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(54) Title: COATING OF CETYL MYRISTATE AND/OR CETYL PALMITATE PARTICLES

(57) Abstract: This invention is related to coated particles of cetylated fatty acids, especially cetyl myristate or cetyl palmitate or combination of cetyl myristate and cetyl palmitate by using wet granulation techniques.

Description

Title of Invention: COATING OF CETYL MYRISTATE AND/OR CETYL PALMITATE PARTICLES

[1] This invention is related to coated particles of cetyl myristate or cetyl palmitate or combination of cetyl myristate and cetyl palmitate by using wet granulation techniques. In this invention, cetyl myristate or cetyl palmitate or combination of cetyl myristate and cetyl palmitate are used as active pharmaceutical ingredients or dietary supplement.

[2] Cetyl palmitate is derived from the fatty acid, palmitic acid which occurs as the glycerol ester in many oils and fats such as palm oil or Chinese vegetable tallow. A synthetic method of preparation is to react palmitoyl chloride and cetyl alcohol in the presence of magnesium. See the Merck Index, 12th edition at page 336. Reference is also made to US US3169099A (SOCONY MOBIL OIL CO INC) 02.09.1965 patent which discloses a biosynthetic method of producing cetyl palmitate.

[3] US 4,113,881A (DIEHL HARRY WELDON) 12.09.1978 discloses that the administration of an effective amount of cetyl myristoleate to a mammal is useful in inhibiting or relieving the symptoms of inflammatory rheumatoid arthritis in mammals.

[4] US 5569676A (DIEHL, HARRY W) 29. 10. 1996 US 5,569,676 discloses the use of cetyl myristoleate in the treatment of osteo-arthritis.

[5] WO 01/85162A (MERACOL CORP LTD ET.AL.) 15.1 1.2001 discloses the use of cetyl myristate and/or cetyl palmitate in the treatment of irritable bowel syndrome or disease. Patent embraces that cetyl myristate comprises 50-98 wt.% of the mixture, preferably, the myristate and palmitate are in a weight ratio of 95:5. The oral dosage unit is a capsule and contains 5-400 mg of the cetyl myristate or the mixture of the cetyl myristate and the cetyl palmitate. It also includes an excipient and/or diluent, preferably silicon dioxide, calcium phosphate and/or magnesium oxide. Preferably said mixture is in a capsule and it includes a pharmaceutically acceptable excipient and/or diluents. Preferably the dosage unit includes silicon dioxide, calcium phosphate and/or magnesium oxide. Liquid formulation, where an amount of liquid equivalent to at least 4 capsules is prescribed which is to be taken 3 times daily. That is 4200 mg of cetyl myristate or the mixture of cetyl myristate and cetyl palmitate.That mixture comprises by weight 95% cetyl myristate and 5% cetyl palmitate by weight In addition added excipients were present in the non gelatin two part capsule case.

[6] WO 01/85163A (MERACOL CORP LTD ET.AL.) 15.1 1.2001 discloses the use of cetyl myristate and/or cetyl palmitate in the treatment of eczema and/or psoriasis. Accordingly, capsule also includes a pharmaceutically acceptable excipient and/or

diluent. These are silicon dioxide, calcium phosphate and/or magnesium oxide. The dosage unit can also be a wax-like solid or can be an orally consumable liquid composition (eg; made up with a general pharmacy type carrier such as methyl cellulose).

[7] WO 2005/118070A (MERACOL CORP LTD ET.AL.) 15.12.2005 discloses the treatment of multiple sclerosis with the use of cetyl myristate and/or cetyl palmitate.The cetyl myristate; or combination of cetyl myristate and cetyl palmitate is administered simultaneously, separately or sequentially.

[8] WO 03/018731A (MERACOL CORP LTD) 06.03.2003 defines the process prepares a mixture of cetyl myristate (50-98 wt.%) and cetyl palmitate, for use in the formulation of cosmetics and pharmaceuticals.

