

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 1211-622		FOR FURTHER ACTION See Form PCT/IPEA/416	
International application No. PCT/BR2022/050017	International filing date (<i>day/month/year</i>) 19 January 2022	Priority date (<i>day/month/year</i>)	
International Patent Classification (IPC) or both national classification and IPC A61K 8/14(2006.01)i; A61Q 17/04(2006.01)i CPC: A61K 8/14, A61Q 17/04			
Applicant ACHÉ LABORATÓRIOS FARMACÊUTICOS S.A.			

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36. 2. This REPORT consists of a total of <u> 4 </u> sheets, including this cover sheet. 3. This report is also accompanied by ANNEXES, comprising: a. ☒ (<i>sent to the applicant and to the International Bureau</i>) a total of <u> 26 </u> sheets, as follows: ☒ sheets of the description, claims and/or drawings which have been amended and/or sheets containing rectifications authorized by this Authority, unless those sheets were superseded or cancelled, and any accompanying letters (see Rules 46.5, 66.8, 70.16, 91.2, and Section 607 of the Administrative Instructions). ☐ sheets containing rectifications, where the decision was made by this Authority not to take them into account because they were not authorized by or notified to this Authority at the time when this Authority began to draw up this report, and any accompanying letters (Rules 66.4bis, 70.2(e), 70.16 and 91.2). ☐ superseded sheets and any accompanying letters, where this Authority either considers that the superseding sheets contain an amendment that goes beyond the disclosure in the international application as filed, or the superseding sheets were not accompanied by a letter indicating the basis for the amendments in the application as filed, as indicated in item 4 of Box No. I and the Supplemental Box (see Rule 70.16(b)). b. ☐ (<i>sent to the International Bureau only</i>) a total of (indicate type and number of electronic carrier(s)) _____ containing a sequence listing, in the form of an Annex C/ST.25 text file, as indicated in the Supplemental Box Relating to Sequence Listing (see paragraph 3ter of Annex C of the Administrative Instructions). 4. This report contains indications relating to the following items: ☒ Box No. I Basis of the report ☐ Box No. II Priority ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability ☐ Box No. IV Lack of unity of invention ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement ☐ Box No. VI Certain documents cited ☐ Box No. VII Certain defects in the international application ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand 02 June 2023	Date of completion of this report 30 June 2023
Name and mailing address of the IPEA/BR National Institute of Industrial Property (Brazil) Rua Mayrink Veiga, 9, 6º andar, CEP 20.090-910 Rio de Janeiro – RJ Brazil	Authorized officer Rodrigo BARBOSA FERRARO
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Box No. I Basis of the report

1. With regard to the **language**, this report is based on:
- ☒ the international application in the language in which it was filed.
- ☐ a translation of the international application into _____ which is the language of a translation furnished for the purposes of:
- ☐ international search (Rules 12.3(a) and 23.1(b)).
- ☐ publication of the international application (Rule 12.4(a)).
- ☐ international preliminary examination (Rules 55.2(a) and/or 55.3(a) and (b)).
2. With regard to the **elements** of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):
- ☐ the international application as originally filed/furnished, or
- ☒ the description:
pages **1 to 12** as originally filed/furnished.
pages* _____ received by this Authority on _____
pages* _____ received by this Authority on _____
- ☒ the claims:
Nos. _____ as originally filed/furnished.
Nos.* _____ as amended (together with any statement) under Article 19
Nos.* **1 to 23** received by this Authority on **02.06.2023**
- ☒ the drawings:
pages **1 to 3** as originally filed/furnished.
pages* _____ received by this Authority on _____
pages* _____ received by this Authority on _____
- ☐ a sequence listing - see Supplemental Box Relating to Sequence Listing.
3. ☒ The amendments have resulted in the cancellation of:
- ☐ the description, pages _____
- ☒ the claims, Nos. **24-26**
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since either they are considered to go beyond the disclosure as filed, or they were not accompanied by a letter indicating the basis for the amendments in the application as filed, as indicated in the Supplemental Box (Rules 70.2(c) and (c-bis)):
- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
5. ☐ This report has been established:
- ☐ taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rules 66.1(d-bis) and 70.2(e)).
- ☐ without taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91(Rules 66.4bis and 70.2(e)).
6. With regard to top-up searches (Rules 66.1ter and 70.2(f)):
- ☐ A top-up search was carried out by this Authority on _____
- ☐ Additional relevant documents have been discovered during the top-up search.
- ☒ No top-up search was carried out by this Authority because it would serve no useful purpose.
7. ☐ Supplementary international search report(s) from Authority(ies) _____ has/
have been received and taken into account in establishing this report (Rule 45bis.8(b) and (c)).

* If item 4 applies, some or all of those sheets may be marked "superseded."

Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement		
1. Statement			
Novelty (N)	Claims	1 - 23	YES
	Claims		NO
Inventive step (IS)	Claims	1 - 23	YES
	Claims		NO
Industrial applicability (IA)	Claims	1 -23	YES
	Claims		NO
2. Citations and explanations(Rule 70.7)			
1 - References:			
D1 - BR 102019013856 – 2021-01-12			
D2 - BR 102017004724 – 2020-04-07			
D3 - WO 2017185155 – 2017-11-02			
D4 - BR PI0801545 – 2010-01-12			
D5 - Dario et al,Synergistic photoprotective activity of nanocarrier containing oil of Acrocomia aculeata (Jacq.) Lodd. Ex. Martius—Arecaceae, Industrial Crops and Products, Volume 112, 2018, Pages 305-312 - 2017-12-09			
D6 - Nikolić et al, Skin photoprotection improvement: Synergistic interaction between lipid nanoparticles and organic UV filters, International Journal of Pharmaceutics, Volume 414, Issues 1–2, 2011, Pages 276-284 - 2011-05-10			
D7 - Felippim et al. Development of Photoprotective Formulations Containing Nanostructured Lipid Carriers: Sun Protection Factor, Physical-Mechanical and Sensorial Properties. AAPS PharmSciTech 21, 311 - 2020-11-08			
D8 - Cordenonsi et al The role of chitosan as coating material for nanostructured lipid carriers for skin delivery of fucoxanthin, International Journal of Pharmaceutics, Volume 567, 2019, 118487 - 2019-07-02			
D9 - Coêlho et al, Plant-Derived Butters as Lipid Nanocarriers: A Systematic and Prospective Review. Recent Patents on Nanotechnology. 14. Issue 4, 262-275 - 2020-01-01			
D10 - ALMEIDA, Claudia Wanessa Monteiro. Estudo de misturas binárias de gorduras vegetais amazônicas para o desenvolvimento de carreadores lipídicos. Undergraduate thesis, (Bachelor of Industrial Chemistry) – Faculty of Chemistry, Institute of Exact and Natural Sciences, Federal University of Pará, Belém, Brazil - 2018-01-26			
2 - Novelty – Article 33(2) PCT:			
The document D1, discloses a nanostructured lipid carrier and composition for dermocosmetic treatement with vegetal butter (katité, cacau. murumuru, cupuaçu, bacuri, ucuuba and tucumã), a liquid vegetal oil (peanut oil, Brazil nut, corn, cotton, grape seed, sesame, soybean, walnut and sunflower), and surfactants.			
The document D2, discloses a nanostructured lipid carrier and composition with vegetable lipids, like vegetal butter (murumuru, cupuaçu, bacuri, ucuuba and tucumã), a liquid vegetal oil (buriti and Brazil nut), and surfactants.			
The document D3, a nanostructured lipid carrier, methods and compositions for cosmeceutical cosmetic and skin-care applications with vegetal butter (murumuru, cupuaçu, bacuri, ucuuba and tucumã), a liquid vegetal oil (buriti oil, Brazil nut oil, cannabis oil , sunflower oil and others oils), and surfactants. The composition of this document also provide UV photoprotection.			
Thus, compared to the prior art, and after the analysis of the comments and the amended claims 1 to 23 are now considered novels and therefore also meet the requirement of inventive step, in sense of PCT Article 33(2) and Article 33(3), respectively.			
3 – Inventive Step – Article 33(3) PCT:			

Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
	Given the withdrawal of the novelty objection and the analysis of the comments and the amended claims, the news claims 1 to 23 does involve an inventive step for the reasons above and therefore does comply with PCT Article 33(3). 4 – Industrial Applicability – Article 33(4) PCT: The subject matter in claims 1 to 23 are considered to be industrially applicable and thus complies with the PCT Article 33(4).



São Paulo, June 2nd, 2023.

TO THE INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY (IPEA/BR)

Comments on the written opinion of the Authority Responsible for the International Search

Applicant: ACHÉ LABORATÓRIOS FARMACÊUTICOS S.A.

Our ref.: 1211-622

Dear sirs,

Please find bellow some arguments, comments, and observations in response to the Written Opinion of the International Searching Authority, issued on October 24th, 2022 (PCT/ISA/237 form – total of 4 pages), for continuation of the international preliminary examination.

On the same date, we are also submitting the payment for the preliminary examination fee (R\$630.00), as well as the handling fee (200CHF = R\$1.108,90), based on the conversion of June 1st, 2023).

Therefore, the Applicant requests that its arguments be considered for the Preliminary International Examination.

➤ **SUMMARY OF THE WRITTEN OPINION:**

Ten prior art documents were cited. They are as follows:

D1 - BR 102019013856	– 2021-01-12
D2 - BR 102017004724	– 2020-04-07
D3 - WO 2017185155	– 2017-11-02
D4 - BR PI0801545	– 2010-01-12

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- D5 - Dario et al, **Synergistic photoprotective activity of nanocarrier containing oil of *Acrocomia aculeata* (Jacq.) Lodd. Ex. Martius—Arecaceae, *Industrial Crops and Products***, Volume 112, 2018, Pages 305-312 - 2017-12-09
- D6 - Nikolić et al, **Skin photoprotection improvement: Synergistic interaction between lipid nanoparticles and organic UV filters, *International Journal of Pharmaceutics***, Volume 414, Issues 1–2, 2011, Pages 276-284 - 2011-05-10
- D7 - Felippin et al, **Development of Photoprotective Formulations Containing Nanostructured Lipid Carriers: Sun Protection Factor, Physical-Mechanical and Sensorial Properties, *AAPS PharmSciTech* 21**, 311 - 2020-11-08
- D8 - Cordenonsi et al **The role of chitosan as coating material for nanostructured lipid carriers for skin delivery of fucoxanthin, *International Journal of Pharmaceutics***, Volume 567, 2019, 118487 - 2019-07-02
- D9 - Coêlho et al, **Plant-Derived Butters as Lipid Nanocarriers: A Systematic and Prospective Review. *Recent Patents on Nanotechnology***, 14, Issue 4, 262-275 - 2020-01-01
- D10 - ALMEIDA, Claudia Wanessa Monteiro, **Estudo de misturas binárias de gorduras vegetais amazônicas para o desenvolvimento de carreadores lipídicos**, Undergraduate thesis, (Bachelor of Industrial Chemistry) – Faculty of Chemistry, Institute of Exact and Natural Sciences, Federal University of Pará, Belém, Brazil - 2018-01-26

REGARDING NOVELTY: The Examiner acknowledged the novelty of the subject matter of claims 2 to 20 and 22 to 26. However, he understood that the subject matter of claims 1 and 21 is not novel in view of prior art documents **D1**, **D2** and **D3**.

REGARDING INVENTIVE STEP: The Examiner pointed that the subject matter of claims 1 to 26 does not have inventive step in view of **D1** to **D10**.

REGARDING INDUSTRIAL APPLICATION: The Examiner understood that the subject matter of claims 1 to 26 presents industrial applicability.

➤ **APPLICANT'S RESPONSE - ARGUMENTS**

• **PRELIMINARY COMMENTS**

Initially, the Applicant believes that it is necessary to highlight some aspects regarding the technical field to which the present invention is inserted. More specifically, the present patent application is related to the field of nanotechnology. In this sense, among the various aspects associated with this knowledge area, the Applicant purposely draws attention to structures called lipid nanoparticles.

This type of nanoparticle is of special interest to the pharmaceutical and cosmetic industries, since it has unique physicochemical properties and is very attractive for the preparation of formulations with a variety of different purposes. Some of the properties studied in this type of particle are stability, biocompatibility and, in certain cases, its ability to encapsulate and/or release active ingredients in a given system.

