produce the final pharmaceutical composition. This approach is preferred if, for example, it is desired to achieve a defined ratio by weight of individual cannabinoids in the final formulation. Alternatively, plant material from one or more *cannabis* plant varieties of defined cannabinoid content may be mixed together prior to extraction of a single botanical drug substance having the desired cannabinoid content, which may then be formulated into a final pharmaceutical composition.

The extract may be formulated with any convenient pharmaceutically acceptable diluents, carriers or excipients to produce a pharmaceutical composition. The choice of diluents, carriers or excipients will depend on the desired dosage form, which may in turn be dependent on the intended route of administration to a patient. Preferred dosage forms include, liquid dosage forms for administration via pump-action or aerosol sprays, tablets, pastilles, gels, capsules, suppositories, powders, etc. and vaporizers. Such dosage forms may be prepared in accordance with standard principles of pharmaceutical formulation, known to those skilled in the art.

Liquid formulations are particularly preferred. A particularly preferred formulation for administration of cannabinoids, though not intended to be limiting to the invention, is a liquid formulation of the extracts according to the invention infused with a medium chain triglyceride (MCT). The MCT suitable for human consumption. The MCT may be composed of any combinations of C-6; C-8; C-10:C12 fatty acids. For example, the MCT is composed of 97%:3% C-8:C10; C-12 fatty acids (e.g., NEOBEE 895). Preferably the pH of the formulation is at least pH 8.0. The formulations are suitable for oral, sublingual, buccal, or topical administration. When used for sublingual administration the formulation optionally comprises a sweetener such as *stevia* extract and or a flavoring such as for example lemon oil, orange oil or both.

A preferred formulation includes a cannabinoid mixture where THCa is greater than or equal to 95%; a CBDa is less than 1%; CBNa is less than 3%; and CBCa is less than 1%. In some aspects the formulation further includes d-limonene, linalool, 1,8-cineole (eucalyptol), α-pinene, terpineol-4-ol, p-cymene, bomeol, Δ-3-carene, β-sitosterol, cannflavin A, apigenin, and quercetin. This preferred formulation is referred to herein as PRANA 1.

Another preferred formulation includes a cannabinoid mixture where the THCa is less than or equal to 35%; CBDa is greater than or equal to 60%; THC is less than 1%; CBN is less than 1%; and CBC is less than 1%. In some aspects the formulation further includes d-limonene, linalool, 1,8-cineole (eucalyptol), α-pinene, terpineol-4-ol, p-cymene, bomeol, Δ-3-carene, β-sitosterol, cannflavin A, apigenin, and quercetin. This preferred formulation is referred to herein as PRANA 2.

In yet another preferred embodiment the formulation includes a cannabinoid mixture where the THCa is greater than or equal to 40%; CBDa is greater than or equal to 40%; THC is less than 1%; CBN is less than 1%; and CBC is less than 1%. In some aspects the formulation further includes β-myrcene, β-caryophyllene, pulegone, α-terpineol, β-sitosterol, cannflavin A, apigenin, and quercetin. This preferred formulation is referred to herein as PRANA 3.

In a further embodiment the formulation includes a cannabinoid mixture THC is less than or equal to 9%; CBD is greater than or equal to 40%; CBN is greater than or equal to 40%; and CBS is less than 1%. In some aspects the formulation further includes β-myrcene, β-caryophyllene, pulegone, α-terpineol, β-sitosterol, cannflavin A, apigenin, and quercetin. This preferred formulation is referred to herein as PRANA 4.

The extract is formulated for oral use (e.g. capsules) in dosage forms that provide 5 mg, 10 mg, 20 mg, or 50 mg of total cannabinoids per dose. For sublingual use, the extract is formulated to provide 0.5, 1 mg, or 2 mg, per drop.

In some applications, the patient may find it advantageous to activate (i.e., decarboxylate) the inactive (i.e. carboxylic acid form) cannabinoids in the extracts and formulations of the invention. The inactive cannabinoids (e.g., THCa and CBDa) of the extracts and formulation of the invention can be converted to active cannabinoids (THC and CBD) by heating the extracts and formulation at a temperature above 160° F. For example, a vessel containing the extracts and formulations of the invention are placed in boiling water (212° F.) for about 30 minutes.

According the invention further contemplates extracts and formulations thereof having the same ratio of cannabinoids as PRANA 1, PRANA 2 and PRANA3 where the THA and the CBD is in its activated decarboxylated form.

The methods of the invention may be used to prepare a cannabinoid—rich extract from *cannabis* plant material. The method includes providing fresh or live *cannabis* plant material; extracting the cannabinoids from the fresh or live plant material to produce a first extract; winterizing the first to produce a winterized extract and purging the winterized

extract to produce a *cannabis* extract. Optionally, the method includes decarboxylating the phytocannabinoids prior the extraction step.

Decarboxylation of cannabinoid acids is a function of time and temperature, thus at higher temperatures a shorter period of time will be taken for complete decarboxylation of a given amount of cannabinoid acid. In selecting appropriate conditions for decarboxylation consideration must, however, be given to minimising thermal degradation of the desirable, pharmacological cannabinoids into undesirable degradation products, particularly thermal degradation of THC to cannabinol (CBN). Preferably, decarboxylation is carried out in a multi-step heating process. For example, Phytocannabinoids are decarboxylated for example by heating the dried plant material at a temperature of about 221° F. for at least 15 minutes followed by heating at about 284° F. for at least 45 minutes. Other suitable methods of decarboxylating phytocannabinoids known in the art may be used.

In some aspects resultant *cannabis* extract is heated at 284° F. for at about 45-74 minutes followed by heating at about 293° F. for at least about 55-90 minutes.

The *cannabis* plant material consists of flowers or flowers and leaves. Preferably, the *cannabis* plant material is frozen at a temperature between at least −10° F. to −50° F. for at least 36 hours prior to being dried.

The *cannabis* plant material has been propagated from a single seed source or a tissue culture or clone with specific ratios of cannabinoids.

Any suitable method for extraction known in the art may be used. For example extraction is hydrocarbon extraction, supercritical C02 or NEOBEE 896 MCT.

The first extract may be winterizing by any method known in the art. For example the first extract is winterized by comprises adding cold ethanol or by storing the first extract at temperature of about −20° F. to about −75° F. for about 48 hours. Winterization produces a waxy precipitate. The waxy precipitate is removed by filtration. Optionally, the winterized extract through activated charcoal.

In some aspects the *cannabis* plant material is derived from a *cannabis* strain having a minimum of 15% THC and less that 1% CBD. In other aspects the *cannabis* plant material is derived from *cannabis* strains having a minimum of 10% CBD and less than 10% THC. For example the *cannabis* plant material is derived from Sour Tsunami× Catatonic Sour Tsunami×Sour Tsunami, Sour Tsunami, Harlequin, R4 or ACDC strains. In other embodiments the *cannabis* plant material is derived from CBD1, Sour Pineapple, CBD Diesel, Harlequin, ACDC or R4. In yet another embodiment the *cannabis* plant material is derived from Sour Tsunami×Catatonic, Sour Tsunami×Sour Tsunami, Sour Tsunami, Harlequin, R4, Swiss Gold, ACDC, CBD1, Sour Pineapple, or CBD Diesel.

The invention also provides a method for preparing *cannabis* juice comprising blanching fresh *cannabis* leaves obtained from a *cannabis* plant in the vegetative stage in cold water; juicing the leaves in a cold press juicer or masticating juicer; filtering the juice through a filter to remove particulates. Optionally, the juice freeze dried. The juicer is a cold press juicer or a masticating juicer. In some aspects the juice further includes *cannabis* juice obtained from *cannabis* flowers, *cannabis* roots or both.

The juice of raw *cannabis* provides unique healing benefits. Plant chemicals known as cannabinoid acids such as CBD-acids, and THC-acids break down quickly after harvest, so these compounds are not available in traditional preparations such as cooked 'medibles', smoking, or vaporizing The healing benefits of cannabinoid-acids are only present for a short period of time before the chemicals break down, so juicing needs to be done quickly after harvest. Fan leaves should make up the majority of the juice, and adding a small amount of *cannabis* flowers can be beneficial.

Cannabis extracts and juice have wide-ranging beneficial effects on a number of medical conditions.

Chronic pain, paralysis, neuropathy, Crohn's Disease, inflammatory bowel disorders (IBS and IBD), glaucoma, PTSD, anxiety, seizures, epilepsy, autoimmune disorders, autism, tumors, and cancer have all been shown by several studies to be controlled by use of *Cannabis*. In addition, nausea and vomiting that are unresponsive to other medications have been shown to be helped through the use of *Cannabis*. Dependency on opiates have also been shown to be controlled by the use of *Cannabis*

Accordingly the invention also includes methods of alleviating a symptom associated with anxiety, post-traumatic stress disorder, chronic pain, or opiate dependency, paralysis, neuropathy, Crohn's disease, inflammatory bowel disorders, glaucoma, seizures, epilepsy, autism, or cancer comprising administering to a subject any one of the formulation according to the invention. In some embodiments the subject receives both a formulation containing a *cannabis* extract and raw *cannabis* in the form of a juice.

In some embodiments the formulation are administered four times daily. For example, the formulations are administered in the morning, afternoon, evening and at bedtime. The formulations are administered such that the ratio of cannabinoids are different depending upon the time of day administered. For example, formulations containing lower amounts of THC (and higher amounts of THCa) are administered during waking hours of the day. Whereas, formulations containing higher amounts of THC (and lower amounts of THCa) are administered prior to bedtime. Exemplary day time formulations include a cannabinoid mixture where THCa is greater than or equal to 95%; a CBDa is less than 1%; CBNa is less than 3%; and CBCa is less than 1%; a cannabinoid mixture where the THCa is less than or equal to 35%; CBDa is greater than or equal to 60%; THC is less than 1%; CBN is less than 1%; and CBC is less than 1%; or a cannabinoid mixture where the THCa is greater than or equal to 40%; CBDa is greater than or equal to 40%; THC is less than 1%; CBN is less than 1%; and CBC is less than 1%. An exemplary bedtime formulation includes a cannabinoid mixture THC is less than or equal to 9%; CBD is greater than or equal to 40%; CBN is greater than or equal to 40%; and CBS is less than 1%.

Preferably a formulation including a cannabinoid mixture where THCa is greater than or equal to 95%; a CBDa is less than 1%; CBNa is less than 3%; and CBCa is less than 1% is administered in the morning. Preferably a cannabinoid mixture where the THCa is less than or equal to 35%; CBDa is greater than or equal to 60%; THC is less than 1%; CBN is less than 1%; and CBC is less than 1% is administered in the afternoon. Preferably, a cannabinoid mixture where the THCa is greater than or equal to 40%; CBDa is greater than or equal to 40%; THC is less than 1%; CBN is less than 1%; and CBC is less than 1% is administered in the evening.

In various aspects the method of the invention include administering the cannabinoids containing compounds by employing an escalating dosing regimen where the total amount of cannabinoids are increased over time. For example, the amount of cannabinoids administered is increased week by week until a certain saturation point that is based on response, weight, and monthly-quarterly test results. To treat opioid dependency, opiates are gradually replaced cannabinoids.

In a preferred method cancer is treated by administering to a subject a total daily doses of:

a. 20 mg of cannabinoid extract and 50 mg of raw *cannabis* juice for seven days;
b. 40 mg of cannabinoid extract and 50 mg of raw *cannabis* juice for seven days;
c. 80 mg of cannabinoid extract and 50 mg of raw *cannabis* juice for seven days;
d. 120 mg of cannabinoid extract and 50 mg of raw *cannabis* juice for seven days; and
e. 160 mg of cannabinoid extract and 100 mg of raw *cannabis* juice for seven days.

In some embodiments, this dosing regimen is followed by administering the subject a total daily dose of 200 mg cannabinoid extract and 100 mg of raw *cannabis* juice every day thereafter. In another embodiment this dosing regimen is followed by administering the subject 200 mg of cannabinoid extract and 100 mg of raw *cannabis* juice for seven days; and 400 mg of cannabinoid extract and 100 mg of raw *cannabis* juice every day thereafter.

EXAMPLES

Example 1: Preparation & Storage of *Cannabis*

Fresh *cannabis* plant material (flowers/flower leaves) is harvested from plants propagated from cuttings taken from the mother plants, originating from a single seed source or tissue culture with specific starting ratio's of cannabinoids

Cannabis Plant material (flowers/flower leaves) is stored in a fresh frozen state immediately after harvesting.

Preferably the plant material is flash frozen for 10 minutes at a temperature between −10° F. and −50° F. The plant material is stored in vacuum seal bags for a minimum of 36 hrs prior to extraction. The starting *cannabis* plant material is extracted at a 90% cannabinoid and/or phytocannabinoid concentrated form.