[9] WO 03/045374A (MERACOL CORP LTD ET.AL.) 05.06.2003 discloses the use of cetyl myristate and/or cetyl palmitate in a method of treatment and/or prophylaxis of a mammal for at least the symptoms of treating asthma, chronic obstruc tive pulmonary disease and/or other respiratory difficulties.

[10] WO 03/026640A (MERACOL CORP LTD ET.AL.) 03.04.2003 discloses the use of cetyl myristate and/or cetyl palmitate in the treatment of food allergies and/or food intolerances.

[11] WO 01/85164A (MERACOL CORP LTD ET.AL.) 15.11.2001 discloses the use of cetyl myristate and/or cetyl palmitate in the treatment of herpes.

[12] This invention discloses that particles of cetylated fatty acids, especially cetyl myristate or cetyl palmitate or combination of cetyl palmitate and cetyl myristate are coated. Present invention also embraces wet granulation method of cetyl myristate or cetyl palmitate or combination of cetyl palmitate and cetyl myristate.

[13] Cetyl myristate or cetyl palmitate or combination of cetyl myristate and cetyl palmitate can be used as active pharmaceutical ingredients (API) in pharmaceutical formulations in addition to excipient properties. However both cetyl myristate and cetyl palmitate are waxy ingredients and thus in formulation stage, they are adhered onto the surfaces of formulation equipments therefore it is hard to granulate such API's in processes. Thus such processes that non-adhering and eligible granulation methods are needed .

[14] It is invented that sticking problem is solved by coating of particles of cetyl myristate and cetyl palmitate by using wet granulation techniques. Coating provides a minimisation and isolation of the waxy surface of particles. In terms of solution,it is also delineated that percentages of API's and excipients, weight ratios, useful solvents and temporary conditions.

[15] Cetyl myristate and cetyl palmitate are sticky and tend to adhere to surfaces of granulation and formulation equipments .

[16] This invention discloses processability of cetyl myristate and cetyl palmitate and also

the ability not to stick or adhere to equipments.

[17] This invention also embraces to provide a wet granulation and/or coating method free from adhesion .

[18] According to this invention, it is invented that adhering problems in Cetyl myristate and cetyl palmitate formulations are eliminated by coating of particles of active ingredients. Coating can be carried out by fluid bed,high or low shear mixer, etc.

[19] In one aspect of this invention particles of cetyl myristate and cetyl palmitate are coated in unison. Accordingly particles of cetyl myristate and cetyl palmitate can be directly coated or can be coated after admixturing with pharmaceutical excipient or mixtures of pharmaceutical excipients .

[20] In another aspect of this invention,cetyl myristate and cetyl palmitate particles can be coated after treatment with a pharmaceutical excipient or mixtures of pharmaceutical excipients.

[21] In a further aspect of this invention cetyl myristate and cetyl palmitate particles can be treated with a pharmaceutical excipient or mixtures of pharmaceutical excipients in the course of coating.

[22] Yet another aspect of this invention, cetyl myristate and cetyl palmitate granules can be coated. Granulation can be made through using of wet granulation, dry granulation and other suitable granulation methods. Wet granulation is preferred.

[23] Coating can be performed by known methods of pharmaceutical technology such as fluid bed, high shear mixer,low sheer mixer etc.

[24] In coating, wet granulation method is preferred. However in wet granulation it is required that a technical problem should be solved. Said problem arises from using of water in wet granulation. When water is used alone as a solvent,huge parts of cetyl myristate and cetyl palmitate start to gel and thus preparing of pharmaceutical formulation becomes nearly impossible. To solve said technical problem it is invented that in wet granulation phase solvent or mixtures of solvents are used other than solely water . Water can be used as a mixed manner with a solvent or mixtures of solvents but according to this invention it *per se* cannot be used in wet granulation.