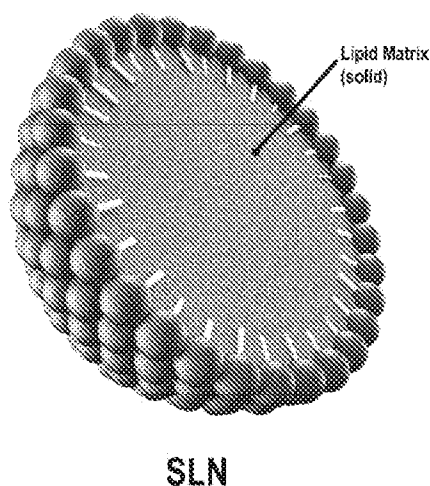


In response to specific needs and application interests, different lipid nanoparticles have been developed and researched over time, so that some of the most important currently are:

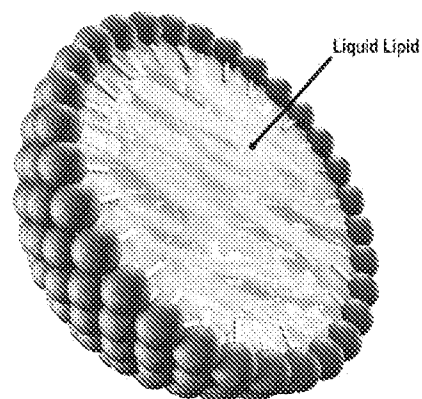
- i) solid lipid nanoparticles (SLN);
- ii) nanostructured lipid carriers (NLC);
- iii) nanoemulsion (NE) particles;
- iv) self-emulsifying drug delivery (SEDDs) particles/systems; and
- v) liposomes.

Each of these particles has specific structures, which directly impacts the physicochemical properties of these nanoparticles and, consequently, their respective applications, as can be seen below in a simplified way:

- The solid lipid nanoparticles (SLN) have a solid core and are formed from solid lipids at room and body temperatures, stabilized by surfactants in the external portion:

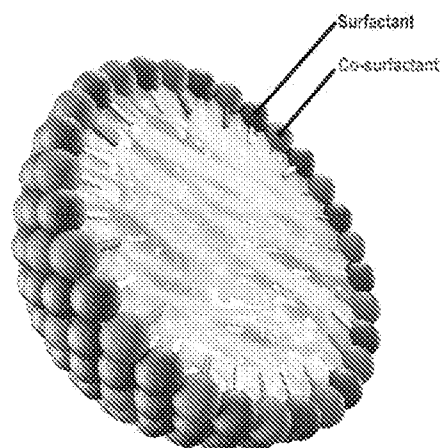


- Nanoemulsions (NE) are particles that have a lipid core that is exclusively liquid at room and body temperatures and surfactants in the external portion.



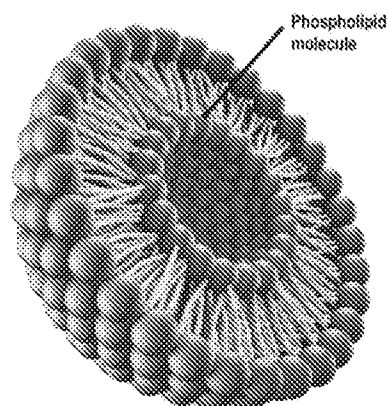
NE

- SEDDs are self-emulsifying systems whose particles are formed *in situ* and structurally have an exclusively liquid core, as well as a primary surfactant and an additional secondary one:



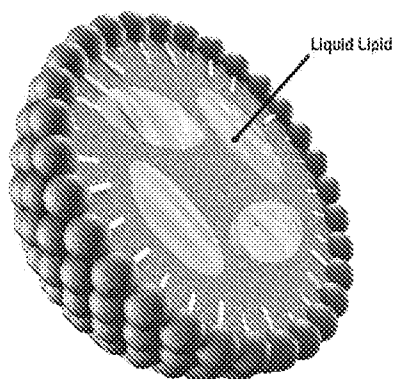
SEDDS

- Liposomes are vesicles formed by phospholipid bilayers:



LIPOSOME

- Finally, the nanostructured lipid carriers (NLC) are effectively the structures of interest of the present invention. NLCs are formed from a mixture of liquid lipids and solid lipids at room and body temperatures, presenting a structured solid matrix with imperfections that allow a greater degree of encapsulation and stability when compared to SLN, for example. These carriers have surfactant in the external portion.



NLC

• REGARDING THE PRESENT INVENTION

First, the Applicant would like to highlight the scope of the present invention.

The present invention relates to:



- 1) Nanostructured lipid carriers (NLC) comprising:
 - a. at least one solid lipid selected from a refined vegetable butter (between 6% and 10%);
 - b. at least one liquid lipid selected from a refined vegetable oil (between 2% and 4%); and
 - c. at least one surfactant (between 2% and 15%).

The solid lipids used are selected from the following butters: bacuri, cacau, cupuaçu, murumuru, ucuuba, tucumã, karité or mixtures thereof.

The liquid lipids employed are selected from: Brazil nut oil, hemp seed oil, corn oil, cotton seed oil, grape seed oil, peanut oil, sesame oil, soybean oil, walnut oil, sunflower oil, raspberry seed oil or mixtures thereof.

- 2) Use of the nanostructured lipid carriers to boost the photoprotective action of ultraviolet (UV) filters, through a synergistic effect.
- 3) Photoprotective composition comprising the NLC, at least one free UV filter (non-encapsulated) and cosmetically acceptable excipients. The NLCs may also comprise encapsulated UV filters.
- 4) Method for skin protection through the application of the photoprotective composition.

• DOCUMENTS D1 to D10

As explained in the specification of the present invention, there is currently a need for new strategies to reduce and optimize the use of sunscreens, for example, compositions that provide improvements in efficiency, safety, and sensory aspects, in addition to reducing the concentration of UV filters and, consequently, production cost, environmental impacts and bioaccumulation processes. The present invention efficiently meets this need.

The prior art documents **D1** to **D10** do not solve this need in the same way as the present invention (which highlights the novelty of the claimed subject matter), nor does it even suggest ways that would lead a person skilled in the art to achieve the present invention in an obvious or evident manner, even when taking the references individually or in combination (which evidences the inventive activity of the claimed subject matter). These aspects will become more evident from the comments below.

Novelty:

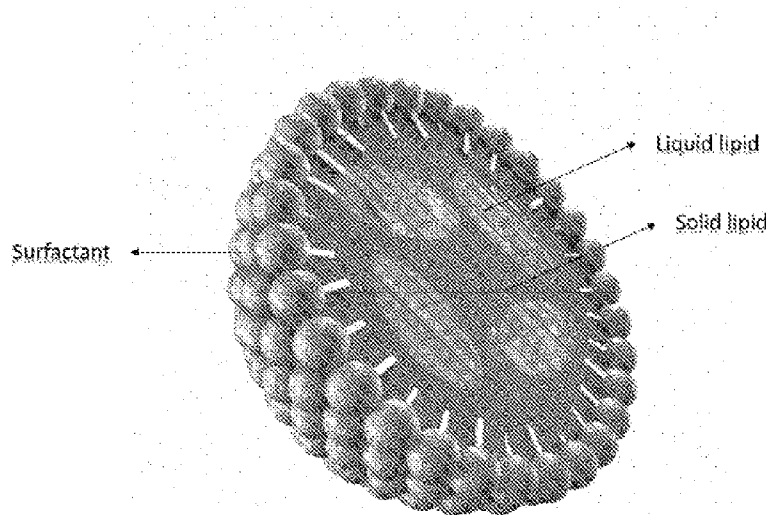
D1: BR 102019013856

The prior art document **D1** discloses a solid lipid composition for producing an NLC, in which the solid composition is obtained by the melting method followed by recrystallization. The composition taught in **D1** necessarily uses the following components: at least one wax, one butter, one oil and one surfactant.



