

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
2 June 2005 (02.06.2005)

PCT

(10) International Publication Number
WO 2005/048931 A2

(51) International Patent Classification⁷: **A61K**
(21) International Application Number:
PCT/US2004/037796
(22) International Filing Date:
12 November 2004 (12.11.2004)
(25) Filing Language: English
(26) Publication Language: English
(30) Priority Data:
60/519,852 13 November 2003 (13.11.2003) US

(71) Applicant (for all designated States except US): **DBC, LLC** [US/US]; 3098 West Executive Parkway, Lehi, Utah 84043-4713 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **KUPPER, Roman** [CH/US]; 1261 Pacific Avenue, Erlanger, Kentucky 41018 (US). **SMOTHERS, Marlene** [US/US]; 1261 Pacific Avenue, Erlanger, Kentucky 41018 (US).

(74) Agent: **JARVIS, Lawrence M.**; MCANDREWS, HELD & MALLOY, LTD., 500 W. Madison Street, Suite 3400, Chicago, Illinois 60661 (US).

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

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

Published:

— without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: DISSOLVING THIN FILM XANTHONE SUPPLEMENT

(57) Abstract: A nutraceutical composition containing xanthenes for oral ingestion is disclosed. The composition is a rapidly dissolving film comprising water soluble polymers and xanthenes. The xanthenes are, preferably, derived from natural plant sources, especially from fruit of *Garcinia mangostana* L. plant.



WO 2005/048931 A2

DISSOLVING THIN FILM XANTHONE SUPPLEMENT

FIELD OF THE INVENTION

[0001] The presently described technology relates to a nutraceutical composition for use in the oral cavity that contains xanthonenes. More particularly, the presently described technology relates to a rapidly dissolving film for oral ingestion comprising xanthonenes, for example, derived from fruit of the *Garcinia mangostana* L. plant.

BACKGROUND OF THE INVENTION

[0002] Rapidly dissolving thin films for oral ingestion are well-known in the art. These films are a recognized alternative to pills, tablets, liquids and other forms of consumable therapeutic or cosmetic substances. These thin films offer several advantages over prior art forms. They are compact and easily carried about, usually via a plastic case having a pliable hinge that allows repeated opening and closing. They are also capable of being ingested discretely, as opposed to ingestion of pills or tablets that generally require movement of the mouth or jaws.

[0003] Further advantages of thin films for oral ingestion are explained in detail in U.S. Patent No. 6,177,096, which is incorporated herein by reference, U.S. Patent No. 6,419,903, which is incorporated herein by reference, and U.S. Patent Application No. 2003/0206942, which is also incorporated herein by reference. These references further disclose the general chemistry and technology associated with thin films and various methods of manufacturing them.

[0004] It is also generally known in the art that rapidly dissolving films can be used for delivering therapeutic amounts of pharmaceutically active ingredients and cosmetically active ingredients. For example, as disclosed in U.S. Patent No. 6,177,096, thin films can be used to deliver cosmetic agents such as breath freshening compounds, flavors for oral hygiene, fragrances for oral hygiene, active ingredients for oral cleansing and active ingredients for dental cleansing, as well as drugs such as hypnotics, sedatives, antiepileptics, antispasmodics, diuretics, antitussive expectorants and antibiotics.

[0005] The medicinal properties of the *Garcinia mangostana* L. plant have increasingly been the subject of recent pharmacological and clinical studies. These studies have shown that some of the natural compounds derived from the plant yield surprising medicinal benefits, especially the xanthone compounds.

5 The history of the *Garcinia mangostana* L. plant and the pharmacological benefits of individual xanthone compounds is described in more particular detail in U.S. Patent No. 6,730,333 (Garrity et al.), which is incorporated herein by reference.

[0006] Despite the known use of rapidly dissolving films for oral ingestion and
10 the documented medicinal benefits of natural xanthenes, the combination of these two distinct fields has been heretofore unknown. Accordingly, there exists a need in the art for a rapidly dissolving film material comprising xanthenes suitable for oral ingestion. Moreover, there is a need in the art for a simple method of delivering therapeutic amounts of xanthenes. There is a further need
15 in the art for a xanthone product that can be easily and unobtrusively consumed. There exists a further need in the art for a consumable xanthone product that comprises xanthenes derived from the fruit of the *Garcinia mangostana* L. plant, otherwise known as the mangosteen plant.

BRIEF SUMMARY OF THE INVENTION

20 [0007] The present technology described herein uniquely provides a source of natural xanthenes that can be easily transported and inconspicuously consumed. In particular, the presently described technology relates to a rapidly dissolving film for oral ingestion comprising xanthenes.

[0008] In one aspect, the presently described technology provides orally
25 consumable film composition comprising at least one ingredient selected from the group consisting of saliva inducing agents, surfactants, stabilizing agents, emulsifiers, thickeners, plasticizers, antimicrobials, water, water soluble polymers, binders, polyethylene oxides, propylene glycols, sweeteners, flavor enhancers, colorants, polyalcohols, and combinations thereof; and at least one
30 xanthone.