[25] Wet granulation method includes following intragranulation and extragranulation steps : **I.Intragranulation** : a. a binder ,a disintegrant, cetyl myristate, cetyl palmitate are mixed, b.a binder and plasticizer is dissolved in a solvent other than solely water, c. materials obtained from step a and step b are mixed in a mixer,preferably high shear mixer, **II.Extragranulation:** a.obtained granules from intragranulation step are dried, b. disintegrant and lubricant are mixed, c. obtained materials from step a and step b are mixed in a mixer.

[26] In combination of cetyl myristate and cetyl palmitate, granules of each active pharmaceutical ingredients can be seperately granulated and then assemblied or both active

pharmaceutical ingredient can be granulated together or one active pharmaceutical ingredient is granulated and then it is assemblied with other non-granulated active pharmaceutical ingredient. It is mostly preferred that both active pharmaceutical ingredients are granulated together.

[27] Final materials can be filed into capsules or can be pressed as tablet or can be another suitable pharmaceutical form.

[28] Intragranulation phase comprises filler is from about 0,5 % to about 10 % , disintegrant is from about 1 % to about 10 %, cetyl myrisate as active pharmaceutical ingredient is from about 40 % to about 99,5 % ,cetyl palmitate as active pharmaceutical ingredient is from about 0,5 % to about 10 %, plasticizer is from about 0,25 % to about 6 %, binder is from about 1 % to about 6 % by weight of total intragranulation phase.

[29] Intragranulation phase preferably comprises filler is 3,76 % , disintegrant is 5,00 %, cetyl myrisate as active pharmaceutical ingredient is 83,32 % ,cetyl palmitate as active pharmaceutical ingredient is 4,17 %, plasticizer is 1,25 %, binder is 2,50 % by weight of total intragranulation phase.

[30] Most preferably, intragranulation phase comprises filler is 15 mg , disintegrant is 20 mg, cetyl myrisate as active pharmaceutical ingredient is 333,3 mg ,cetyl palmitate as active pharmaceutical ingredient is 16,7 mg, plasticizer is 5 mg, binder is 10 mg.

[31] Extragranulation comprises intragranular material obtained from intragranulation phase, lubricant and disintegrant.

[32] Extragranulation phase comprises intragranular material is from about 40 % to 99,5, lubricant is from about 0,5 % to 10 %, disintegrant is from about 0,5 % to 10 % by weight of total extragranulation phase.

[33] Extragranulation phase preferably comprises intragranular material is 95,2 %, lubricant is 2,3 %, disintegrant is 2,3 % by weight of total extragranulation phase.

[34] Most preferably,extragranulation phase comprises intragranular material is 400 mg, lubricant is 10 mg and disintegrant is 10 mg.

[35] Pharmaceutical composition comprising extragranulation and intragranulation in a weight ratio of intragranulation phase to extragranulation phase is from 5:1 to 1:5. Preferably weight ratio is 1:1,05

[36] According to this invention pharmaceutical composition comprises diluent/filler is from 0.5% to 20%, disintegrant is from 1% to 15%, cetyl myrisate as active pharmaceutical ingredient is from 40% to 99.5%,cetyl palmitate as active pharmaceutical ingredient is from 0.5% to 30%,plasticizer is from 0.1% to 10%, binder is from 0.1% to 20%, lubricant is from 0.1% to 20 %, by weight of total pharmaceutical composition. Preferebly pharmaceutical composition comprises diluents/filler is 3.5%, disintegrant is 7.2%, cetyl myrisate as active pharmaceutical ingredient is 79.3% ,cetyl palmitate as active pharmaceutical ingredient is 3.9%,plasticizer is 1.2% , binder is 2.5% , lubricant

is 2.4%, by weight of total pharmaceutical composition. If pharmaceutical composition is filled into a capsule, capsule weight is not included to 'total pharmaceutical composition'.

[37] In accordance with present invention, the pharmaceutical composition of cetyl myristate and cetyl palmitate combination comprises disintegrant, lubricant, binder,diluent/filler,coating agents and the like.