However, unlike **D1**, the NLC of the present invention have, internally, **solid (solid lipid - butter) and liquid (liquid lipid - oil) portions coexisting**, as can be seen from figure 1 of the present invention:

[Fig. 1]



Furthermore, the NLC of the present invention **do not** incorporate any type of wax as an essential component, only: at least one solid lipid (refined vegetable butter), at least one liquid lipid (refined vegetable oil) and at least one surfactant.

D2: BR 102017004724

The prior art document **D2** describes a process for obtaining solid lipid nanoparticles of nanostructured lipid carriers type composed by mixing two solid vegetable lipids with a liquid vegetable lipid, stabilized in an emulsifying system by surfactants, with the incorporation of a drug for application in the treatment of tumor cells (abstract). Furthermore, the lipid nanoparticles claimed in claim 15 of **D2** require a high amount of solid lipids (50 to 90%).

Like **D1**, reference **D2** does not teach the NLC of the present invention, since the nanoparticles of **D2** are solid (abstract) and the NLC of the present invention have, internally, solid and liquid portions coexisting. Furthermore, the solid lipids of the present invention are limited to an amount that varies from 6 to 10%, which is a much lower range than that taught in **D2**.

D3: WO 2017185155

The prior art document **D3** discloses nanostructured lipid vehicles (or carriers) comprising a combination of murumuru seed butter, bis-diglyceryl polyacyladipate-2 (BDP-2) and oil, as presented in paragraph [001]. Furthermore, in the brief description of the



invention, more specifically in paragraph [011], it is disclosed that NLC also comprise surfactants.

The essential component BDP-2 used in **D3** to the obtainment of the NLC is a solid lipid of synthetic origin. However, in direct opposition to this aspect, all lipids (solid or liquid) utilized to obtain the NLC of the present invention are explicitly selected from butters or oils of **vegetable origin, that is, natural origin**.

Inventive step:

1) Types of lipid nanoparticles and their compositions

The embodiment of lipid nanoparticles of the present invention is related to a NLC that has, internally, solid and liquid lipid portions coexisting. The solid lipid portion comprises at least one solid lipid selected from a refined vegetable butter. The liquid lipid portion is constituted by at least one liquid lipid selected from a refined vegetable oil.

D1: BR 102019013856

As previously mentioned, the constituent composition of the nanoparticles from **D1** is related to a solid composition, which essentially comprises: at least one wax, one butter, one oil and one surfactant.

As stated in paragraph [004] of **D1**, "(...). The lipid composition of the oil phase has a special impact on the stability of the nanostructured lipid carrier, requiring experimental evaluations to determine the most appropriate proportion of lipid constituents and surfactants that favor the stability of the particles" (emphasis added). Therefore, the composition of **D1** was studied to obtain stable solid nanoparticles, with wax being an essential component for this purpose.

This became evident from paragraph [065], which explains that carrying out a lipid mixture using wax is the main reason for the technological advantage of the nanoparticles taught in **D1**: "(...) the solid lipid composition proposed in the present invention, due to its character of mixing lipids with different melting points, originates a solid and consistent mixture at room temperature, but with a lower melting point when compared to that of the wax."

As opposed to **D1**, the NLC of the present invention have solid and liquid portions coexisting. Therefore, it would not be obvious to remove an essential component of **D1**, transforming the solid lipid composition into a composition with coexisting solid and liquid portions, since this modification would render the technology from **D1** inoperative for the purpose initially intended.



D2: BR 102017004724

As previously mentioned, **D2** discloses solid lipid nanoparticles (SLN) of the carrier type, in which these nanoparticles are destined for the encapsulation of drugs for the application in the treatment of tumor cells (abstract). Furthermore, to obtain the nanoparticles of **D2**, the lipid composition necessarily requires the use of 50 to 90% of solid lipids (claim 15).

As opposed to **D2**, in addition to having NLC with solid and liquid portions coexisting, the present invention also uses a much lower amount of solid lipids - about **5 to 9 times lower** considering the maximum amount of solid lipids in the NLC of the present invention.

Therefore, an expressive reduction of solid lipids and the formation of NLC with solid and liquid portions coexisting would not be obvious modifications based on the teachings of **D2**, since these conditions would make the technology of **D2** inoperative for its purpose initially intended.

Additionally, it should be noted that the NLC of the present invention promotes, in combination with ultraviolet filters, a synergistic effect of increasing the sun protection factor (SPF), which is not seen in **D2**, which uses the nanoparticles as carriers to encapsulate pharmaceutically active ingredients for the treatment of tumor cells.

D3: WO 2017185155

In accordance with the above discussed, document **D3** discloses nanostructured lipid carriers comprising a combination of the following essential components: murumuru seed butter, bis-diglyceryl polyacyladipate-2 (BDP-2), oil and surfactants.

The compound BDP-2 is of synthetic origin and is essential for the obtainment of the NLC of **D3**, as it is the directly responsible for the reduction of the enthalpy of the carriers, which directly and positively impacts in the crystallinity of these carriers, as explained in example 2 of **D3**. In contrast, the NLC of the present invention employs only lipids of vegetable origin.

Therefore, it would not be obvious for a person skilled in the art, from the teachings of **D3**, to promote the removal precisely of the essential component of the lipid composition (BDP-2) since it is the mainly responsible for the advantageous feature of enthalpy and crystallinity of the NLC of **D3**. In other words, the removal of this component would render the technology of **D3** unusable.

D4: PI 0801545

The prior art document **D4** discloses nanoparticles prepared based on natural waxes from the Amazon. More specifically, the document discloses biodegradable and biocompatible nanoparticles composed of waxes from the Amazon. It should be noted that the document only vaguely mentions the possibility of using butters or oils for the



construction of the nanoparticles of **D4**. Therefore, it is not even possible to know if the components could at some point be combined or if they should be used separately. In addition to not directing any type of combination, the document also does not suggest the quantities of the components of these combinations.

Additionally, as pointed out on page 3, lines 12 to 15, "The nanoparticles described in the present invention are quite similar to solid lipid nanoparticles, with the difference of being made up of **waxes** of Amazonian origin **and not of lipids**" (emphasis added). Therefore, the subject matter of **D4** is directed specifically to nanoparticles using wax and **clearly teaches away a person skilled in the art from the use of lipids**.