[0009] Preferably, xanthoness to be used in the presently described technology are derived from natural plant sources, especially from fruit of *Garcinia mangostana* L. plant. For example, the pericarp of the fruit of *Garcinia mangostana* L. plant can be used alone or in combination with the pulp of the fruit as an excellent
5 source of xanthoness.

BRIEF DESCRIPTION OF SEVERAL VIEWS OF THE DRAWINGS

[0010] [Not Applicable]

DETAILED DESCRIPTION OF THE INVENTION

[0011] It is understood that the terminology used herein is used for the purpose of
10 describing particular embodiments only, and is not intended to limit the scope of the presently described technology. It is also understood that, as used herein and in the appended claims, the singular forms "a," "an," and "the" include plural reference, unless the context clearly dictates otherwise.

[0012] Unless defined otherwise, all technical and scientific terms used herein
15 have the same meanings as commonly understood by one of ordinary skill in the art to which this invention belongs. While various methods, compositions, and materials of the presently described technology are described herein, any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the presently described technology. All references cited
20 herein are incorporated by reference in their entirety.

[0013] The film, which is normally a thin film, of the presently described technology is instantly wettable and rapidly dissolving. Thus, the film adheres to the roof of one's mouth or tongue, quickly and totally dissolves. The film comprises xanthone compounds for delivery through oral consumption.

25 [0014] In one embodiment of the invention, the xanthoness are derived from natural plant sources. Preferably, the xanthoness can be derived from fruit of the *Garcinia mangostana* L. plant. In one preferred embodiment of the presently described technology, the xanthoness are derived from the pericarp of mangosteen fruit. In another preferred embodiment, the xanthoness are derived from a mixture

of mangosteen fruit pulp and pericarp, thus ensuring a natural, holistic source of xanthonenes.

[0015] In addition to xanthone compounds, the film of the presently described technology can comprise one or more of the following ingredients: saliva
5 inducing agents, surfactants, stabilizing agents, emulsifiers, thickeners, plasticizers, antimicrobials, water, water soluble polymers, binders, polyethylene oxides, propylene glycols, sweeteners, flavor enhancers, colorants and polyalcohols.

[0016] Any number of saliva enhancing agents can be used in the presently
10 described technology. These agents are well known in the art, which include common food-grade sweeteners such as glucose, dextrose, fructose, lactose, maltose, xylose, sucrose, corn sugar syrup, and other sweet mono- or di-saccharides. A combination of synthetic sweeteners plus a non-sugar, sugar-related compound such as sorbitol, hexitol, maltitol, xylitol, and mannitol, or
15 starch hydrolysate such as Lycansin, or the like is also advantageous in the presently described technology. Aspartame may also be used.

[0017] The surfactants that may be used in the presently described technology can vary, but generally compromise one or more anionic surfactants. For example, when a combination of surfactants is used, the first component may be a
20 polyoxyethylene alkyl ether and the second component may be a polyoxyethylene sorbitan fatty acid ester. The ether compound may have an HLB value of 14-16, while the ester compound may have an HLB value of between 10 and 20. Of course, these values can vary, as one of ordinary skill in the art will appreciate.

[0018] Stabilizers useful in the presently described technology include xanthan
25 gums, carrageenan, and the like. In one embodiment of the presently described technology, antimicrobials are included in the formulation. These compounds include essential oils such as eucalyptol, menthol, vacrol, thymol, methyl salicylate, verbenone, eugenol, gerianol and combinations thereof.

[0019] The water soluble polymers of the presently described technology can exhibit film forming properties, so the xanthone-containing mixture can be spread into a thin film with sufficient tensile strength to withstand cutting, dicing and packaging of the product. Typical polymers include, but are not limited to, 5 amylase, arabic gum, carboxymethyl cellulose, carboxyvinyl polymers, collagen, dextrin, gluten, guar gum, acacia gum, high amylase starch, hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxypropylated high amylase starch, hydroxypropylmethyl cellulose, methylmethacrylate copolymers, polyacrylic acid, polyethylene glycol, polyvinyl alcohol, polyvinyl pyrrolidone, pullulan, 10 sodium alginate, tragacanth gum, whey protein isolate, and combinations thereof.

[0020] Polyalcohols give a soft feel to the film and allow the film to conform to the contours of the oral cavity. Useful polyalcohols for purposes of the presently described technology include glycerol, polyethylene glycol, propylene glycol, glycerol monoesters with fatty acids or other known polyalcohols. If colorants 15 are used in the presently described technology, they should be non-toxic and approved by the Food and Drug Administration.