Example 2: Extraction of Inactive Cannabinoids

Cannabis flowers stored in a flash frozen state (see Example 1), and gently spread apart on curing screens while still in a frozen state. Gently break apart and spread the fresh frozen plant material into small sized pieces less than 0.7 inches on a 160u-220u screen to be air dried out.

The plant material (inactive plant matter) is placed in a stainless steel cylinder inside a closed loop hydrocarbon extraction machine such as the Emotek Obe Dos, or equal supercritical $C0_2$ extraction equipment/methods that meet these specific requirements.

Liquid hydrocarbon (99%) is run thru the product and held under pressure of (45 pounds of pressure) for approximately 45 min at a temperature −20° F. fahrenheit to −75° F.

The result material is winterized to remove inert waxy material. Winterization is accomplished by applying a secondary gas to the liquid hydrocarbon; a cold ethanol wash that is filtered out, or by storing the extract solution at −20° F. to −75° F. for approximately 48 hrs. The resultant waxy precipitate is removed by filtration through a twenty μm membrane and passed through activated charcoal.

Finally, the extract is purged under a vacuum pressurized unit Across International Digital Vacuum Drying Oven with a solvent rated recovery pump with a min ½ hp 3425 rip oil-less compressor for approximately 48 hrs.

The final product is removed and stored in amber glass storage containers without light exposure and stored at temps below 40° F. until needed for formulation of products.

Example 3: Extraction of Active Cannabinoids

Cannabis flowers are air dried as in Example 2. Once the *cannabis* flowers are air dried the *cannabis* plant material is placed in a scientific sterile containment oven for 15 min @ 221° F. degrees, and again at 284° F.degrees for 45 min. The process in order decarboxylates the phytocannabinoids. Once the *cannabis* plant material has been decarboxylated it is extracted in an ACTIVE

The fresh *cannabis* plant material (ACTIVE plant material) is placed in a stainless steel cylinder inside a closed loop hydrocarbon extraction Liquid hydrocarbon (99%) is run thru the product and held under pressure of (45 pounds of pressure) for approximately 45 min at a temperature −20° F. fahrenheit to −75° F.

The result material is winterized to remove inert waxy material. Winterization is accomplished by applying a secondary gas to the liquid hydrocarbon; a cold ethanol wash that is filtered out, or by storing the extract solution at −20° F. to −75° F. for approximately 48 hrs. The resultant waxy precipitate is removed by filtration through a twenty μm membrane and passed through activated charcoal.

Finally, the extract is purged under a vacuum pressurized unit Across International Digital Vacuum Drying Oven with a solvent rated recovery pump with a min ½ hp 3425 rip oil-less compressor for approximately 48 hrs.

The resultant decarboxylated CBD:THC oil is converted to CBD:CBN (defined as >90% CBD:THC) oil by heating the oil at 284° F. for 45-75 minutes, and a second temperature at 293° F. for 55 min-90 min.

The final product is removed and stored in amber glass storage containers without light exposure and stored at temps below 40° F. until needed for formulation of products.

Example 3: Extraction Using NEOBEE 895 MCT

Start with cured and dried *cannabis* flowers, flower rosin, hash rosin, hashish, or kif with specific starting ratio's of cannabinoids 1:1, 2:1, 3:1, 4:1, 8:1, 18:1, 20:1, 30:1, 50:1, 70:1. *Cannabis* flowers should be dried out with a moisture content of below 3% and gently broken apart into small sized pieces less then 0.7 inches, or finely milled into 2 mm to 3 mm sized pieces. *Cannabis* flowers, flower rosin, hash rosin, hashish, or kif are combined with NEOBEE 895 MCT. The ratio of *cannabis* to MCT is determined based on the starting material, test results, ratio's, and desired mg per ml outcome. Example 50 g of 20% *Cannabis* flowers combined with 100 ml of MCT oil. The MCT Oil and starting *cannabis* material is heated together in a brewer, double boiler, or on a heat plate at 41 celsius/106 fahrenheit for a minimum of 3 hrs in order to extract and infuse the desired cannabinoids into the MCT oil. The oil is strained thru a 15 micron stainless steel filter, or silk screen to separate the *cannabis* content from the oil. Utilizing a Buchner funnel and 5 micron filtration system under vacuum will provide the best results for flirtation. The soaked *cannabis* content is pressed to remove all remaining oil, filtered, and added back to the concentrated infused THCa and/or CBDa NEOBEE 895 MCT mixture. This initial mixture is considered a INACTIVE state since the cannabinoids are still in the acid forms of THCa and/or CBDa. The infused *cannabis* and NEOBEE 895 MCT oil can be heated at 105 celsius/221 fahrenheit for 15 min, and repeated at 140 celsius/284 fahrenheit 45 min-120 min to ACTIVATE the phytocannabinoids into THC and/or CBD. Decarboxylate *cannabis* flowers, flower rosin, hash rosin, hasish, or kif THC, or CBN, can also be combined to the NEOBEE 895 MCT and heated together at

41 celsius/106 fahrenheit for a minimum of 3 hrs in order to infuse the ACTIVE content into the MCT oil. This process is used to create all products with specific ratio's and milligram to milliliter dosages for capsules, sublingual's, topical, transdermal, etc.

Example 4: Flower & Hash Rosin Extraction

Cannabis flowers are cured until moisture is below 10%. Once the *cannabis* flowers are air dried the *cannabis* plant material is placed in a stainless steel, or nylon silk screen sleeves with a micron ratings ranging including 15u, 25u, 90u, and 120u. Desired micron rating is used based on the starting material flower vs separated trichome heads only known as bubble hash or kif. The flowers, hash, or kif in these sleeves are placed between PTFE 3× flourmer coated sheets, or non-stick parchment paper. The sheets are a min of 2× wider then the nylon or stainless steel screens to collect the extracted cannabinoid oils and resin. A mechanical heat platen press is used with min pressure of 2500 psi with heat applied at ranges between 100-300 degree's for a range of 4 seconds to 3 min depending on the desired out come. This process mechanically separates the cannabinoids and terpenes present in the raw *cannabis* flowers with concentrations of THCa, THC, CBDa, CBD, CBGa, CBG, CBN, CBL. The resin is collected from the PTFE or non stick parchment paper, weighed, and stored in a plastic seal bag or glass pyrex at temperatures of 32 degrees fahrenheit or below. This type of mechanically separated *cannabis* resin and extract is later combined with NEOBEE 895 MCT to make desired formulations, ratio's, and concentrations for the various delivery methods described in this document i.e. capsule, topical, transdermal, sublingual.

Example 5: Preparation of Raw Cannabinoids

Plants with high CBD content are best for juicing as they contain more CBD-acids than non-CBD producing strains.

Process:

1. We remove ONLY fresh *cannabis* leaves during vegetation NOT during the flowering cycle.

2. Leaves are blanched in cold water for cleaning

3. Leaves are then juiced using a cold press juicer or commercial masticating juice

4. The juice is filtered thru a stainless steel filter to remove any particulates.

5. Juice is immediately poured into 1 oz containers or 10 oz containers and freeze-dried at −50° F. degrees.

6. Freeze-dried *cannabis* juice can be used in capsule form, packets, or infused with a medical food.

Example 6: Formulation of *Cannabis* Extracts

Mix 1 gram of *cannabis* oil produced by the above methods with a min of 95% total cannabinoid concentration per 40 ml of NEOBEE 895 for approximately 24 hrs at a temperature under 90° F. but not lower than 70° F. without exposure to light. The resultant infusion is mixed with NEOBEE 895 to produce capsules at 5 mg, 10 mg, 20 mg, and 50 mg total cannabinoids. For subligual formulations 0.5 g or 350 mg of the resultant infusion is combined with 9 ml of NEOBEE 895 and 1 ml of natural sweeteners and flavor additives. (*stevia*, truvia, xyotol, lemon, orange)

Example 7: Exemplary Stacking Protocol for Cancer/Tumor Treatment and Management

Week #1
Morning:
+Frozen ¼ ounce of proprietary blend of Fresh Frozen Raw *Cannabis* Juice (50 mg Raw) or Powdered Raw *Cannabis* Juice added to apple juice, super smoothie, or anti-inflammatory juice beverage.
+5 mg Prana P1 Capsules
Afternoon:
+5 mg Prana P2 Capsules
Dinner:
+5 mg Prana P3 Capsules
Bedtime: (30 min Prior)
+5 mg Prana P4 Capsules
Total Cannabinoids Absorbed Daily: 20 mg+50 mg Raw
Week #2
Morning:
+Frozen ¼ ounce of proprietary blend of Fresh Frozen Raw *Cannabis* Juice (50 mg Raw) or Powdered Raw *Cannabis* Juice added to apple juice, super smoothie, or anti-inflammatory juice beverage.
+10 mg Prana P1 Capsules
Afternoon:
+10 mg Prana P2 Capsules
Dinner:
+10 mg Prana P3 Capsules
Bedtime: (30 min Prior)
+10 mg Prana P4 Capsules
Total Cannabinoids Absorbed Daily: 40 mg+50 mg Raw
Week #3 (Min Holding Dose)
Morning:
+Frozen ¼ ounce of proprietary blend of Fresh Frozen Raw *Cannabis* Juice (50 mg Raw) or Powdered Raw *Cannabis* Juice added to apple juice, super smoothie, or anti-inflammatory juice beverage.
+20 mg Prana P1 Capsules
Afternoon:
+20 mg Prana P2 Capsules
Dinner:
+20 mg Prana P3 Capsules
Bedtime: (30 min Prior)
+20 mg Prana P4 Capsules
Total Cannabinoids Absorbed Daily: 80 mg+50 mg Raw
Week #4
Morning:
+Frozen ¼ ounce of proprietary blend of Fresh Frozen Raw *Cannabis* Juice (50 mg Raw) or Powdered Raw *Cannabis* Juice added to apple juice, super smoothie, or anti-inflammatory juice beverage.
+30 mg Prana P1 Capsules
Afternoon:
+30 mg Prana P2 Capsules
Dinner:
+30 mg Prana P3 Capsules
Bedtime: (30 min Prior)
+30 mg Prana P4 Capsules
Total Cannabinoids Absorbed Daily: 120 mg+50 mg Raw
Week #5
Morning:
+Frozen 0.5 ounce of proprietary blend of Fresh Frozen Raw *Cannabis* Juice (100 mg Raw) or Powdered Raw *Cannabis* Juice added to apple juice, super smoothie, or anti-inflammatory juice beverage.
+40 mg Prana P1 Capsules

Afternoon:
+40 mg Prana P2 Capsules
Dinner:
+40 mg Prana P3 Capsules
Bedtime: (30 min Prior)
+40 mg Prana P4 Capsules
Total Cannabinoids Absorbed Daily: 160 mg+100 mg Raw
Week #6 (Advanced Holding Dose)
Morning:
+Frozen 0.5 ounce of proprietary blend of Fresh Frozen Raw *Cannabis* Juice (100 mg Raw) or Powdered Raw *Cannabis* Juice added to apple juice, super smoothie, or anti-inflammatory juice beverage.
+50 mg Prana P1 Capsules
Afternoon:
+50 mg Prana P2 Capsules
Dinner:
+50 mg Prana P3 Capsules
Bedtime: (30 min Prior)
+50 mg Prana P4 Capsules
Total Cannabinoids Absorbed Daily: 200 mg+100 mg Raw
Week #7-Week #12 (Advanced Stages)
Morning:
+Frozen 0.5 ounce of proprietary blend of Fresh Frozen Raw *Cannabis* Juice (100 mg Raw) or Powdered Raw *Cannabis* Juice added to apple juice, super smoothie, or anti-inflammatory juice beverage.
+100 mg Prana P1 Capsules
Afternoon:
+100 mg Prana P2 Capsules
Dinner:
+100 mg Prana P3 Capsules
Bedtime: (30 min Prior)
+100 mg Prana P4 Capsules

Example 7: Exemplary Protocol for Anxiety/PTSD

Morning
+5 mg-10 mg Prana P2 CBD AM Capsules (2:1 to 3:1, THC:CBD)
+2 mg to 4 mg Prana P4 CBD:CBN Sublingual (1:1)
Afternoon:
+2 mg to 4 mg Prana P4 CBD:CBN Sublingual (1:1)
Used when feeling anxiety or PSTD throughout the day.
After Dinner:
+5 mg-10 mg Prana P3 CBD PM Capsules (2:1 to 1:1, THCa:CBDa)
+4 mg Prana P4 CBD:CBN Sublingual (1:1)
Bedtime:
+10 mg Prana P4 CBN Capsules