In this manner, the present invention differs considerably from **D4** mainly because it does not incorporate an element pointed out as essential by the prior art document, which would lead to an unusability of the technology developed and disclosed by **D4**. Finally, the referred prior art document also **does not** teach or suggest, under any circumstances, a nanostructured lipid carrier (NLC) constituted by solid and liquid lipids of vegetable origin associated with a surfactant, wherein both a solid lipid portion and a liquid lipid portion coexist within the carrier.

D9: Coêlho et al.

Document **D9** addresses the use of lipid derivatives for the construction of lipid nanocarriers. The content addressed by the reference is directed only to carriers with a solid core lipid composition (butters). In opposition to the teachings of **D9**, the NLC of the present invention has both a solid lipid portion and a liquid lipid portion coexisting.

In addition, nothing in **D9** teaches or directs a person skilled in the art to the obtainment of the NLCs with the essential features of the present invention and which have a synergistic effect when associated with UV filters (encapsulated or free) in the improvement of the SPF.

D10: Almeida

The study carried out on **D10** aimed to analyze the physicochemical properties of the murumuru and bacuri fats, in order to evaluate their use as lipid matrices in nanoparticles. The content covered by the document is directed only to solid core nanoparticles, formed by fats and butters. However, the NLC of the present invention necessarily presents a liquid portion coexisting with a solid portion.

Furthermore, although it is not the focus of the study, in item 2.2.2 of **D10**, is also disclosed, in a non-specific manner, a composition comprising cetyl palmitate as a solid lipid and a liquid oil. Cetyl palmitate is a synthetic solid lipid. In opposition, the NLC of the present invention only uses lipids of natural origin.

Finally, also in item 2.2.2, the use of liquid lipids in the preparation of NLC is pointed out as negative, as it results in problems in the retention of the encapsulated active, that



is, leading to excessive release of the active. According to the teachings of **D10**, the replacement of a liquid lipid with a semi-solid one could lead to the overcoming of said disadvantage. Therefore, document **D10** clearly teaches how to replace the use of liquid lipids with semi-solid lipids in the construction of lipid nanoparticles, distancing the person skilled in the art from the present invention.

In this manner, nothing in **D10** teaches or directs a person skilled in the art to the obtainment of the NLCs with the essential features of the present invention and which have a synergistic effect when associated with UV filters (encapsulated or free) in the improvement of the SPF.

In this manner, there is no reason to combine **D1** to **D4**, **D9** and/or **D10** to any of the prior art document and, even in this remote possibility, a person skilled in the art would never be motivated to achieve the essential features of the present invention, especially in relation to the NLC of claim 1 as amended.

2) Synergism

Synergism is a common approach in cosmetic product formulations. It can be defined as the combination of active ingredients that produce a combined effect greater than the sum of their individual effects.

An essential point to be considered is that the synergistic effect cannot be extrapolated from one system to another due to the existence of variations in factors such as the nature of the compounds and their concentrations, environmental conditions, and modes of action.

In the present invention, the synergy of improvement of the sun protection factor (SPF) is observed in compositions that contain the combination of ultraviolet (UV) filters and nanostructured lipid carriers (NLC) as defined in claim 1 now amended, in which the UV filters can be free (unencapsulated), or encapsulated in NLC, or even encapsulated and free, at the same time.

D5: Dario et al.

Document **D5** discloses a synergistic photoprotective activity generated by a composition comprising bocaiuva oil (liquid lipid) and cetyl palmitate (solid lipid). The document does not mention the use of butters.

As previously discussed, the cetyl palmitate is a solid lipid of synthetic origin. On the other hand, the solid lipid used in the present invention is related to a **butter of vegetable origin**, that is, of natural origin. This aspect indicates that there would be **no** motivation to combine butters and natural vegetable oils for the obtainment of the NLC of the present invention.



In addition, the study carried out on **D5** evaluates, in a comparative way, the NLC comprising two combinations of solid and liquid lipids as constituents, namely:

- bocaiúva pulp oil with cetyl palmitate; and
- bocaiúva almond oil with cetyl palmitate.

The first combination (bocaiúva pulp oil with cetyl palmitate) resulted in a non-observance of synergism, but in the second combination the synergistic effect was identified for the combination of bocaiúva almond oil and cetyl palmitate.

Therefore, it becomes evident that the synergistic effect cannot be extrapolated from **D5**, since only one of the combinations studied in this previous article led to the observation of synergistic effects, even with the use of oils from different parts of the same plant. The second paragraph on page 311 highlights this note.

Therefore, there are no indications that the synergism of the combinations of the present invention would be obvious from the information of **D5** since the difference in components and concentrations are very expressive between the prior art document and the present invention. Furthermore, the development of stable NLCs from natural compounds (butter and vegetable oils) is challenging, due to the complexity that the mixture of ingredients in vegetable products impose.

D6: Nikolic et al.

Document **D6** discloses NLCs that, by encapsulating organic UV filters, showed a synergistic photoprotective effect. Note that the prior art document necessarily teaches how to use a wax as a solid lipid. On the other hand, the present invention necessarily uses a vegetable butter as a solid lipid and in a very well-defined concentration.

D6 also discloses attempts at the technique that were used for the construction of lipid nanoparticles, which consisted of only solid lipids, only liquid lipids, or a mixture of solid and liquid lipids but, in the last case, generating lipid nanoparticles with an exclusively solid core. On the other hand, the embodiment of lipid nanoparticles of the present invention is a NLC that has, internally, both solid and liquid portions coexisting. The non-obviousness of this modification has already been ostensibly discussed above.

Furthermore, there are no indications that the synergism of the combinations of the present invention would be obvious from the information in **D6** since the difference in components and concentrations is very expressive between the prior art document and the present invention.

An aspect that is in line with this understanding is pointed out in the conclusion of the article, which states that the synergistic effect can only be achieved with the choice of an adequate solid lipid but does not indicate or suggest which are these lipids, nor mention any possible combination between vegetable butters and vegetable oils. The clear only suggestion in **D6** is that the suitable solid lipid is a wax.



D7: Felippim et al.

Document **D7** discloses NLC obtained from vegetable lipid sources. The objective of the study is to provide photoprotective compositions containing a nanoencapsulated antioxidant (quercetin). Furthermore, the abstract specifies that the formulations responsible for presenting a synergistic effect were those that necessarily contained nanoencapsulated quercetin.

In opposition to this aspect, the NLCs of the present invention do not comprise nanoencapsulated quercetin. The material that may or may not be encapsulated in the NLC of the present invention are the UV filters. It would therefore not be obvious for a person skilled in the art to remove an essential component, responsible for the main effect (synergy) observed on the composition of **D7**.