[0021] Although there are a number of different methods of producing the thin films of the presently described technology, one method is as follows: The non-water soluble plasticizers, surfactants, and polyalcohols are dissolved in an 20 appropriate amount of solvent, which may include water-alcohol mixtures. The other water soluble ingredients and xanthenes are then slowly added until a single homogeneous solution is obtained. It may be necessary to heat the solution to accommodate thorough mixture and dissolving of all ingredients. The resulting soup mixture is then poured or coated onto a non-stick drying surface that allows 25 even spreading of the mixture across its surface. The mixture is slowly cooled and/or dried until it hardens and the thin film is formed. The thin films are then cut into shapes suitable for packing.

[0022] The invention will now be explained with reference to the following example, which are given for illustration only and are not intended to be limiting 30 thereof.

Example 1

[0023] A rapidly dissolving thin film was made by combining the ingredients listed below:

<u>Ingredients</u>	<u>Amount</u>
Natural compounded liquid mangosteen flavor	4.5% - 4.9%
Mangosteen fruit extract	0.1% - 0.5%
Vitamin C	0.2%
Aspartame	0.04%
Xanthan gums	2% - 3%
Water	Remainder

5 [0024] In this example, whole fruit of the mangosteen fruit is ground into a mixture containing pericarp and fruit pulp. Xanthonenes are then extracted from the mangosteen whole fruit mixture by dissolving the whole fruit mixture in an alcohol based solvent. The solvent containing extracted xanthonenes is then mixed with other ingredients in the amount of from about 0.1% to about 0.5% to make a
 10 mixture solution. The mixture solution is rolled out on a sheet, and water is evaporated off using an airflow cooling tunnel over a period of about 24 hours. The resulted thin film is then cut into desired shapes and sizes.

[0025] The presently described technology may be embodied in other specific forms without departing from its spirit or essential characteristics. The described
 15 embodiments are to be considered in all respects only as illustrative and not restrictive. The scope of the presently described technology is, therefore, indicated by the appended claims rather than by the foregoing description. All changes that come within the meaning and range of equivalency of the claims are to be embraced within their scope.

CLAIMS

What is claimed is:

1. An orally consumable film composition comprising:

5 at least one ingredient selected from the group consisting of saliva inducing agents, surfactants, stabilizing agents, emulsifiers, thickeners, plasticizers, antimicrobials, water, water soluble polymers, binders, polyethylene oxides, propylene glycols, sweeteners, flavor enhancers, colorants, polyalcohols, and combinations thereof; and

at least one xanthone.

- 10 2. The film composition of claim 1, wherein the at least one xanthone is derived from natural plant sources.

3. The film composition of claim 1, wherein the at least one xanthone is derived from fruit of *Garcinia mangostana* L. plant.

- 15 4. The film composition of claim 1, wherein the at least one xanthone is derived from pericarp of fruit of *Garcinia mangostana* L. plant.

5. The film composition of claim 1, wherein the at least one xanthone is derived from a mixture of pulp and pericarp of fruit of *Garcinia mangostana* L. plant.

6. The film composition of claim 1, wherein the at least one xanthone is derived from fruit of *Garcinia mangostana* L. plant by a process comprising:

20 grinding whole fruit of *Garcinia mangostana* L. plant into a mixture of pericarp and fruit pulp; and

extracting xanthoness from the mixture.

7. The film composition of claim 1, wherein the water soluble polymers are selected from the group consisting of amylase, arabic gum, carboxymethyl
25 cellulose, carboxyvinyl polymers, collagen, dextrin, gluten, guar gum, acacia

- 5 gum, high amylase starch, hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxypropylated high amylase starch, hydroxypropylmethyl cellulose, methylmethacrylate copolymers, polyacrylic acid, polyethylene glycol, polyvinyl alcohol, polyvinyl pyrrolidone, pullulan, sodium alginate, tragacanth gum, whey protein isolate, and combinations thereof.
8. The film composition of claim 1, wherein the salvia inducing agents are selected from the group consisting of glucose, dextrose, fructose, lactose, maltose, xylose, sucrose, corn sugar syrup, sorbitol, hexitol, maltitol, xylitol, mannitol, starch hydrolysate, aspartame and combinations thereof.
- 10 9. The film composition of claim 1, wherein the surfactants comprise one or more anionic surfactants.
10. The film composition of claim 1, wherein the stabilizers are selected from the group consisting of xanthan gums, carrageenan, antimicrobials, and combinations thereof.
- 15 11. The film composition of claim 10, wherein the antimicrobials comprising one or more essential oils.
12. The film composition of claim 11, wherein the essential oils are selected from the group consisting of eucalyptol, menthol, vacrol, thymol, methyl salicylate, verbenone, eugenol, gerianol and combinations thereof.
- 20 13. The film composition of claim 1, wherein the polyalcohols are selected from the group consisting of glycerol, polyethylene glycol, propylene glycol, glycerol monoesters with fatty acids, and combinations thereof.