Example 8: Exemplary Protocol for Chronic Pain

Morning:
+5 mg Prana P2 CBD AM Capsules (2:1 to 3:1, THC:CBD)
+2 mg to 4 mg Prana P1 THCa Sublingual
Afternoon:
+5 mg Prana P2 CBD AM Capsules (2:1 to 3:1, THC:CBD)
+2 mg to 4 mg Prana P1 THCa Sublingual (As Needed)
Dinner:
+10 mg Prana P3 CBD PM Capsules (2:1 to 1:1, THCa:CBDa)
+2 mg to 4 mg Prana P1 THCa Sublingual
Bedtime:
+10 mg Prana P4 CBN Capsules

Example 9: Exemplary Protocol for Opiate Dependency

Note: This is a 16 week program.
Week #1 & Week #2
Morning:
+Prana P5-100 gms raw or 10 gms powder
+5 mg Prana P1 Prana Capsule
+2 mg Prana P2 CBD AM Sublingual (2:1 to 3:1, THC:CBD)
Afternoon:
+5 mg Prana P1 Prana Capsule
+2 mg Prana P2 CBD AM Sublingual (2:1 to 3:1)
Dinner:
+5 mg Prana P1 Prana Capsule
+2 mg Prana P2 CBD AM Sublingual (2:1 to 3:1)
Bedtime: (30 min Prior)
+10 mg Prana P3 CBD PM Capsules (2:1 to 1:1)
+2 mg Prana P4 Sublingual CBD:CBN (1:1)
Total Cannabinoids Daily: 31 mg+50 mg Raw
Reduce Opiates by 10%-20%
Week #3 & Week #4
Morning:
+Prana P5-100 gms raw or 10 gms powder
+10 mg Prana P1 Capsules
+4 mg Prana P2 CBD AM Sublingual (2:1 to 3:1)
Afternoon:
+10 mg Prana P1 THCa Capsules
+4 mg Prana P2 CBD AM Sublingual (2:1 to 3:1)
Dinner:
+10 mg Prana P1 THCa Capsules
+4 mg Prana P2 CBD AM Sublingual (2:1 to 3:1)
Bedtime: (30 min Prior)
+10 mg Prana P3 CBD PM Capsules (2:1 to 1:1)
+4 mg Prana P4 Sublingual CBD:CBN (1:1)
Total Cannabinoids Absorbed Daily: 56 mg+50 mg Raw
Reduce Opiates by 10%-20%
Week #5 & Week #6
Morning:
+Prana P5-100 gms raw or 10 gms powder
+15 mg Prana P1 THCa Capsules
+6 mg Prana P2 CBD AM Sublingual (2:1 to 3:1)
Afternoon:
+15 mg Prana P1 THCa Capsules
+6 mg Prana P2 CBD AM Sublingual (2:1 to 3:1)
Dinner:
+15 mg Prana P1 THCa Capsules
+6 mg Prana P2 CBD AM Sublingual (2:1 to 3:1)
Bedtime: (30 min Prior)
+15 mg Prana P3 CBD PM Capsules (2:1 to 1:1)
+6 mg Prana P4 Sublingual CBD:CBN (1:1)
Total Cannabinoids Absorbed Daily: 84 mg+50 mg Raw
Reduce Opiates by 10%-20%
Week #7 & Week #8
Morning:
+Prana P5-100 gms raw or 10 gms powder
+20 mg Prana P1 Prana Capsule
+6 mg Prana P2 CBD AM Sublingual (2:1 to 3:1)
Afternoon:
+20 mg Prana P1 Prana Capsule
+6 mg Prana P2 CBD AM Sublingual (2:1 to 3:1)
Dinner:
+20 mg Prana P1 THC Capsules
+6 mg Prana P2 CBD AM Sublingual (2:1 to 3:1)

Bedtime: (30 min Prior)
+20 mg Prana P3 CBD PM Capsules (2:1 to 1:1)
+6 mg Prana P4 Sublingual CBD:CBN (1:1)
Total Cannabinoids Absorbed Daily: 104 mg+50 mg Raw
Reduce Opiates by 10%-20%
Week #8 & Week #9
Morning:
+Prana P5-100 gms raw or 10 gms powder
+15 mg Prana P1 Prana Capsule
+6 mg Prana P2 CBD AM Sublingual (2:1 to 3:1)
Afternoon:
+15 mg Prana P1 Prana Capsule
+6 mg Prana P2 CBD AM Sublingual (2:1 to 3:1)
Dinner:
+15 mg Prana P1 Prana Capsule
+6 mg Prana P2 CBD AM Sublingual (2:1 to 3:1)
Bedtime: (30 min Prior)
+20 mg Prana P3 CBD PM Capsules (2:1 to 1:1)
+6 mg Prana P4 Sublingual CBD:CBN (1:1)
Total Cannabinoids Absorbed Daily: 89 mg+50 mg Raw
Reduce Opiates by 10%-20%
Week #10 & Week #11
Morning:
+Prana P5-100 gms raw or 10 gms powder
+10 mg Prana P1 Prana Capsule
+6 mg Prana P2 CBD AM Sublingual (2:1 to 3:1)
Afternoon:
+10 mg Prana P1 Prana Capsule
+6 mg Prana P2 CBD AM Sublingual (2:1 to 3:1)
Dinner:
+10 mg Prana P1 Prana Capsule
+6 mg Prana P2 CBD AM Sublingual (2:1 to 3:1)
Bedtime: (30 min Prior)
+15 mg Prana P3 CBD PM Capsules (2:1 to 1:1)
+6 mg Prana P4 Sublingual CBD:CBN (1:1)
Total Cannabinoids Absorbed Daily: 69 mg+50 mg Raw
Reduce Opiates by 10%-20%
Week #12 & Week #13
Morning:
+Prana P5-100 gms raw or 10 gms powder
+5 mg Prana P1 Prana Capsule
+6 mg Prana P2 CBD AM Sublingual (2:1 to 3:1)
Afternoon:
+5 mg Prana P1 Prana Capsule
+6 mg Prana P2 CBD AM Sublingual (2:1 to 3:1)
Dinner:
+5 mg Prana P1 Prana Capsule
+6 mg Prana P2 CBD AM Sublingual (2:1 to 3:1)
Bedtime: (30 min Prior)
+10 mg Prana P3 CBD PM Capsules (2:1 to 1:1)
+6 mg Prana P4 Sublingual CBD:CBN (1:1)
Total Cannabinoids Absorbed Daily: 49 mg+50 mg Raw
Reduce Opiates by 10%-20%
Week #14 & Week #15
Morning:
+Prana P5-100 gms raw or 10 gms powder
+4 mg Prana P1 THCa Sublingual
+5 mg Prana P2 CBD AM Capsule (2:1 to 3:1)
Afternoon:
+4 mg Prana P1 THCa Sublingual
+5 mg Prana P2 CBD AM Capsule (2:1 to 3:1)
Dinner:
+4 mg Prana P1 THCa Sublingual
+5 mg Prana P2 CBD AM Capsule (2:1 to 3:1)
Bedtime: (30 min Prior)
+10 mg Prana P3 CBD PM Capsules (2:1 to 1:1)
+4 mg Prana P4 Sublingual CBD:CBN (1:1)
Total Cannabinoids Absorbed Daily: 41 mg+50 mg Raw
Opiates should be Reduced by 80-90%
Week #16+
+Every 3rd Day+Prana P5-100 gms raw or 10 gms powder
Morning:
+10 mg Prana P2 CBD AM Capsule (2:1 to 3:1)
+4 mg Prana P1 THCa Sublingual (Only As Needed for Pain)
Afternoon:
+4 mg Prana P1 THCa Sublingual (Only As Needed for Pain)
Dinner:
+10 mg Prana P3 CBD PM Capsule (2:1 to 1:1)
+4 mg Prana P1 THCa Sublingual (Only As Needed for Pain)
Bedtime: (30 min Prior)
+4 mg Prana P4 Sublingual CBD:CBN (1:1)
Total Cannabinoids Absorbed Daily: 36 mg+25 mg Raw
Opiates should be Reduced by 90%-100%.

OTHER EMBODIMENTS

While the invention has been described in conjunction with the detailed description thereof, the foregoing description is intended to illustrate and not limit the scope of the invention, which is defined by the scope of the appended claims. Other aspects, advantages, and modifications are within the scope of the following claims.

What is claimed is:

1. A cannabinoid formulation, wherein the cannabinoid formulation is selected from the group consisting of:

(a) a formulation wherein 95% or more of the total cannabinoids in the formulation is tetrahydrocannabinolic acid (THCa), cannabidiolic acid (CBDa) is less than 1%, cannabinolic acid (CBNa) is less than 3% and cannabichromenic acid (CBCa) is less than 1%;

(b) a formulation wherein 95% or more of the total cannabinoids in the formulation is tetrahydrocannabinol (THC), cannabidiol (CBD) is less than 1%, cannabinol (CBN) is less than 3% and cannabichromene (CBC) is less than 1%;

(c) a formulation wherein THCa is less than or equal to 35%, CBDa is greater than or equal to 60%, THC is less than 1%, CBN is less than 1% and CBC is less than 1%;

(d) a formulation wherein THCa is greater than or equal to 40%, CBDa is greater than or equal to 40%, THC is less than 1%, CBN is less than 1% and CBC is less than 1%;

(e) a formulation wherein THC is less than or equal to 35%, CBD is greater than or equal to 60%, CBN is less than 1%, and CBC is less than 1%;

(f) a formulation wherein THC is greater than or equal to 40%, CBD is greater than or equal to 40%, CBN is less than 1% and CBC is less than 1%; and

(g) a formulation wherein THC is less than or equal to 9%, CBD is greater than or equal to 40%, CBN is greater than or equal to 40% and CBC is less than 1%.

2. The cannabinoid formulation of claim **1**, wherein the cannabinoid formulation further comprises one or more terpene and/or flavonoid.

3. The cannabinoid formulation of claim **1**, wherein the cannabinoid formulation is infused in a medium chain triglyceride (MCT).

4. The cannabinoid formulation of claim **3**, wherein the MCT is composed of any combination of C-6, C-8, C-10 and C-12 fatty acids.

5. The cannabinoid formulation of claim 1, wherein the cannabinoid formulation is a liquid.

6. The cannabinoid formulation of claim 1, wherein the terpene comprises β-myrcene, β-caryophyllene, or d-limonene.

7. The cannabinoid formulation of claim 1, wherein the terpene comprises β-myrcene, β-caryophyllene, and d-limonene.

8. The cannabinoid formulation of claim 1, wherein the pH of the cannabinoid formulation is at least pH 8.0.

9. The cannabinoid formulation of claim 1, wherein THCa is greater than or equal to 40%, CBDa is greater than or equal to 40%, CBN is less than 1% and CBC is less than 1%, and wherein the ratio of THCa to CBDa is 1:1.

10. The cannabinoid formulation of claim 1, wherein THCa and CBDa are in their activated decarboxylated forms THC and CBD, wherein THC is greater than or equal to 40%, CBD is greater than or equal to 40%, CBN is less than 1% and CBC is less than 1%, and wherein the ratio of THC to CBD is 1:1.

11. The cannabinoid formulation of claim 1, wherein THC is less than or equal to 9%, CBD is greater than or equal to 40%, CBN is greater than or equal to 40% and CBC is less than 1%, and wherein the ratio of CBD to CBN is 1:1.

12. A method of relieving symptoms associated with anxiety, post-traumatic stress disorder, chronic pain, or opiate dependency, paralysis, neuropathy, Crohn's disease, inflammatory bowel disorders, glaucoma, seizures, epilepsy, autism, or cancer in a subject, comprising administering any one or more of the formulations of claim 1.

13. The method of claim 12, wherein the formulation is administered four times daily.

* * * * *

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(54) Title: CANNABIS EXTRACTS AND METHODS OF PREPARING AND USING SAME

(57) Abstract: The invention relates to the extraction of pharmaceutically active components from plant materials, and more particularly to the preparation of a botanical drug substance (BDS) for incorporation in to a medicament. It also relates to a BDS, for use in pharmaceutical formulations. In particular it relates to BDS comprising cannabinoids obtained by extraction from cannabis.

CANNABIS EXTRACTS AND METHODS OF PREPARING AND USING SAME

RELATED APPLICATIONS

[0001] This application claims priority to, and the benefit of U.S. Provisional Application No. 62/066,795 filed on October 21, 2014 and U.S. Provisional Application No. 62/068,278 filed on October 24, 2014, the contents of which are incorporated by reference in their entireties.