Therefore, there are no indications that the synergism of the combinations of the present invention would be obvious from the information of **D7**, since it is not at all plausible to assume that compositions free of nanoencapsulated quercetin would present any type of synergism. In other words, document **D7**, therefore, teaches away a person skilled in the art from the present invention.

Furthermore, **D7** uses different ingredients from the present invention (ilipe butter and calendula oil) to specifically encapsulate 0.6% of quercetin (antioxidant with molecular mass of 302.2 g/mol). In the present invention, the NLC is suitable for encapsulation of high concentration of chemical filters (much greater than 0.6%) and molecules with totally different physicochemical features, for example, with higher molecular weight (above 500 g/mol).

In this manner, there is no reason to combine **D5**, **D6** or **D7** to any of the prior art documents and, even if there were, a person skilled in the art would never be motivated to reach the conditions determined as essential of the present invention, especially with regard to the NLC of claim 1, as amended.

3) Specific application

The present invention aims, among other embodiments, a photoprotective cosmetic application. In addition, a synergy of improvement of the sun protection factor (SPF) is observed in compositions that contain a combination of ultraviolet (UV) filters and nanostructured lipid carriers (NLC), in which the UV filters can be free (not encapsulated), or encapsulated in the NLC, or even encapsulated and free at the same time.

D8: Cordenonsi et al.

Document **D8** is related to an article aimed at evaluating the role of chitosan as a coating for nanostructured lipid carriers for the delivery of fucoxanthin to the skin. The only similarity that the nanostructured carriers of **D8** have in relation to the NLC of the present invention are the vegetable lipids.



The objective of **D8** is very different from the objective of the present invention, as it is directed towards the delivery of a specific drug for the treatment of psoriasis. On the other hand, the present invention aims to provide NLC for the application in a **photoprotective** formulation, which has a **synergistic effect on SPF**, wherein the NLC are **not** intended towards the delivery of actives. When encapsulated, the UV filters must remain inside the NLC and not be released or delivered, unlike the drug of the prior art document **D8**.

Nothing in **D8** teaches or directs a person skilled in the art to the obtainment of the NLCs with the essential features of the present invention and which have a synergistic effect when associated with UV filters (encapsulated or free) in the improvement of the SPF.

➤ **CONCLUSIONS AND FINAL COMMENTS:**

The constitution of the lipid nanoparticles of the documents **D1** to **D10** pointed out in the Written Opinion of the Authority Responsible for the International Search is notoriously different from the constitution of the NLC of the present invention, as discussed above.

As to the structure, none of the prior art documents mentioned, including **D1**, **D2**, **D4**, **D6**, **D9** and **D10**, presents or suggests the same composition, qualitatively and quantitatively defined, according to the present invention.

Furthermore, the synergism of the prior art documents **D5**, **D6** and **D7** pointed out in the Written Opinion is extremely specific and cannot be extrapolated, as discussed above for each of these references.

Finally, the application of documents **D2** and **D8** are highly discrepant with that intended in the present invention, which is directed to a photoprotective cosmetic application (among other embodiments), and which has a synergistic effect of improving the SPF when in combination with encapsulated or free (non-encapsulated) UV filters.

In this manner, the person skilled in the art would not be led to conceive the NLC, the composition comprising the NLC, the use of the NLC and the method of protection using the composition comprising the NLC according to the present invention by combining the documents pointed out herein to obtain the advantages claimed and shown in the present patent application.

➤ **ADDITIONAL COMMENTS:**

The new pages with the set of claims aim to highlight the distinct technical features of the present invention. Therefore, it is requested that these new pages to be considered during the International Examination.



We are at your entire disposal for any further clarification, and we look forward to the continuation of the International Examination.

Yours sincerely,



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Chemical Engineer
Master in Law
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Specialist in Cosmetics
Specialist in Chemistry

ANNEX – AMENDED SET OF CLAIMS (MARKED-UP VERSION)

Claims

[Claim 1] A nanostructured lipid carrier comprising a solid and a liquid portion characterized by comprising:

- (i) from 6% to 10% of At least one solid lipid selected from a refined vegetal butter comprising a melting point between 50 and 70°C, palmitic acid between 50 and 70%, and oleic acid between 15 and 30%, wherein the at least one solid lipid is selected from butter of Bacuri (Gen. Platania), Cacau (Gen. Theobroma), Cupuaçu (Gen. Theobroma), Murumuru (Gen. Astrocaryum), Ucuuba (Gen. Virola), Tucumã (Gen. Astrocaryum), Karité (Gen. Butyrospermum) or mixtures thereof.
- (ii) from 2% to 4% of At least one liquid lipid selected from a refined vegetal oil comprising high levels of polyunsaturated and low levels of saturated fat, wherein the at least one liquid lipid is selected from Brazil nut oil (Gen. Bertholletia), Hemp seed oil (Gen. Cannabis), corn oil (Gen. Zea), cotton seed oil (Gen. Gossypieae), grape seed oil (Gen. Vitis), peanut oil (Gen. Arachis), sesame oil, soybean oil (Gen. Glycine), walnut oil (Gen. Juglans), sunflower oil (Gen. Helianthus), raspberry seed oil (Gen. Rubus) or mixtures thereof, and
- (iii) from 2% to 15% of at least one surfactant.

~~[Claim 2] The nanostructured lipid carrier according to claim 1 characterized by (i) the solid lipid selected from the butter of Bacuri (Gen. Platania), Cacau (Gen. Theobroma), Cupuaçu (Gen. Theobroma), Murumuru (Gen. Astrocaryum), Ucuuba (Gen. Virola), Tucumã (Gen. Astrocaryum), Karité (Gen. Butyrospermum) or mixtures thereof.~~

~~[Claim 3]~~ [Claim 2] The nanostructured lipid carrier according to claim 1 characterized by (i) the solid lipid is selected from bacuri butter.

~~[Claim 4]~~ [Claim 3] The nanostructured lipid carrier according to claim 1 characterized by (ii) the liquid lipid comprises oleic acid (5-35%), linoleic acid (40-65%), linolenic acid (20-35%).

~~[Claim 5] The nanostructured lipid carrier according to claim 4 characterized by (ii) the liquid lipid is selected from Brazil nut oil (Gen. Bertholletia), Hemp seed oil (Gen. Cannabis), corn oil (Gen. Zea), cotton seed oil (Gen. Gossypieae), grape seed oil (Gen. Vitis), peanut oil (Gen. Arachis), sesame oil, soybean oil (Gen. Glycine), walnut oil (Gen. Juglans),~~

~~sunflower oil (Gen. Helianthus), raspberry seed oil (gen. Rubus) or mixtures thereof.~~

~~[Claim 6]~~[Claim 4] The nanostructured lipid carrier according to claim 15 characterized by (ii) the liquid lipid is selected from raspberry seed oil.