[38] According to this invention the pharmaceutical composition of cetyl myristate or cetyl palmitate or combination of cetyl myristate and cetyl palmitate comprising multistage disintegrant accompanying wherein disintegrant or mixture of disintegrants are separated into two parts wherein initial part of disintegrant or mixture of disintegrants are used in first phase and residual portion of said disintegrant or mixture of disintegrants are used in additional phase or additional phases. Herein,first phase is preferably intragranular phase and additional phase is preferably extragranular phase. Multistage disintegrant accompanying can be performed without separation of a disintegrant mass.

[39] Weight ratio of extragranular disintegrant and intragranular disintegrant is from5: 1 to 1:5. Preferably weight ratio is 1:2 (extragranular disintegrant : intragranular disintegrant).

[40] In another aspect, it is invented that pharmaceutical composition of cetyl myristate or cetyl palmitate or combination of cetyl myristate and cetyl palmitate should be granulated and granules are dried under 45°C. Exceeding 45°C, active ingredient becomes a coagulate and smear form and granulation is impossible. For instance granules are preferably dried maximum 40°C.

[41] In yet another aspect of this invention is to provide a specific proportional weight ratio of excipients to active pharmaceutical ingredients. If a weight ratio is not taken into account,total weight of pharmaceutical composition wold be so heavy and huge volume for ingestion of patients. To solve this technical problem, it is invented that weight ratio of excipients to active pharmaceutical ingredients should not exceed 1:30 in intragranulation phase. Preferably weight ratio of excipients to active pharmaceutical ingredients is 1:7 in intragranulation phase. In extragranular phase, weight ratio of excipients to active pharmaceutical ingredients should not exceed 1:50. Preferably weight ratio of excipients to active pharmaceutical ingredients is 1:17,5 in extragranulation phase.

[42] Disintegrants are, but not limited to, alginic acid, chitosan, pectins, cation exchange resins, magnesium silicates, aluminium silicates, mixtures thereof and the like.

[43] Lubricants/Glidants are, but not limited to, magnesium stearate,calcium stearate,hydrogenated castor oil,glyceryl behenate,glyceryl monostearate,glyceryl palmitostearate,leucine,mineral oil, light mineral oil, myristic acid,palmitic

acid,polyethylene glycol,potassium benzoate,sodium benzoate,sodium lauryl sulfate,sodium stearyl fumarate,stearic acid,talc, hydrogenated vegetable oil,zinc stearate, magnesium lauryl sulphate,sodium stearyl fumarate, polyethylene glycol, stearic acid, colloidal silicon dioxide or mixtures thereof and the like. Preferred lubricant is magnesium stearate. Two different kinds of lubricants are preferred to be benefited from different proporties of lubrication.

[44] Binders are, but not limited to, sodium alginate, cellulose, methylcellulose, ethyl-cellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose, sodium carboxymethyl cellulose, polypropylpyrrolidone, polyvinylprrolidone, gelatin, polyethylene glycol, starch, pre-gelatinized starch, sugars, trehalose, glucose,tragacanth, sorbitol, acacia, alginates, carrageenan, xanthan gum, locust bean gum and gum arabic, waxes,polyacrylamide , mixtures thereof, and the like.

[45] Diluents/fillers are, but not limited to, mannitol, sorbitol, xylitol, microcrystalline cellulose, silicified microcrystalline cellulose , hydroxypropyl methylcellulose, hydroxypropyl cellulose , pullulan and fast dissolving carbohydrates such as Pharmaburst™, mixtures thereof and the like.

[46] Plasticizers are , but not limited to, polyethylene glycol, propylene glycol, triacetin, dimethyl phthalate, diethyl phthalate, dibutyl phthalate, dibutyl sebacate, triethyl citrate, tributyl citrate, triethyl acetyl citrate, castor oil , acetylated monoglycerides, mixtures thereof and the like. Plasticizer is used to have hard granulate.