FIELD OF THE INVENTION

[0002] This invention relates to the extraction of pharmaceutically active components from plant materials, and more particularly to botanical drug substance (BDS) comprising cannabinoids obtained by extraction from cannabis. Methods of using the extracts to treat chronic pain, paralysis, neuropathy, Crohn's Disease, IBS, glaucoma, PTSD, anxiety, seizures, epilepsy, autoimmune disorders autism, tumors, and cancer are also included.

BACKGROUND OF THE INVENTION

[0003] Cannabis products have been consumed in various forms for thousands of years. The first descriptions of the medical uses date from Chinese herbal texts in the first century A.D. Cannabis products were taken orally in an herbal tea concoction and were used for their pain-relieving and sleep- inducing properties.

[0004] There presently exists the need to provide more effective and safer cannabis extracts for various medical uses, extraction methods that provide unique active compounds that are useful to treat pain and various medical conditions. Additionally, presently known extraction procedures do not provide the desired active ingredient(s) for the particular medical purpose. The present invention overcomes these limitations and provides other related advantages.

SUMMARY OF THE INVENTION

[0005] The invention provides an extract comprising a mixture of at least 95% total cannabinoids, and at least one terpene /flavonoid. The extract contains at least 4, 5, 6 , 7 or more cannabinoids. The cannabinoids are selected from tetrahydrocannabinolic acid (THCa), cannabidiolic acid (CBDa), cannabinolic acid (CBNa) cannabichromenic acid (CBCa), tetrahydrocannabinol (THC), cannabinol (CBN), cannabidiol (CBD) or cannabichromene (CBC). In some aspect the cannabinoids are THCa and CBDa and at least two cannabinoids selected from CBNa, CBCa, THC, CBN and CBC. In a preferred embodiment the cannabinoids are

THC, CBN, CBC and CBD. In another preferred embodiment the cannabinoids are THCa, CBDa, CBNa and CBCa. In yet another preferred embodiment the cannabinoids are THCa, CBDa, THC, CBN, and CBC.

[0006] The terpene/flavonoid is for example, d-limonene linalool, 1,8-cineole (eucalyptol), α-pinene, terpineol-4-ol, p-cymene, borneol, Δ-3-carene, β-sitosterol, β-myrcene, or β-caryophyllene.cannflavin A, apigenin, quercetin or pulegone,.

[0007] Also provided by the invention are formulations containing the extracts according to the invention. For example the formulation contains any of the extracts according to the invention infused with a medium chain triglyceride (MCT). The MCT is for example, NEOBEE 895.

[0008] Preferably, the pH of the formulation is at least pH 8.0.

[0009] In some formulations the concentration of THCa is greater than or equal to 95%; CBDa is less than 1%; CBNa is less than 3%; and CBCa is less than 1%. Optionally the formulation further contains d-limonene, linalool, 1,8-cineole (eucalyptol), α-pinene, terpineol-4-ol, p-cymene, borneol, Δ-3-carene, β-sitosterol, cannflavin A, apigenin, quercetin

[0010] In other formulations the concentration of THCa is less than or equal to 35%; CBDa is greater than or equal to 60%; THC is less than 1%; CBN is less than 1%; and CBC is less than 1%. Optionally, the formulation further contains d-limonene, linalool, 1,8-cineole (eucalyptol), α-pinene, terpineol-4-ol, p-cymene, borneol, Δ-3-carene, β-sitosterol, cannflavin A, apigenin, quercetin

[0011] In another formulation the concentration of THCa is greater than or equal to 40%;CBDa is greater than or equal to 40%; THC is less than 1%; CBN is less than 1%; and CBC is less than 1%. Optionally, the formulation further conatains β-myrcene, β-caryophyllene, pulegone, α-terpineol, β-sitosterol, cannflavin A, apigenin, quercetin

[0012] In yet another formulation the concentration of THC is less than or equal to 9%; CBD is greater than or equal to 40%; CBN is greater than or equal to 40%; and CBS is less than 1%. Optionally, the formulation further containsβ-myrcene, β-caryophyllene, pulegone, α-terpineol, β-sitosterol, cannflavin A, apigenin, quercetin.

[0013] In various aspects the formulation of the invention are formulated for r oral, sublingual, buccal, or topical administration. The sublingual formulation further contains a sweetener such as a stevia extract. Optionally, the sublingual formulation further contains lemon oil, orange oil or both.

[0014] In other aspects the invention provides a method of preparing a cannabis extract providing fresh or live cannabis plant material; extracting the cannabinoids from the plant material to produce a first extract; winterizing and purging the winterized extract. Optionally, the method further incudes decarboxylating the phytocannabinoids prior to extraction. The decarboxylation is accomplished for example, by heating the dried plant material at a temperature of about 221^0F for at least 15 minutes followed by heating at about 284^0F for at least 45 minutes. In some aspects the winterized extract is heated at 284 ^{0}F for at about 45-74 minutes followed by heating at about 293^0F for at least about 55- 90 minutes.

[0015] Extraction is for example by hydrocarbon extraction. Winterizing includes adding cold ethanol to the first extract or storing the first extract at a temperature of about -20° to about -75° F for about 48 hours to produce a waxy precipitate and removing the waxy precipitate by filtration. Optionally, the winterized extract is filtered through activated charcoal.

[0016] The cannabis plant material consists of flowers or flowers and leaves. In some aspects the cannabis plant material is frozen at a temperature between at least -10^0F to -50^0F for at least 36 hours prior to being extracted. Preferably, the cannabis plant material has been propagated from a single seed source or a tissue culture with specific ratios of cannabinoids. In some aspects the cannabis plant material is derived from a cannabis strain having a minimum of 15% THC and less that 1% CBD. In others aspect the cannabis plant material is derived from Sour Tsunami x Catatonic Sour Tsunami x Sour Tsunami, Sour Tsunami, Harlequin, R4 ACDC strains. In yet other as aspects the cannabis plant material is derived from CBD1, Sour Pineapple, CBD Diesel, Harlequin, ACDC or R4. In yet a further aspect the cannabis plant material is derived from Sour Tsunami x Catatonic, Sour Tsunami x Sour Tsunami, Sour Tsunami, Harlequin, R4, Swiss Gold, ACDC, CBD1, Sour Pineapple, or CBD Diesel.

[0017] The invention further provides a method for preparing cannabis juice by blanching fresh cannabis leaves obtained from a cannabis plant in the vegetative stage in cold water; juicing the leaves in a cold press juicer or masticating juicer; and filtering the juice through a filter to remove particulates. Optionally, filter juice is freeze dried.

[0018] The juicer is for example, a cold press juicer or a masticating juicer. Also included in the invention is juice produced according to the method of the invention. In some embodiments the cannabis juice is obtained from cannabis flowers, cannabis roots or both.

[0019] The invention also provides method of relieving symptoms associated with anxiety, post traumatic stress disorder, chronic pain, or opiate dependency, paralysis, neuropathy,

Crohns disease, inflammatory bowel disorders, glaucoma, seizures, epilepsy, autism, or cancer comprising administering to a subject in need thereof one or more of the formulations or juice according to the invention. The formulations are administered four times daily. For example the formulation is administered in the morning; afternoon, evening and at bedtime.

[0020] In specific embodiments the invention provides a method of treating cancer by administering to a subject a total daily doses of: 20 mg of cannabinoid extract and 50 mg of raw cannabis juice for seven days; 40 mg of cannabinoid extract and 50 mg of raw cannabis juice for seven days; 80 mg of cannabinoid extract and 50 mg of raw cannabis juice for seven days; 120 mg of cannabinoid extract and 50 mg of raw cannabis juice for seven days; and 160 mg of cannabinoid extract and 100 mg of raw cannabis juice for seven days. In some aspects the method further includes administering a total daily dose of 200 mg cannabinoid extract and 100 mg of raw cannabis juice every day thereafter or administering 200 mg of cannabinoid extract and 100 mg of raw cannabis juice for seven days; and 400 mg of cannabinoid extract and 100 mg of raw cannabis juice every day thereafter.

[0021] In another embodiment the invention provides method of treating opioid dependency by reducing the amount of opiates used per day by at least 10% and administering to a subject a total daily doses of: 31 mg of cannabinoid extract and 50 mg of raw cannabis for fourteen days; 56 mg of cannabinoid extract and 50 mg of raw cannabis for fourteen days; 84 mg of cannabinoid extract and 50 mg of raw cannabis juice for fourteen days; 104 mg of cannabinoid extract and 50 mg of raw cannabis for fourteen days; 89 mg of cannabinoid extract and 50 mg of raw cannabis for fourteen days; 69 mg of cannabinoid extract and 50 mg of raw cannabis for fourteen days; 49 mg of cannabinoid extract and 50 mg of raw cannabis for fourteen days; and 41 mg of cannabinoid extract and 50 mg of raw cannabis for fourteen days.

[0022] Optionally, the method further includes administering a total daily dose of 36 mg cannabinoid extract and 25 mg of raw cannabis every day thereafter and a single dose of 50 mg raw cannabis every three days.

[0023] In another embodiment, the invention provides a method of treating anxiety/PTSD by administering to a subject a total daily doses of about 28 mg to 42 mg of cannabinoid extract.

[0024] In a further embodiment, the invention includes a method of treating chronic pain by administering to a subject a total daily doses of about 36 mg to 48 mg of cannabinoid extract.

[0025] The formulations are administered four times daily. For example, the formulation is administered in the morning; afternoon, evening and at bedtime.

[0026] Other features and advantages of the invention will be apparent from and are encompassed by the following detailed description and claims.

DETAILED DESCRIPTION

[0027] The present invention is based in part upon extraction procedures and delivery approaches that allow selective utilization of various cannabinoid molecules and terpenes from the whole cannabis sativa plant. These various cannabinoid compounds are designed to selectively affect various cannabinoid receptors in the nervous system, immune system and other tissues. The extract is an oil-based whole plant product that contains inactive and active compounds contained in the cannabis plant such as cannabinoids, terpenes and/or flavonoids. Compositions of the invention and methods of extraction disclosed herein provide an extract with specific physiological properties that are mediated through separate pathways and receptors, which provide numerous benefits and advantages.

[0028] The extracts and/or delivery methods of the invention allows a wide range of prevention, treatment and management options for patients. In some aspects the delivery methods of the invention employs micro-dosing with a stacking method of cannabinoid administration week by week until a certain saturation point that is based on response, weight, and monthly-quarterly test results.

[0029] Surprisingly, it was discovered that the age or the cannabis plant material, the temperature in which it is stored and processed is critical and the ratio of the specific cannabinoids extract is critical to effectiveness of the final formulation. Importantly, for an extract to maintain non-psychoactive properties the cannabis plant material is never heated above 160^0F. Preferably, the non-psychoactive extracts according to the invention are formulated at 110^0F or below.

[0030] Cannabis is a genus of flowering plants that includes three different species, *Cannabis sativa*, *Cannabis indica* and *Cannabis ruderalis*. The term "Cannabis plant(s)" encompasses wild type Cannabis and also variants thereof, including cannabis chemovars which naturally contain different amounts of the individual cannabinoids. For example, some Cannabis strains have been bred to produce minimal levels of THC, the principal psychoactive constituent responsible for the high associated with it and other strains have been selectively bred to produce high levels of THC and other psychoactive cannabinoids.

[0031] Cannabis plants produce a unique family of terpeno-phenolic compounds called cannabinoids, which produce the "high" one experiences from consuming marijuana. There are 483 identifiable chemical constituents known to exist in the cannabis plant, and at least 85 different cannabinoids have been isolated from the plant. The two cannabinoids usually produced in greatest abundance are cannabidiol (CBD) and/or Δ9-tetrahydrocannabinol (THC), but only THC is psychoactive. Cannabis plants are categorized by their chemical phenotype or "chemotype," based on the overall amount of THC produced, and on the ratio of THC to CBD. Although overall cannabinoid production is influenced by environmental factors, the THC/CBD ratio is genetically determined and remains fixed throughout the life of a plant. Non-drug plants produce relatively low levels of THC and high levels of CBD, while drug plants produce high levels of THC and low levels of CBD.

[0032] The best studied cannabinoids include tetrahydrocannabinol (THC), cannabidiol (CBD) and cannabinol (CBN). Other cannabinoids include for example, cannabichromene (CBC), cannabigerol (CBG) cannabinidiol (CBND), Cannabicyclol (CBL), Cannabivarin (CBV), Tetrahydrocannabivarin (THCV), Cannabidivarin (CBDV), Cannabichromevarin (CBCV) Cannabigerovarin (CBGV),Cannabigerol Monomethyl Ether (CBGM).

[0033] Cannabinoids are derived from their respective 2-carboxylic acids (2-COOH) by decarboxylation (catalyzed by heat, light, or alkaline conditions). As a general rule, the carboxylic acids form of the cannabinoid have the function of a biosynthetic precursor.