~~[Claim 7]~~[Claim 5] The nanostructured lipid carrier according to claim 1 characterized by the vegetable oil has photoprotective activity or potentiates photoprotective activity, or combinations thereof.

~~[Claim 8]~~[Claim 6] The nanostructured lipid carrier according to claim 1 characterized by all vegetable sources have anti-inflammatory, antioxidant and moisturizing activity or potentiates anti-inflammatory, antioxidant and moisturizing activity, or combinations thereof.

~~[Claim 9]~~[Claim 7] The nanostructured lipid carrier according to claim 1 characterized by the (iii) surfactant is selected from triblock copolymer of polyethylene oxide-polypropylene oxide-polyethylene oxide, copolymer of ethylene oxide and propylene oxide blocks, steareth, polysorbate 20, polysorbate 40, polysorbate 60, polysorbate 80, sodium lauryl sulfate, polyglycerol oleate, lauryl glucoside, polyoxyl-35 castor oil, polyoxyl 40 hydrogenated castor oil, lecithin and derivatives thereof, phospholipids and derivatives thereof, sorbitan monostearate and/or C₈₋₁₀ mono- and di-glycerides.

~~[Claim 10]~~[Claim 8] The nanostructured lipid carrier according to claim 70 characterized by (iii) the surfactant is selected from polyglycerol oleate, polysorbate 60 and/or copolymer of ethylene oxide and propylene oxide blocks.

~~[Claim 11] The nanostructured lipid carrier according to any of claims 1 to 10 characterized by comprising:~~

- ~~(i) 6% to 10% of refined vegetal butter;~~
- ~~(ii) 2% to 4% of refined vegetal oil;~~
- ~~(iii) 2% to 15% of surfactant.~~

~~[Claim 12]~~[Claim 9] The nanostructured lipid carrier according to any of claims 1 to 844, characterized by the carrier has a particle size in a range from about 100 nm to about 300nm.

~~{Claim-13}~~~~[Claim 10]~~.....The nanostructured lipid carrier according to any of claims 1 to ~~8~~14, characterized by the carrier has a polydispersion index in a range from about 0.001 to about 0.5.

~~{Claim-14}~~~~[Claim 11]~~.....The nanostructured lipid carrier according to any of claims 1 to ~~10~~14, characterized by the carrier has a surface potential in a range from about -50mV to about +30mV.

~~{Claim-15}~~~~[Claim 12]~~.....The nanostructured lipid carrier according to any of claims 1 to ~~11~~14, characterized by the carrier has an encapsulation efficiency greater or equal than 70%.

~~{Claim-16}~~~~[Claim 13]~~.....The nanostructured lipid carrier according to any of claims 1 to ~~12~~14 characterized by further comprising at least one inorganic or organic ultraviolet filter.

~~{Claim-17}~~~~[Claim 14]~~.....The nanostructured lipid carrier according to claim ~~13~~6 characterized by the inorganic ultraviolet filter is selected from at least one of titanium dioxide, zinc oxide, colloidal silicon dioxide and derivatives thereof.

~~{Claim-18}~~~~[Claim 15]~~.....The nanostructured lipid carrier according to claim ~~13~~6 characterized by the organic ultraviolet filter is selected from camphor benzalkonium methosulfate, terephthalylidene dicamphor sulfonic acid, methoxydibenzoylmethane, benzylidene camphor sulfonic acid, octocrylene, cinoxate, menthyl anthranilate, tea-salicylate phenylbenzimidazole sulfonic acid, ethylhexyl methoxycinnamate, benzophenone-3, benzophenone-4, benzophenone-5, paba, homosalate, polyacrylamidomethyl benzylidene camphor, peg-25 paba, ethylhexyl dimethyl paba, ethylhexyl salicylate, isoamyl p-methoxycinnamate, 4-methyl benzylidene camphor, 3-benzylidene camphor, ethylhexyl triazone, drometrizole trisiloxane, diethylhexyl butamido triazone, methylene bis-benzotriazolyl tetramethylbutylphenol, disodium phenyl dibenzimidazole tetrasulfonate, bis-ethylhexyloxyphenol methoxyphenyl triazine, polysilicone-15, diethylamino hydroxybenzoyl hexyl benzoate, tris-biphenyl triazine, bis -ethylhexylolxyphenol methoxyphenyl triazine, diethylamino hydroxybenzoyl hexyl benzoate, ethylhexyl triazone, avobenzene, octocrylene or mixtures thereof.

~~[Claim 19]~~[Claim 16]..... Use of the nanostructured lipid carrier as defined in one of claims 1 to 158 characterized by being an ultraviolet filter booster.

~~[Claim 20]~~[Claim 17]..... The use of the nanostructured lipid carrier as defined in one of claims 1 to 158 characterized by being for the preparation of a photoprotective composition.

~~[Claim 24]~~[Claim 18]..... A photoprotective composition characterized by comprising:

- (i) nanostructured lipid nanocarrier as defined in any of claims 1 to 158;
- (ii) at least one free ultraviolet filter;
- (iii) acceptable cosmeceutical excipients.

~~[Claim 22]~~[Claim 19]..... The photoprotective composition, according to claim 1824, characterized by comprising:

- (i) 10% to 30% of a nanostructured lipid nanocarrier as defined in one of claims 1 to 18 based on the total weight of the photoprotective composition;
- (ii) 70% to 90% of a free filter based on the total weight of the photoprotective composition;
- (iii) acceptable cosmeceutical excipients.

~~[Claim 23]~~[Claim 20]..... The photoprotective composition, according to claim 1923, characterized by the free ultraviolet filter is selected from inorganic or organic ultraviolet filters.

~~[Claim 24]~~[Claim 21]..... The photoprotective composition, according to claim 2025, characterized by the inorganic ultraviolet filter is selected from at least one of titanium dioxide, zinc oxide, colloidal silicon dioxide and derivatives thereof.