[47] **Example :**

[Table 1]

Table 1

INGREDIENTS/FUNCTIONS	**mg**
INTRAGRANULAR PHASE	
Cetyl Myristate/API	333.3
Cetyl Palmitate/API	16.7
Disintegrant	20.0
Diluent/Filler	15.0
Binder	10.0
Plasticizer	5.0
Ethanol (Evapourated,not calculated in final granules)	120
TOTAL (INTRAGRANULAR PHASE)	**400**
EXTRAGRANULAR PHASE	
Lubricant	10
Disintegrant	10
TOTAL (EXTRAGRANULAR PHASE)	20
TOTAL(EXTRAGRANULAR+INTRA GRANULAR)	420.0

Claims

[Claim 1] A pharmaceutical or dietary supplement composition comprising **(a)** cetyl myristate, or **(b)** cetyl palmitate or **(c)** cetyl myristate and cetyl palmitate and pharmaceutically acceptable excipient or mixtures of excipients characterized in that particles of cetyl myristate,or cetyl palmitate,or combination of cetyl myristate and cetyl palmitate are coated.

[Claim 2] Coating of particles of **(a)** cetyl myristate, or **(b)** cetyl palmitate or **(c)** cetyl myristate and cetyl palmitate , as claimed in claim 1, is performed by wet granulation.

[Claim 3] As claimed in claim 2, wet granulation comprises intragranular and extragranular phases.

[Claim 4] As claimed in claim 3, intragranular phase comprises filler is from 0,5 % to 10 % , disintegrant is from 1 % to 10 %, cetyl myrisate as active pharmaceutical ingredient is from 40 % to 99,5 % ,cetyl palmitate as active pharmaceutical ingredient is from 0,5 % to 10 %, plasticizer is from 0,25 % to 6 %, binder is from 1 % to 6 % by weight of total intragranulation phase.

[Claim 5] As claimed in claim 4, intragranulation phase preferably comprises filler is 3,76 % , disintegrant is 5,00 %, cetyl myrisate as active pharmaceutical ingredient is 83,32 % ,cetyl palmitate as active pharmaceutical ingredient is 4,17 %, plasticizer is 1,25 %, binder is 2,50 % by weight of total intragranulation phase.

[Claim 6] As claimed in claim 5, most preferably, intragranulation phase comprises filler is 15 mg , disintegrant is 20 mg, cetyl myrisate as active pharmaceutical ingredient is 333,3 mg ,cetyl palmitate as active pharmaceutical ingredient is 16,7 mg, plasticizer is 5 mg, binder is 10 mg.

[Claim 7] As claimed in claim 3, extragranular phase comprises intragranular material is from about 40 % to 99,5, lubricant is from about 0,5 % to 10 %, disintegrant is from about 0,5 % to 10 % by weight of total extragranulation phase.

[Claim 8] As claimed in claim 7, extragranulation phase preferably comprises intragranular material is 95,2 %, lubricant is 2,3 %, disintegrant is 2,3 % by weight of total extragranulation phase.

[Claim 9] As claimed in claim 8, most preferably, extragranulation phase comprises intragranular material is 400 mg, lubricant is 10 mg and dis-

integrant is 10 mg.

[Claim 10] As claimed in claim 3, extragranulation and intragranulation are in a weight ratio from 5:1 to 1:5, preferably 1:1,05.

[Claim 11] A pharmaceutical or dietary supplement composition of cetyl myristate or cetyl palmitate or combination of cetyl myristate and cetyl palmitate comprising multistage disintegrant accompanying wherein an amount of disintegrant or mixture of disintegrants are separated into two lots wherein an amount of disintegrant or mixture of disintegrants are used in intragranular phase and an amount of disintegrant or mixture of disintegrants are used in extragranular phase.