[0034] As used herein THC, CBD, CBN, CBC, CBG, CBND, CBL, CBV, THCV, CBDV,, CBCV, CBGV and CBGM refer to the decarboxylated form of the cannabinoid. Whereas, THCa, CBDa, CBNa, CBCa, CBGa, CBNDa, CBLa, CBVa, THCVa, CBDVa, CBCVa, CBGVa and CBGM refer to the acid form of the cannabinoid.

[0035] Tetrahydrocannabinol (THC) is the primary psychoactive component of the Cannabis plant. THC is only psychoactive in is decarboxylated state. The carboxylic acid form (THCa) is non-psychoactive.

[0036] Delta-9-tetrahydrocannabinol (Δ9-THC, THC) and delta-8-tetrahydrocannabinol (Δ8-THC), mimic the action of anandamide, a neurotransmitter produced naturally in the body. These two THCs produce the effects associated with cannabis by binding to the CB1 cannabinoid receptors in the brain. THC appears to ease moderate pain (analgesic) and to be neuroprotective, while also offering the potential to reduce neuroinflammation and to stimulate neurogenesis. THC has approximately equal affinity for the CB1 and CB2 receptors.

[0037] Cannabidiol (CBD) is not psychoactive, and was thought not to affect the psychoactivity of THC. However, recent evidence shows that smokers of cannabis with a higher CBD/THC ratio were less likely to experience schizophrenia-like symptoms.[15] This is supported by psychological tests, in which participants experience less intense psychotic-like effects when intravenous THC was co-administered with CBD (as measured with a PANSS test). Cannabidiol has little affinity for CB1 and CB2 receptors but acts as an indirect antagonist of cannabinoid agonists. Recently it was found to be an antagonist at the putative new cannabinoid receptor, GPR55, a GPCR expressed in the caudate nucleus and putamen. Cannabidiol has also been shown to act as a 5-HT1A receptor agonist, an action that is involved in its antidepressant, anxiolytic, and neuroprotective effects.

[0038] It appears to relieve convulsion, inflammation, anxiety, and nausea. CBD has a greater affinity for the CB2 receptor than for the CB1 receptor. CBD shares a precursor with THC and is the main cannabinoid in low-THC Cannabis strains. CBD apparently plays a role in preventing the short-term memory loss associated with THC in mammals.

[0039] Cannabinol (CBN) is the primary product of THC degradation, and there is usually little of it in a fresh plant. CBN content increases as THC degrades in storage, and with exposure to light and air. It is only mildly psychoactive. Its affinity to the CB2 receptor is higher than for the CB1 receptor

[0040] Cannabigerol (CBG) is non-psychotomimetic but still affects the overall effects of Cannabis. It acts as an α2-adrenergic receptor agonist, 5-HT1A receptor antagonist, and CB1 receptor antagonist.[31] It also binds to the CB2 receptor.[31]

[0041] Tetrahydrocannabivarin (THCV) is prevalent in certain central Asian and southern African strains of Cannabis. It is an antagonist of THC at CB1 receptors and attenuates the psychoactive effects of THC.

[0042] Cannabidivarin (CBDV) is usually a minor constituent of the cannabinoid profile.

[0043] Cannabichromene (CBC) is non-psychoactive and does not affect the psychoactivity of THC. More common in tropical cannabis varieties. Effects include anti-inflammatory and analgesic.

[0044] In addition to cannabinoids, cannabis plants produce terpenes, a diverse group of organic hydrocarbons that are the building blocks of the cannabinoids.

[0045] Over 100 different terpenes have been identified in the cannabis plant, and every strain tends toward a unique terpene type and composition. The terpenes act synergistically with

the cannabinoids to provide a therapeutic effect. Examples of some common terpenes found in Cannabis include:

[0046] Borneol- menthol, camphor, pine, woody. Can be easily converted into menthol. It is considered a "calming sedative" in Chinese medicine. It is directed for fatigue, recovery from illness and stress.

[0047] Caryophyllene - spicy, sweet, woody, clove, camphor, peppery. It binds weakly to CB2 receptor. As a topical it is one of the constituents of an anti-inflammatory and analgesic treatment for toothache. In high amounts, it's a calcium and potassium ion channel blocker. As a result, it impedes the pressure exerted by heart muscles.

[0048] Cineole/Eucalyptol- spicy, camphor, refreshing, minty. It is used to increase circulation, pain relief and easily crosses the blood-brain-barrier to trigger fast olfactory reaction.

[0049] Delta3Carene- sweet, pine, cedar, woodsy, pungent. In aroma therapy, cypress oil, high in D-3-carene, is used to dry excess fluids, tears, running noses, excess menstrual flow and perspiration.

[0050] Limonene- citrus (orange, tangerine, lemon, and grapefruit), rosemary, juniper, peppermint. Repulsive to predators. Found in the rinds of many fruits and flowers. With the presence of other certain terpenes, Limonene can be an anti-bacterial, anti-fungal, anti-depressant and anti- carcinogen. It can synergistically promote the absorption of other terpenes by quickly penetrating cell membranes. The result can be increased systolic blood pressure.

[0051] Linolool- floral (spring flowers), lily, citrus and candied spice. Possesses anti-anxiety and sedative properties.

[0052] Myrcene – clove like, earthy, green-vegetative, citrus, fruity with tropical mango and minty nuances. The most prevalent terpene found in most varieties of marijuana. It's a building block for menthol, citronella, and geraniol. It possesses antimicrobial, antiseptic, analgesic, antioxidant, anti-carcinogen, anti depressant, anti-inflammatory, and muscle relaxing effects. Myrcene affects the permeability of the cell membranes, allowing more THC to reach brain cells.

[0053] Pinene- Alpha: pine needles, rosemary Beta: dill, parsley, rosemary, basil, yarrow, rose, hops, the familiar odor associated with pine trees and their resins. Pinene can increase mental focus and energy, as well as act as an expectorant, bronchodilator, and topical antiseptic. It easily crosses the blood-brain barrier where it inhibits activity of acetylcholinesterase, which

destroys acetylcholine, an information transfer molecule, resulting in better memory. It may counteract THC's activity, which leads to low acetylcholine levels.

[0054] Pulegone- mint, camphor, rosemary, candy. Pulegone is an acetylcholinesterase inhibitor. That is, it stops the action of the protein that destroys acetylcholine, which is used by the brain to store memories.

[0055] In various aspects the invention provides cannabis extracts with predefined ratios of cannabinoids. Standard conditions for cannabinoid assays, and methods of calculating cannabinoid content (as %) are well known in the art.

[0056] The extracts are mixture of at least 95% total cannabinoids and include terpenes and/or flavonoids. Preferably the extracts contains a mixture of at least cannabinoids four cannabinoid such as tetrahydrocannabinolic acid (THCa), cannabidiolic acid (CBDa), cannabinolic acid (CBNa) cannabichromenic acid (CBCa), tetrahydrocannabinol (THC), cannabinol (CBN), cannabidiol (CBD)and cannabichromene (CBC).

[0057] In some embodiments the extract contains THCa and CBDa and at least two cannabinoids selected from CBNa, CBCa, THC, CBN and CBC. In other embodiments the extract includes THC, CBN, CBC and CBD. In further embodiments the extract includes THCa, CBDa, CBNa and CBCa. In other embodiments the extract includes THCa, CBDa, THC, CBN, and CBC.

[0058] The terpene and/or flavonoids in the extract include for example, terpene is linalool, 1,8-cineole (eucalyptol), α-pinene, terpineol-4-ol, p-cymene, borneol, Δ-3-carene, β-sitosterol, β-myrcene, β-caryophyllene.d-limonene, cannflavin A, apigenin, quercetin or pulegone.

[0059] The extracts of the invention may be formulated with one or more pharmaceutically acceptable carriers, diluents or excipients or deposited on a pharmaceu- tically acceptable surface for vaporisation in order to produce pharmaceutical formulations containing cannabinoids as the pharmaceutically active agents.

[0060] Therefore, in a further aspect the invention provides a method of making a pharmaceutical composition comprising, as an active agent, a substance which is an extract from at least one cannabis plant variety.

[0061] Separate extracts may be prepared from single cannabis plant varieties having differing cannabinoid content (e.g. high THC and high CBD plants) and then mixed or blended together prior to formulation to produce the final pharmaceutical composition. This approach is

preferred if, for example, it is desired to achieve a defined ratio by weight of individual cannabinoids in the final formulation. Alternatively, plant material from one or more cannabis plant varieties of defined cannabinoid content may be mixed together prior to extraction of a single botanical drug substance having the desired cannabinoid content, which may then be formulated into a final pharmaceutical composition.

[0062] The extract may be formulated with any convenient pharmaceutically acceptable diluents, carriers or excipients to produce a pharmaceutical composition. The choice of diluents, carriers or excipients will depend on the desired dosage form, which may in turn be dependent on the intended route of administration to a patient. Preferred dosage forms include, liquid dosage forms for administration via pump-action or aerosol sprays, tablets, pastilles, gels, capsules, suppositories, powders, etc. and vaporizers. Such dosage forms may be prepared in accordance with standard principles of pharmaceutical formulation, known to those skilled in the art.

[0063] Liquid formulations are particularly preferred. A particularly preferred formulation for administration of cannabinoids, though not intended to be limiting to the invention, is a liquid formulation of the extracts according to the invention infused with a medium chain triglyceride (MCT). The MCT suitable for human consumption. The MCT may be composed of any combinations of C-6; C-8; C-10:C12 fatty acids. For example, the MCT is composed of 97%:3% C-8:C10;C-12 fatty acids (e.g., NEOBEE 895). Preferably the pH of the formulation is at least pH 8.0. The formulations are suitable for oral, sublingual, buccal, or topical administration. When used for sublingual administration the formulation optionally comprises a sweetener such as stevia extract and or a flavoring such as for example lemon oil, orange oil or both.

[0064] A preferred formulation includes a cannabinoid mixture where THCa is greater than or equal to 95%; a CBDa is less than 1%; CBNa is less than 3%; and CBCa is less than 1%. In some aspects the formulation further includes d-limonene, linalool, 1,8-cineole (eucalyptol), α-pinene, terpineol-4-ol, p-cymene, borneol, Δ-3-carene, β-sitosterol, cannflavin A, apigenin, and quercetin. This preferred formulation is referred to herein as PRANA 1.

[0065] Another preferred formulation includes a cannabinoid mixture where the THCa is less than or equal to 35%; CBDa is greater than or equal to 60%;THC is less than 1%; CBN is less than 1%; and CBC is less than 1%. In some aspects the formulation further includes d-limonene, linalool, 1,8-cineole (eucalyptol), α-pinene, terpineol-4-ol, p-cymene, borneol, Δ-3-

carene, β-sitosterol, cannflavin A, apigenin, and quercetin. This preferred formulation is referred to herein as PRANA 2.

[0066] In yet another preferred embodiment the formulation includes a cannabinoid mixture where the THCa is greater than or equal to 40%; CBDa is greater than or equal to 40%; THC is less than 1%; CBN is less than 1%; and CBC is less than 1%. In some aspects the formulation further includes β-myrcene, β-caryophyllene, pulegone, α-terpineol, β-sitosterol, cannflavin A, apigenin, and quercetin. This preferred formulation is referred to herein as PRANA 3.

[0067] In a further embodiment the formulation includes a cannabinoid mixture THC is less than or equal to 9%; CBD is greater than or equal to 40%; CBN is greater than or equal to 40%; and CBS is less than 1%. In some aspects the formulation further includes β-myrcene, β-caryophyllene, pulegone, α-terpineol, β-sitosterol, cannflavin A, apigenin, and quercetin. This preferred formulation is referred to herein as PRANA 4.

[0068] The extract is formulated for oral use (e.g. capsules) in dosage forms that provide 5 mg, 10 mg, 20 mg, or 50 mg of total cannabinoids per dose. For sublingual use, the extract is formulated to provide 0.5, 1 mg, or 2 mg, per drop.

[0069] In some applications, the patient may find it advantageous to activate (i.e.,decarboxylate) the inactive (i.e. carboxylic acid form) cannabinoids in the extracts and formulations of the invention. The inactive cannabinoids (e.g., THCa and CBDa) of the extracts and formulation of the invention can be converted to active cannabinoids (THC and CBD) by heating the extracts and formulation at a temperature above 160^0F. For example, a vessel containing the extracts and formulations of the invention are placed in boiling water (212^0F) for about 30 minutes.

[0070] According the invention further contemplates extracts and formulations thereof having the same ratio of cannabinoids as PRANA 1, PRANA 2 and PRANA3 where the THA and the CBD is in its activated decarboxylated form.

[0071] The methods of the invention may be used to prepare a cannabinoid –rich extract from cannabis plant material. The method includes providing fresh or live cannabis plant material; extracting the cannabinoids from the fresh or live plant material to produce a first extract; winterizing the first to produce a winterized extract and purging the winterized extract to produce a cannabis extract. Optionally, the method includes decarboxylating the phytocannabinoids prior the extraction step.

[0072] Decarboxylation of cannabinoid acids is a function of time and temperature, thus at higher temperatures a shorter period of time will be taken for complete decarboxylation of a given amount of cannabinoid acid. In selecting appropriate conditions for decarboxylation consideration must, however, be given to minimising thermal degradation of the desirable, pharmacological cannabinoids into undesirable degradation products, particularly thermal degradation of THC to cannabinol (CBN). Preferably, decarboxylation is carried out in a multi-step heating process. For example, Phytocannabinoids are decarboxylated for example by heating the dried plant material at a temperature of about 221^0F for at least 15 minutes followed by heating at about 284^0F for at least 45 minutes. Other suitable methods of decarboxylating phytocannabinoids known in the art may be used.

[0073] In some aspects resultant cannabis extract is heated at 284 ^{0}F for at about 45-74 minutes followed by heating at about 293^0F for at least about 55- 90 minutes.

[0074] The cannabis plant material consists of flowers or flowers and leaves. Preferably, the cannabis plant material is frozen at a temperature between at least $^-10^0$F to $^-50^0$F for at least 36 hours prior to being dried.

[0075] The cannabis plant material has been propagated from a single seed source or a tissue culture or clone with specific ratios of cannabinoids.

[0076] Any suitable method for extraction known in the art may be used. For example extraction is hydrocarbon extraction, supercritical C02 or NEOBEE 896 MCT.

[0077] The first extract may be winterizing by any method known in the art. For example the first extract is winterized by comprises adding cold ethanol or by storing the first extract at temperature of about $^-20^o$ Fto about $^-75^o$ F for about 48 hours. Winterization produces a waxy precipitate. The waxy precipitate is removed by filtration. Optionally, the winterized extract through activated charcoal.

[0078] In some aspects the cannabis plant material is derived from a cannabis strain having a minimum of 15% THC and less that 1% CBD. In other aspects the cannabis plant material is derived from cannabis strains having a minimum of 10% CBD and less than 10% THC. For example the cannabis plant material is derived from Sour Tsunami x Catatonic Sour Tsunami x Sour Tsunami, Sour Tsunami , Harlequin, R4 or ACDC strains. In other embodiments the cannabis plant material is derived from CBD1, Sour Pineapple, CBD Diesel, Harlequin, ACDC or R4. In yet another embodiment the cannabis plant material is derived from

Sour Tsunami x Catatonic, Sour Tsunami x Sour Tsunami, Sour Tsunami, Harlequin, R4, Swiss Gold, ACDC, CBD1, Sour Pineapple, or CBD Diesel.

[0079] The invention also provides a method for preparing cannabis juice comprising blanching fresh cannabis leaves obtained from a cannabis plant in the vegetative stage in cold water; juicing the leaves in a cold press juicer or masticating juicer; filtering the juice through a filter to remove particulates. Optionally, the juice freeze dried. The juicer is a cold press juicer or a masticating juicer. In some aspects the juice further includes cannabis juice obtained from cannabis flowers, cannabis roots or both.

[0080] The juice of raw cannabis provides unique healing benefits. Plant chemicals known as cannabinoid acids such as CBD-acids, and THC-acids break down quickly after harvest, so these compounds are not available in traditional preparations such as cooked 'medibles', smoking, or vaporizingThe healing benefits of cannabinoid-acids are only present for a short period of time before the chemicals break down, so juicing needs to be done quickly after harvest. Fan leaves should make up the majority of the juice, and adding a small amount of cannabis flowers can be beneficial.

[0081] Cannabis extracts and juice have wide-ranging beneficial effects on a number of medical conditions.

[0082] Chronic pain, paralysis, neuropathy, Crohn's Disease, inflammatory bowel disorders (IBS and IBD), glaucoma, PTSD, anxiety, seizures, epilepsy, autoimmune disorders, autism, tumors, and cancer have all been shown by several studies to be controlled by use of Cannabis. In addition, nausea and vomiting that are unresponsive to other medications have been shown to be helped through the use of Cannabis. Dependency on opiates have also been shown to be controlled by the use of Cannabis

[0083] Accordingly the invention also includes methods of alleviating a symptom associated with anxiety, post-traumatic stress disorder, chronic pain, or opiate dependency, paralysis, neuropathy, Crohn's disease, inflammatory bowel disorders, glaucoma, seizures, epilepsy, autism, or cancer comprising administering to a subject any one of the formulation according to the invention. In some embodiments the subject receives both a formulation containing a cannabis extract and raw cannabis in the form of a juice.

[0084] In some embodiments the formulation are administered four times daily. For example, the formulations are administered in the morning, afternoon, evening and at bedtime. The formulations are administered such that the ratio of cannabinoids are different depending

upon the time of day administered. For example, formulations containing lower amounts of THC (and higher amounts of THCa) are administered during waking hours of the day. Whereas, formulations containing higher amounts of THC (and lower amounts of THCa) are administered prior to bedtime. Exemplary day time formulations include a cannabinoid mixture where THCa is greater than or equal to 95%; a CBDa is less than 1%; CBNa is less than 3%; and CBCa is less than 1%; a cannabinoid mixture where the THCa is less than or equal to 35%; CBDa is greater than or equal to 60%;THC is less than 1%; CBN is less than 1%; and CBC is less than 1%; or a cannabinoid mixture where the THCa is greater than or equal to 40%; CBDa is greater than or equal to 40%; THC is less than 1%; CBN is less than 1%; and CBC is less than 1%. An exemplary bedtime formulation includes a cannabinoid mixture THC is less than or equal to 9%; CBD is greater than or equal to 40%; CBN is greater than or equal to 40%; and CBS is less than 1%.

[0085] Preferably a formulation including a cannabinoid mixture where THCa is greater than or equal to 95%; a CBDa is less than 1%; CBNa is less than 3%; and CBCa is less than 1% is administered in the morning. Preferably a cannabinoid mixture where the THCa is less than or equal to 35%; CBDa is greater than or equal to 60%;THC is less than 1%; CBN is less than 1%; and CBC is less than 1% is administered in the afternoon. Preferably, a cannabinoid mixture where the THCa is greater than or equal to 40%; CBDa is greater than or equal to 40%; THC is less than 1%; CBN is less than 1%; and CBC is less than 1% is administered in the evening.

[0086] In various aspects the method of the invention include administering the cannabinoids containing compounds by employing an escalating dosing regimen where the total amount of cannabinoids are increased over time. For example, the amount of cannabinoids administered is increased week by week until a certain saturation point that is based on response, weight, and monthly-quarterly test results. To treat opioid dependency, opiates are gradually replaced cannabinoids.

[0087] In a preferred method cancer is treated by administering to a subject a total daily doses of:

a. 20 mg of cannabinoid extract and 50 mg of raw cannabis juice for seven days;
b. 40 mg of cannabinoid extract and 50 mg of raw cannabis juice for seven days;
c. 80 mg of cannabinoid extract and 50 mg of raw cannabis juice for seven days;
d. 120 mg of cannabinoid extract and 50 mg of raw cannabis juice for seven days; and

e. 160 mg of cannabinoid extract and 100 mg of raw cannabis juice for seven days.

[0088] In some embodiments, this dosing regimen is followed by administering the subject a total daily dose of 200 mg cannabinoid extract and 100 mg of raw cannabis juice every day thereafter. In another embodiment this dosing regimen is followed by administering the subject 200 mg of cannabinoid extract and 100 mg of raw cannabis juice for seven days; and 400 mg of cannabinoid extract and 100 mg of raw cannabis juice every day thereafter.

EXAMPLES

[0089] **Example 1: Preparation & Storage of Cannabis**

[0090] Fresh cannabis plant material (flowers / flower leaves) is harvested from plants propagated from cuttings taken from the mother plants, originating from a single seed source or tissue culture with specific starting ratio's of cannabinoids

[0091] Cannabis Plant material (flowers / flower leaves) is stored in a fresh frozen state immediately after harvesting.

[0092] Preferably the plant material is flash frozen for 10 minutes at a temperature between $^{-}10\ ^{0}F$ and $^{-}50^{0}F$. The plant material is stored in vacuum seal bags for a minimum of 36 hrs prior to extraction. The starting cannabis plant material is extracted at a 90% cannabinoid and/or phytocannabinoid concentrated form.

[0093] **EXAMPLE 2: EXTRACTION OF INACTIVE CANNABINOIDS**

[0094] Cannabis flowers stored in a flash frozen state (see Example 1), and gently spread apart on curing screens while still in a frozen state. Gently break apart and spread the fresh frozen plant material into small sized pieces less than 0.7 inches on a 160u - 220u screen to be air dried out.

[0095] The plant material (inactive plant matter) is placed in a stainless steel cylinder inside a closed loop hydrocarbon extraction machine such as the Emotek Obe Dos, or equal supercritical $C0_2$ extraction equipment / methods that meet these specific requirements.

[0096] Liquid hydrocarbon (99%) is run thru the product and held under pressure of (45 pounds of pressure) for approximately 45min at a temperature $^{-}20^{0}F$ fahrenheit to $^{-}75\ ^{0}F$.

[0097] The result material is winterized to remove inert waxy material. Winterization is accomplished by applying a secondary gas to the liquid hydrocarbon; a cold ethanol wash that is filtered out, or by storing the extract solution at $^{-}20^{0}F$ to $^{-}75^{0}F$ for approximately 48 hrs. The resultant waxy precipitate is removed by filtration through a twenty μm membraneand passed through activated charcoal.

[0098] Finally, the extract is purged under a vacuum pressurized unit Across International Digital Vacuum Drying Oven with a solvent rated recovery pump with a min 1/2 hp 3425 rip oil-less compressor for approximately 48 hrs.

[0099] The final product is removed and stored in amber glass storage containers without light exposure and stored at temps below 40 ^{0}F until needed for formulation of products.

[00100] **EXAMPLE 3: EXTRACTION OF ACTIVE CANNABINOIDS**

[00101] Cannabis flowers are air dried as in Example 2. Once the cannabis flowers are air dried the cannabis plant material is placed in a scientific sterile containment oven for 15min @ 221^{0}F degrees, and again at 284 ^{0}Fdegrees for 45min. The process in order decarboxylates the phytocannabinoids. Once the cannabis plant material has been decarboxylated it is extracted in an ACTIVE

[00102] The fresh cannabis plant material (ACTIVE plant material) is placed in a stainless steel cylinder inside a closed loop hydrocarbon extraction Liquid hydrocarbon (99%) is run thru the product and held under pressure of (45 pounds of pressure) for approximately 45min at a temperature $^-$20^{0}F fahrenheit to $^-$75 ^{0}F.

[00103] The result material is winterized to remove inert waxy material. Winterization is accomplished by applying a secondary gas to the liquid hydrocarbon; a cold ethanol wash that is filtered out, or by storing the extract solution at $^-$20^{0}F to $^-$75^{0}F for approximately 48 hrs. The resultant waxy precipitate is removed by filtration through a twenty μm membraneand passed through activated charcoal.

[00104] Finally, the extract is purged under a vacuum pressurized unit Across International Digital Vacuum Drying Oven with a solvent rated recovery pump with a min 1/2 hp 3425 rip oil-less compressor for approximately 48 hrs.

[00105] The resultant decarboxylated CBD:THC oil is converted to CBD:CBN (defined as >90% CBD:THC) oil by heating the oil at 284^{0}F for 45-75 minutes, and a second temperature at 293^{0}F for 55min - 90min.

[00106] The final product is removed and stored in amber glass storage containers without light exposure and stored at temps below 40 ^{0}F until needed for formulation of products.