[Claim 12] As claimed in claim 11, weight ratio of extragranular disintegrant and intragranular disintegrant is from 5:01 to 1:5, preferably weight ratio of extragranular disintegrant to intragranular disintegrant is 1:2.

[Claim 13] A pharmaceutical composition of cetyl myristate or cetyl palmitate or combination of cetyl myristate and cetyl palmitate characterized in that granulation is prepared and/or dried under 45°C.

[Claim 14] As claimed in claim 3, extrgranulation and extragranulation phases are prepared following steps comrising **I.Intragranulation** : a. a binder ,a disintegrant, cetyl myristate, cetyl palmitate are mixed, b.a binder and plasticizer is dissolved in a solvent other than solely water, c. materials obtained from step a and step b are mixed in a mixer,preferably high shear mixer, **II.Extragranulation:** a.obtained granules from intragranulation step are dried, b. disintegrant and lubricant are mixed, c. obtained materials from step a and step b are mixed in a mixer.

[Claim 15] As claimed in claim 3, weight ratio of excipients to active pharmaceutical ingredients are not exceeded 1:30 in intragranular phase, preferably weight ratio of excipients to active pharmaceutical ingredients is 1:7 and weight ratio of excipients to active pharmaceutical ingredients are not exceeded 1:50 in extragranular phase, preferably weight ratio of excipients to active pharmaceutical ingredients is 1:17,5.

[Claim 16] As claimed in claim 1, pharmaceutical composition comprises diluent/ filler is from 0.5% to 20%, disintegrant is from 1% to 15%, cetyl myrisate as active pharmaceutical ingredient is from 40% to 99.5%,cetyl palmitate as active pharmaceutical ingredient is from 0.5% to 30%, plasticizer is from 0.1% to 10%, binder is from 0.1% to 20%, lubricant is from 0.1% to 20 %, by weight of total pharmaceutical composition, preferably pharmaceutical composition comprises diluents/

filler is 3.5%, disintegrant is 7.2%, cetyl myrisate as active pharmaceutical ingredient is 79.3% ,cetyl palmitate as active pharmaceutical ingredient is 3.9%,plasticizer is 1.2% , binder is 2.5% , lubricant is 2.4%, by weight of total pharmaceutical composition.

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2011/054513

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K9/20 A61K31/215
ADD.

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K

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

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal , BIOSIS, EMBASE, MEDLINE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 399 360 A (SURER HANSRUEDI [CH] ET AL) 21 March 1995 (1995-03-21)	1-3, 11
Y	examples 1-8 claims 1-8	1-16

X	GB 2 181 053 A (SANDOZ LTD SANDOZ LTD [CH]) 15 April 1987 (1987-04-15)	1-3, 13
Y	examples 1-21	1-16

X	WO 2004/062643 Al (LIFECYCLE PHARMA AS [DK] ; SCHULTZ KIRSTEN [DK] ; HANSEN TUE [DK] ; HOLM) 29 July 2004 (2004-07-29) example 9	1,2

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

☒ See patent family annex.

* Special categories of cited documents :

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

"E" earlier document but published on or after the international filing date

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

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

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

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

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

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

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
16 January 2012	25/01/2012

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Sindel , Ulrike

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2011/054513

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5399360 A	21-03-1995	NONE	
GB 2181053 A	15-04-1987	CY 1622 A	10-07-1992
		GB 2181053 A	15-04-1987
WO 2004062643 A1	29-07-2004	AU 2003205543 A1	10-08-2004
		WO 2004062643 A1	29-07-2004

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2011/054513

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☒ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-10, 14-16

   Pharmaceutical composition comprising coated particles of cetyl palmitate and/or cetyl myristate

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2. claims: 11, 12

   Pharmaceutical composition comprising cetyl palmitate and/or cetyl myristate and a multistage disintegrant intra- and extragranular

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3. claim: 13

   Pharmaceutical composition comprising cetyl palmitate and/or cetyl myristate, made by a granulation step

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