[00107] **EXAMPLE 3: EXTRACTION USING NEOBEE 895 MCT**

[00108] Start with cured and dried cannabis flowers, flower rosin, hash rosin, hashish, or kif with specific starting ratio's of cannabinoids 1:1, 2:1, 3:1, 4:1, 8:1, 18:1, 20:1, 30:1, 50:1, 70:1. Cannabis flowers should be dried out with a moisture content of below 3% and gently

broken apart into small sized pieces less then .7 inches, or finely milled into 2mm to 3mm sized pieces. Cannabis flowers, flower rosin, hash rosin, hashish, or kif are combined with NEOBEE 895 MCT. The ratio of cannabis to MCT is determined based on the starting material, test results, ratio's, and desired mg per ml outcome. Example 50g of 20% Cannabis flowers combined with 100ml of MCT oil. The MCT Oil and starting cannabis material is heated together in a brewer, double boiler, or on a heat plate at 41 celsius / 106 fahrenheit for a minimum of 3hrs in order to extract and infuse the desired cannabinoids into the MCT oil. The oil is strained thru a 15 micron stainless steel filter, or silk screen to separate the cannabis content from the oil. Utilizing a Buchner funnel and 5 micron filtration system under vacuum will provide the best results for flirtation. The soaked cannabis content is pressed to remove all remaining oil, filtered, and added back to the concentrated infused THCa and/or CBDa NEOBEE 895 MCT mixture. This initial mixture is considered a INACTIVE state since the cannabinoids are still in the acid forms of THCa and/or CBDa. The infused cannabis and NEOBEE 895 MCT oil can be heated at 105 celsius / 221 fahrenheit for 15min, and repeated at 140celsius / 284 fahrenheit 45min - 120min to ACTIVATE the phytocannabinoids into THC and/or CBD. Decarboxylate cannabis flowers, flower rosin, hash rosin, hasish, or kif THC, or CBN, can also be combined to the NEOBEE 895 MCT and heated together at 41 celsius / 106 fahrenheit for a minimum of 3hrs in order to infuse the ACTIVE content into the MCT oil. This process is used to create all products with specific ratio's and milligram to milliliter dosages for capsules, sublingual's, topical, transdermal, etc.

[00109] **EXAMPLE 4: FLOWER & HASH ROSIN EXTRACTION**

[00110] Cannabis flowers are cured until moisture is below 10%. Once the cannabis flowers are air dried the cannabis plant material is placed in a stainless steel, or nylon silk screen sleeves with a micron ratings ranging including 15u, 25u, 90u, and 120u. Desired micron rating is used based on the starting material flower vs separated trichome heads only known as bubble hash or kif. The flowers, hash, or kif in these sleeves are placed between PTFE 3x flourmer coated sheets, or non-stick parchment paper. The sheets are a min of 2x wider then the nylon or stainless steel screens to collect the extracted cannabinoid oils and resin. A mechanical heat platen press is used with min pressure of 2500 psi with heat applied at ranges between 100 - 300 degree's for a range of 4 seconds to 3 min depending on the desired out come. This process mechanically separates the cannabinoids and terpenes present in the raw cannabis flowers with concentrations of THCa, THC, CBDa, CBD, CBGa, CBG, CBN, CBL. The resin is collected

from the PTFE or non stick parchment paper, weighed, and stored in a plastic seal bag or glass pyrex at temperatures of 32 degrees fahrenheit or below. This type of mechanically separated cannabis resin and extract is later combined with NEOBEE 895 MCT to make desired formulations, ratio's, and concentrations for the various delivery methods described in this document i.e. capsule, topical, transdermal, sublingual.

[00111] **EXAMPLE 5: PREPARATION OF RAW CANNABINOIDS**

[00112] Plants with high CBD content are best for juicing as they contain more CBD-acids than non-CBD producing strains.

[00113] Process:

[00114] 1. We remove ONLY fresh cannabis leaves during vegetation NOT during the flowering cycle.

[00115] 2. Leaves are blanched in cold water for cleaning

[00116] 3. Leaves are then juiced using a cold press juicer or commercial masticating juice

[00117] 4. The juice is filtered thru a stainless steel filter to remove any particulates.

[00118] 5. Juice is immediately poured into 1oz containers or 10oz containers and freeze-dried at $^{-}50^{0}$F degrees.

[00119] 6. Freeze-dried cannabis juice can be used in capsule form, packets, or infused with a medical food.

[00120] **EXAMPLE 6: FORMULATION OF CANNABIS EXTRACTS**

[00121] Mix 1 gram of cannabis oil produced by the above methods with a min of 95% total cannabinoid concentration per 40ml of NEOBEE 895 for approximately 24 hrs at a temperature under 90 ^{0}F but not lower than 70 ^{0}F without exposure to light. The resultant infusion is mixed with NEOBEE 895 to produce capsules at 5mg, 10mg, 20mg, and 50mg total cannabinoids. For subligual formulations 0.5 g or 350 mg of the resultant infusion is combined with 9ml of NEOBEE 895 and 1 ml of natural sweeteners and flavor additives. (stevia, truvia, xyotol, lemon, orange)

[00122] **EXAMPLE 7: EXEMPLARY STACKING PROTOCOL FOR CANCER/TUMOR TREATMENT AND MANAGEMENT**

WEEK #1

Morning:

+ Frozen 1/4 ounce of proprietary blend of Fresh Frozen Raw Cannabis Juice (50mg Raw) or Powdered Raw Cannabis Juice added to apple juice, super smoothie, or anti-inflammatory juice beverage.

+ 5mg Prana P1 Capsules

Afternoon:

+ 5mg Prana P2 Capsules

Dinner:

+ 5mg Prana P3 Capsules

Bedtime: (30min Prior)

+ 5mg Prana P4 Capsules

TOTAL CANNABINOIDS ABSORBED DAILY: 20mg + 50mg Raw

WEEK #2

Morning:

+ Frozen 1/4 ounce of proprietary blend of Fresh Frozen Raw Cannabis Juice (50mg Raw) or Powdered Raw Cannabis Juice added to apple juice, super smoothie, or anti-inflammatory juice beverage.

+ 10mg Prana P1 Capsules

Afternoon:

+ 10mg Prana P2 Capsules

Dinner:

+ 10mg Prana P3 Capsules

Bedtime: (30min Prior)

+ 10mg Prana P4 Capsules

TOTAL CANNABINOIDS ABSORBED DAILY: 40mg + 50mg Raw

WEEK #3 (MIN HOLDING DOSE)

Morning:

+ Frozen 1/4 ounce of proprietary blend of Fresh Frozen Raw Cannabis Juice (50mg Raw) or Powdered Raw Cannabis Juice added to apple juice, super smoothie, or anti-inflammatory juice beverage.

+ 20mg Prana P1 Capsules

Afternoon:

+ 20mg Prana P2 Capsules

Dinner:

+ 20mg Prana P3 Capsules

Bedtime: (30min Prior)

+ 20mg Prana P4 Capsules

TOTAL CANNABINOIDS ABSORBED DAILY: 80mg + 50mg Raw

WEEK #4

Morning:

+ Frozen 1/4 ounce of proprietary blend of Fresh Frozen Raw Cannabis Juice (50mg Raw) or Powdered Raw Cannabis Juice added to apple juice, super smoothie, or anti-inflammatory juice beverage.

+ 30mg Prana P1 Capsules

Afternoon:

+ 30mg Prana P2 Capsules

Dinner:

+ 30mg Prana P3 Capsules

Bedtime: (30min Prior)

+ 30mg Prana P4 Capsules

TOTAL CANNABINOIDS ABSORBED DAILY: 120mg + 50mg Raw

WEEK #5

Morning:

+ Frozen .5 ounce of proprietary blend of Fresh Frozen Raw Cannabis Juice (100mg Raw) or Powdered Raw Cannabis Juice added to apple juice, super smoothie, or anti-inflammatory juice beverage.

+ 40mg Prana P1 Capsules

Afternoon:

+ 40mg Prana P2 Capsules

Dinner:

+ 40mg Prana P3 Capsules

Bedtime: (30min Prior)

+ 40mg Prana P4 Capsules

TOTAL CANNABINOIDS ABSORBED DAILY: 160mg + 100mg Raw

WEEK #6 (ADVANCED HOLDING DOSE)

Morning:

+ Frozen .5 ounce of proprietary blend of Fresh Frozen Raw Cannabis Juice (100mg Raw) or Powdered Raw Cannabis Juice added to apple juice, super smoothie, or anti-inflammatory juice beverage.

+ 50mg Prana P1 Capsules

Afternoon:

+ 50mg Prana P2 Capsules

Dinner:

+ 50mg Prana P3 Capsules

Bedtime: (30min Prior)

+ 50mg Prana P4 Capsules

TOTAL CANNABINOIDS ABSORBED DAILY: 200mg + 100mg Raw

WEEK #7 - WEEK #12 (ADVANCED STAGES)

Morning:

+ Frozen .5 ounce of proprietary blend of Fresh Frozen Raw Cannabis Juice (100mg Raw) or Powdered Raw Cannabis Juice added to apple juice, super smoothie, or anti-inflammatory juice beverage.

+ 100mg Prana P1 Capsules

Afternoon:

+ 100mg Prana P2 Capsules

Dinner:

+ 100mg Prana P3 Capsules

Bedtime: (30min Prior)

+ 100mg Prana P4 Capsules

[00123] EXAMPLE 7: EXEMPLARY PROTOCOL FOR ANXIETY / PTSD

Morning

+ 5mg - 10mg Prana P2 CBD AM Capsules (2:1 to 3:1, THC:CBD)

+ 2mg to 4mg Prana P4 CBD:CBN Sublingual (1:1)

Afternoon:

+ 2mg to 4mg Prana P4 CBD:CBN Sublingual (1:1)

Used when feeling anxiety or PSTD throughout the day.

After Dinner:

+ 5mg - 10mg Prana P3 CBD PM Capsules (2:1 to 1:1, THCa:CBDa)

+ 4mg Prana P4 CBD:CBN Sublingual (1:1)

Bedtime:

+ 10mg Prana P4 CBN Capsules

[00124] EXAMPLE 8: EXEMPLARY PROTOCOL FOR CHRONIC PAIN

Morning:

+ 5mg Prana P2 CBD AM Capsules (2:1 to 3:1, THC:CBD)

+ 2mg to 4mg Prana P1 THCa Sublingual

Afternoon:

+ 5mg Prana P2 CBD AM Capsules (2:1 to 3:1, THC:CBD)

+ 2mg to 4mg Prana P1 THCa Sublingual (As Needed)

Dinner:

+ 10mg Prana P3 CBD PM Capsules (2:1 to 1:1, THCa:CBDa)

+ 2mg to 4mg Prana P1 THCa Sublingual

Bedtime:

+ 10mg Prana P4 CBN Capsules

[00125] EXAMPLE 9: EXEMPLARY PROTOCOL FOR OPIATE DEPENDENCY

Note: This is a 16 week program.

WEEK #1 & WEEK #2

Morning:

+ Prana P5 - 100gms raw or 10gms powder

+ 5mg Prana P1 Prana Capsule

+ 2mg Prana P2 CBD AM Sublingual (2:1 to 3:1, THC:CBD)

Afternoon:

+ 5mg Prana P1 Prana Capsule

+ 2mg Prana P2 CBD AM Sublingual (2:1 to 3:1)

Dinner:

+ 5mg Prana P1 Prana Capsule

+ 2mg Prana P2 CBD AM Sublingual (2:1 to 3:1)

Bedtime: (30min Prior)

+ 10mg Prana P3 CBD PM Capsules (2:1 to 1:1)

+ 2mg Prana P4 Sublingual CBD:CBN (1:1)

TOTAL CANNABINOIDS DAILY: 31mg + 50mg Raw

REDUCE OPIATES BY 10%-20%

WEEK #3 & WEEK #4

Morning:

+ Prana P5 - 100gms raw or 10gms powder

+ 10mg Prana P1 Capsules

+ 4mg Prana P2 CBD AM Sublingual (2:1 to 3:1)

Afternoon:

+ 10mg Prana P1 THCa Capsules

+ 4mg Prana P2 CBD AM Sublingual (2:1 to 3:1)

Dinner:

+ 10mg Prana P1 THCa Capsules

+ 4mg Prana P2 CBD AM Sublingual (2:1 to 3:1)

Bedtime: (30min Prior)

+ 10mg Prana P3 CBD PM Capsules (2:1 to 1:1)

+ 4mg Prana P4 Sublingual CBD:CBN (1:1)

TOTAL CANNABINOIDS ABSORBED DAILY: 56mg + 50mg Raw

REDUCE OPIATES BY 10%-20%

WEEK #5 & WEEK #6

Morning:

+ Prana P5 - 100gms raw or 10gms powder

+ 15mg Prana P1 THCa Capsules

+ 6mg Prana P2 CBD AM Sublingual (2:1 to 3:1)

Afternoon:

+ 15mg Prana P1 THCa Capsules

+ 6mg Prana P2 CBD AM Sublingual (2:1 to 3:1)

Dinner:

+ 15mg Prana P1 THCa Capsules

+ 6mg Prana P2 CBD AM Sublingual (2:1 to 3:1)

Bedtime: (30min Prior)

+ 15mg Prana P3 CBD PM Capsules (2:1 to 1:1)

+ 6mg Prana P4 Sublingual CBD:CBN (1:1)

TOTAL CANNABINOIDS ABSORBED DAILY: 84mg + 50mg Raw

REDUCE OPIATES BY 10%-20%

WEEK #7 & WEEK #8

Morning:

+ Prana P5 - 100gms raw or 10gms powder

+ 20mg Prana P1 Prana Capsule

+ 6mg Prana P2 CBD AM Sublingual (2:1 to 3:1)

Afternoon:

+ 20mg Prana P1 Prana Capsule

+ 6mg Prana P2 CBD AM Sublingual (2:1 to 3:1)

Dinner:

+ 20mg Prana P1 THC Capsules

+ 6mg Prana P2 CBD AM Sublingual (2:1 to 3:1)

Bedtime: (30min Prior)

+ 20mg Prana P3 CBD PM Capsules (2:1 to 1:1)

+ 6mg Prana P4 Sublingual CBD:CBN (1:1)

TOTAL CANNABINOIDS ABSORBED DAILY: 104mg + 50mg Raw

REDUCE OPIATES BY 10%-20%

WEEK #8 & WEEK #9

Morning:

+ Prana P5 - 100gms raw or 10gms powder

+ 15mg Prana P1 Prana Capsule

+ 6mg Prana P2 CBD AM Sublingual (2:1 to 3:1)

Afternoon:

+ 15mg Prana P1 Prana Capsule

+ 6mg Prana P2 CBD AM Sublingual (2:1 to 3:1)

Dinner:

+ 15mg Prana P1 Prana Capsule

+ 6mg Prana P2 CBD AM Sublingual (2:1 to 3:1)

Bedtime: (30min Prior)

+ 20mg Prana P3 CBD PM Capsules (2:1 to 1:1)

+ 6mg Prana P4 Sublingual CBD:CBN (1:1)

TOTAL CANNABINOIDS ABSORBED DAILY: 89mg + 50mg Raw

REDUCE OPIATES BY 10%-20%

WEEK #10 & WEEK #11

Morning:

+ Prana P5 - 100gms raw or 10gms powder

+ 10mg Prana P1 Prana Capsule

+ 6mg Prana P2 CBD AM Sublingual (2:1 to 3:1)

Afternoon:

+ 10mg Prana P1 Prana Capsule

+ 6mg Prana P2 CBD AM Sublingual (2:1 to 3:1)

Dinner:

+ 10mg Prana P1 Prana Capsule

+ 6mg Prana P2 CBD AM Sublingual (2:1 to 3:1)

Bedtime: (30min Prior)

+ 15mg Prana P3 CBD PM Capsules (2:1 to 1:1)

+ 6mg Prana P4 Sublingual CBD:CBN (1:1)

TOTAL CANNABINOIDS ABSORBED DAILY: 69mg + 50mg Raw

REDUCE OPIATES BY 10%-20%

WEEK #12 & WEEK #13

Morning:

+ Prana P5 - 100gms raw or 10gms powder

+ 5mg Prana P1 Prana Capsule

+ 6mg Prana P2 CBD AM Sublingual (2:1 to 3:1)

Afternoon:

+ 5mg Prana P1 Prana Capsule

+ 6mg Prana P2 CBD AM Sublingual (2:1 to 3:1)

Dinner:

+ 5mg Prana P1 Prana Capsule

+ 6mg Prana P2 CBD AM Sublingual (2:1 to 3:1)

Bedtime: (30min Prior)

+ 10mg Prana P3 CBD PM Capsules (2:1 to 1:1)

+ 6mg Prana P4 Sublingual CBD:CBN (1:1)

TOTAL CANNABINOIDS ABSORBED DAILY: 49mg + 50mg Raw

REDUCE OPIATES BY 10%-20%

WEEK #14 & WEEK #15

Morning:

+ Prana P5 - 100gms raw or 10gms powder

+ 4mg Prana P1 THCa Sublingual

+ 5mg Prana P2 CBD AM Capsule (2:1 to 3:1)

Afternoon:

+ 4mg Prana P1 THCa Sublingual

+ 5mg Prana P2 CBD AM Capsule (2:1 to 3:1)

Dinner:

+ 4mg Prana P1 THCa Sublingual

+ 5mg Prana P2 CBD AM Capsule (2:1 to 3:1)

Bedtime: (30min Prior)

+ 10mg Prana P3 CBD PM Capsules (2:1 to 1:1)

+ 4mg Prana P4 Sublingual CBD:CBN (1:1)

TOTAL CANNABINOIDS ABSORBED DAILY: 41mg + 50mg Raw

OPIATES SHOULD BE REDUCED BY 80-90%

WEEK #16 +

+ Every 3rd Day + Prana P5 - 100gms raw or 10gms powder

Morning:

+ 10mg Prana P2 CBD AM Capsule (2:1 to 3:1)

+ 4mg Prana P1 THCa Sublingual (Only As Needed for Pain)

Afternoon:

+ 4mg Prana P1 THCa Sublingual (Only As Needed for Pain)

Dinner:

+ 10mg Prana P3 CBD PM Capsule (2:1 to 1:1)

+ 4mg Prana P1 THCa Sublingual (Only As Needed for Pain)

Bedtime: (30min Prior)

+ 4mg Prana P4 Sublingual CBD:CBN (1:1)

TOTAL CANNABINOIDS ABSORBED DAILY: 36mg + 25mg Raw
OPIATES SHOULD BE REDUCED BY 90% - 100%.

[00126] The term 'comprise' and variants of the term such as 'comprises' or 'comprising' are used herein to denote the inclusion of a stated integer or stated integers but not to exclude any other integer or any other integers, unless in the context or usage an exclusive interpretation of the term is required.

OTHER EMBODIMENTS

[00127] In some embodiments there is provided a liquid cannabinoid formulation, wherein at least 95% of the total cannabinoids is tetrahydrocannabinolic acid (THCa), wherein the cannabidiolic acid (CBDa) is less than 1% of the total cannabinoids, the cannabinolic acid (CBNa) is less than 3% of the total cannabinoids and the cannabichromenic acid (CBCa) is less than 1% of the total cannabinoids, and wherein the formulation comprises at least one terpene and/or flavonoid.

[00128] In some embodiments there is provided a liquid cannabinoid formulation, wherein at least 95% of the total cannabinoids is tetrahydrocannabinol (THC), and wherein the formulation comprises at least one terpene and/or flavonoid.

[00129] In some embodiments there is provided a liquid cannabinoid formulation, wherein at least 95% of the total cannabinoids is cannabidiol (CBD), and wherein the formulation comprises at least one terpene and/or flavonoid.

[00130] In some embodiments there is provided a liquid cannabinoid formulation, wherein at least 95% of the total cannabinoids is THCa and cannabidiolic acid (CBDa), and wherein the formulation comprises at least one terpene and/or flavonoid.

[00131] In some embodiments there is provided a liquid cannabinoid formulation, wherein at least 95% of the total cannabinoids are THC and CBD, and wherein the formulation comprises at least one terpene and/or flavonoid.

[00132] In some embodiments there is provided a liquid cannabinoid formulation, wherein at least 95% of the total cannabinoids are CBD, cannabinol (CBN) and THC, and wherein the formulation comprises at least one terpene and/or flavonoid.

[00133] While the invention has been described in conjunction with the detailed description thereof, the foregoing description is intended to illustrate and not limit the scope of

the invention, which is defined by the scope of the appended claims. Other aspects, advantages, and modifications are within the scope of the following claims.

CLAIMS

1. A liquid cannabinoid formulation, wherein at least 95% of the total cannabinoids is tetrahydrocannabinolic acid (THCa), wherein the cannabidiolic acid (CBDa) is less than 1% of the total cannabinoids, the cannabinolic acid (CBNa) is less than 3% of the total cannabinoids and the cannabichromenic acid (CBCa) is less than 1% of the total cannabinoids, and wherein the formulation comprises at least one terpene and/or flavonoid.

2. The formulation of claim 1, wherein the terpene and/or flavonoid is d-limonene linalool, 1,8-cineole (eucalyptol), α-pinene, terpineol-4-ol, p-cymene, borneol, Δ-3-carene, β-sitosterol, β-myrcene, β-caryophyllene, cannflavin A, apigenin, quercetin or pulegone.

3. The formulation of claim 1 or claim 2, wherein the formulation comprises no more than 4% terpene.

4. A liquid cannabinoid formulation, wherein at least 95% of the total cannabinoids is tetrahydrocannabinol (THC), and wherein the formulation comprises at least one terpene and/or flavonoid.

5. The formulation of claim 4, wherein the formulation comprises no more than 4% terpene.

6. The formulation of claim 5, wherein the terpene and/or flavonoid is d-limonene linalool, 1,8-cineole (eucalyptol), α-pinene, terpineol-4-ol, p-cymene, borneol, Δ-3-carene, β-sitosterol, β-myrcene, β-caryophyllene, cannflavin A, apigenin, quercetin or pulegone.

7. The formulation of claim 1 or 4, wherein the formulation comprises no more than 4% terpene, and wherein said terpene comprises myrcene, caryophyllene, and limonene.

8. A liquid cannabinoid formulation, wherein at least 95% of the total cannabinoids is cannabidiol (CBD), and wherein the formulation comprises at least one terpene and/or flavonoid.

9. The formulation of claim 8, wherein the formulation further comprises less than 1% THC.

10. The formulation of claim 8 or claim 9, wherein the formulation comprises no more than 4% terpene.

11. The formulation of any one of claims 8 to 10, wherein the terpene and/or flavonoid is d-limonene linalool, 1,8-cineole (eucalyptol), α-pinene, terpineol-4-ol, p-cymene, borneol, Δ-3-carene, β-sitosterol, β-myrcene, β-caryophyllene, cannflavin A, apigenin, quercetin or pulegone.

12. The formulation of claim 8 or claim 9, wherein the formulation comprises no more than 4% terpene, and wherein said terpene comprises myrcene, caryophyllene, and limonene.

13. A liquid cannabinoid formulation, wherein at least 95% of the total cannabinoids is THCa and cannabidiolic acid (CBDa), and wherein the formulation comprises at least one terpene and/or flavonoid.

14. The formulation of claim 13, wherein the formulation comprises no more than 4% terpene.

15. The formulation of claim 13 or claim 14, wherein the terpene and/or flavonoid is d-limonene linalool, 1,8-cineole (eucalyptol), α-pinene, terpineol-4-ol, p-cymene, borneol, Δ-3-carene, β-sitosterol, β-myrcene, β-caryophyllene, cannflavin A, apigenin, quercetin or pulegone.

16. A liquid cannabinoid formulation, wherein at least 95% of the total cannabinoids are THC and CBD, and wherein the formulation comprises at least one terpene and/or flavonoid.

17. The formulation of claim 16, wherein the formulation comprises no more than 4% terpene.

18. The formulation of claim 16 or claim 17, wherein the terpene and/or flavonoid is d-limonene linalool, 1,8-cineole (eucalyptol), α-pinene, terpineol-4-ol, p-cymene, borneol, Δ-3-carene, β-sitosterol, β-myrcene, β-caryophyllene, cannflavin A, apigenin, quercetin or pulegone.

19. The formulation of claim 13 or 16, wherein the formulation comprises no more than 4% terpene, and wherein said terpene comprises myrcene, limonene, pinene, and caryophyllene.

20. A liquid cannabinoid formulation, wherein at least 95% of the total cannabinoids are CBD, cannabinol (CBN) and THC, and wherein the formulation comprises at least one terpene and/or flavonoid.

21. The formulation of claim 20, wherein the formulation comprises less than 9% THC.

22. The formulation of claim 20 or claim 21, wherein the formulation comprises no more than 4% terpene.

23. The formulation of any one of claims 20 to 22, wherein the terpene and/or flavonoid is d-limonene linalool, 1,8-cineole (eucalyptol), α-pinene, terpineol-4-ol, p-cymene, borneol, Δ-3-carene, β-sitosterol, β-myrcene, β-caryophyllene, cannflavin A, apigenin, quercetin or pulegone.

24. The formulation of claim 20 or claim 21, wherein the formulation comprises no more than 4% terpene, and wherein said terpene comprises myrcene, pinene and caryophyllene.

25. The formulation of any one of the preceding claims, wherein the formulation is infused in a medium chain triglyceride (MCT).

26. The formulation of claim 25, wherein the MCT is NEOBEE 895.

27. The formulation of any one of claims 1 to 26, formulated for oral, sublingual, buccal, or topical administration.

28. The formulation of claim 27, wherein the sublingual formulation further comprises a sweetener.

29. The formulation of claim 28, wherein the sweetener is a stevia extract.

30. The formulation of claim 28 or claim 29, further comprising lemon oil, orange oil or both.