~~[Claim 25]~~[Claim 22]..... The photoprotective composition, according to claim 2025, characterized by the organic ultraviolet filter is selected from camphor benzalkonium methosulfate, terephthalylidene dicamphor sulfonic acid, methoxydibenzoylmethane, benzylidene camphor sulfonic acid, octocrylene, cinoxate, menthyl anthranilate, tea-salicylate phenylbenzimidazole sulfonic acid, ethylhexyl methoxycinnamate, benzophenone-3, benzophenone-4, benzophenone-5, paba,

homosalate, polyacrylamidomethyl benzylidene camphor, peg-25 paba, ethylhexyl dimethyl paba, ethylhexyl salicylate, isoamyl p-methoxycinnamate, 4-methyl benzylidene camphor, 3-benzylidene camphor, ethylhexyl triazone, drometrizole trisiloxane, diethylhexyl butamido triazone, methylene bis-benzotriazolyl tetramethylbutylphenol, disodium phenyl dibenzimidazole tetrasulfonate, bis-ethylhexyloxyphenol methoxyphenyl triazine, polysilicone-15, diethylamino hydroxybenzoyl hexyl benzoate, tris-biphenyl triazine, bis-ethylhexyloxyphenol methoxyphenyl triazine, diethylamino hydroxybenzoyl hexyl benzoate, ethylhexyl triazone, avobenzene, octocrylene or mixtures thereof.

~~{Claim 26}~~{Claim 23}.....A method for skin photoprotection characterized by comprising apply to the skin a photoprotective composition ~~according as defined into~~ any of claims ~~24-18~~ to ~~2225~~.

ANNEX – AMENDED SET OF CLAIMS (CLEAN VERSION)

Claims

[Claim 1] A nanostructured lipid carrier comprising a solid and a liquid portion characterized by comprising:

(i) from 6% to 10% of at least one solid lipid selected from a refined vegetal butter comprising a melting point between 50 and 70°C, palmitic acid between 50 and 70%, and oleic acid between 15 and 30%, wherein the at least one solid lipid is selected from butter of: Bacuri (*Gen. Platonina*), Cacao (*Gen. Theobroma*), Cupuaçu (*Gen. Theobroma*), Murumuru (*Gen. Astrocaryum*), Ucuuba (*Gen. Virola*), Tucumã (*Gen. Astrocaryum*), Karité (*Gen. Butyrospermum*) or mixtures thereof.

(ii) from 2% to 4% of at least one liquid lipid selected from a refined vegetal oil comprising high levels of polyunsaturated and low levels of saturated fat, wherein the at least one liquid lipid is selected from Brazil nut oil (*Gen. Bertholletia*), Hemp seed oil (*Gen. Cannabis*), corn oil (*Gen. Zea*), cotton seed oil (*Gen. Gossypieae*), grape seed oil (*Gen. Vitis*), peanut oil (*Gen. Arachis*), sesame oil, soybean oil (*Gen. Glycine*), walnut oil (*Gen. Juglans*), sunflower oil (*Gen. Helianthus*), raspberry seed oil (*Gen. Rubus*) or mixtures thereof; and

(iii) from 2% to 15% of at least one surfactant.

[Claim 2] The nanostructured lipid carrier according to claim 1 characterized by (i) the solid lipid is selected from bacuri butter.

[Claim 3] The nanostructured lipid carrier according to claim 1 characterized by (ii) the liquid lipid comprises oleic acid (5-35%), linoleic acid (40-65%), linolenic acid (20-35%).

[Claim 4] The nanostructured lipid carrier according to claim 1 characterized by (ii) the liquid lipid is selected from raspberry seed oil.

[Claim 5] The nanostructured lipid carrier according to claim 1 characterized by the vegetable oil has photoprotective activity or potentiates photoprotective activity, or combinations thereof.

[Claim 6] The nanostructured lipid carrier according to claim 1 characterized by all vegetable sources have anti-inflammatory, antioxidant and moisturizing activity or potentiates anti-inflammatory, antioxidant and moisturizing activity, or combinations thereof.

- [Claim 7] The nanostructured lipid carrier according to claim 1 characterized by the (iii) surfactant is selected from triblock copolymer of polyethylene oxide-polypropylene oxide-polyethylene oxide, copolymer of ethylene oxide and propylene oxide blocks, steareth, polysorbate 20, polysorbate 40, polysorbate 60, polysorbate 80, sodium lauryl sulfate, polyglycerol oleate, lauryl glucoside, polyoxyl-35 castor oil, polyoxyl 40 hydrogenated castor oil, lecithin and derivatives thereof, phospholipids and derivatives thereof, sorbitan monostearate and/or C₈₋₁₀ mono- and di-glycerides.
- [Claim 8] The nanostructured lipid carrier according to claim 7 characterized by (iii) the surfactant is selected from polyglycerol oleate, polysorbate 60 and/or copolymer of ethylene oxide and propylene oxide blocks.
- [Claim 9] The nanostructured lipid carrier according to any of claims 1 to 8, characterized by the carrier has a particle size in a range from about 100 nm to about 300nm.
- [Claim 10] The nanostructured lipid carrier according to any of claims 1 to 8, characterized by the carrier has a polydispersion index in a range from about 0.001 to about 0.5.
- [Claim 11] The nanostructured lipid carrier according to any of claims 1 to 10, characterized by the carrier has a surface potential in a range from about -50mV to about +30mV.
- [Claim 12] The nanostructured lipid carrier according to any of claims 1 to 11, characterized by the carrier has an encapsulation efficiency greater or equal than 70%.
- [Claim 13] The nanostructured lipid carrier according to any of claims 1 to 12 characterized by further comprising at least one inorganic or organic ultraviolet filter.
- [Claim 14] The nanostructured lipid carrier according to claim 13 characterized by the inorganic ultraviolet filter is selected from at least one of titanium dioxide, zinc oxide, colloidal silicon dioxide and derivatives thereof.
- [Claim 15] The nanostructured lipid carrier according to claim 13 characterized by the organic ultraviolet filter is selected from camphor benzalkonium methosulfate, terephthalylidene dicamphor sulfonic acid, methoxydibenzoylmethane, benzylidene camphor sulfonic acid,

octocrylene, cinoxate, menthyl anthranilate, tea-salicylate
phenylbenzimidazole sulfonic acid, ethylhexyl methoxycinnamate,
benzophenone—3, benzophenone—4, benzophenone—5, paba,
homosalate, polyacrylamidomethyl benzylidene camphor, peg-25 paba,
ethylhexyl dimethyl paba, ethylhexyl salicylate, isoamyl p—
methoxycinnamate, 4—methyl benzylidene camphor, 3-benzylidene
camphor, ethylhexyl triazone, drometrizole trisiloxane, diethylhexyl
butamido triazone, methylene bis-benzotriazolyl tetramethylbutylphenol,
disodium phenyl dibenzimidazole tetrasulfonate, bis-ethylhexyloxyphenol
methoxyphenyl triazine, polysilicone-15, diethylamino hydroxybenzoyl
hexyl benzoate, tris-biphenyl triazine, bis -ethylhexyloxyphenol
methoxyphenyl triazine, diethylamino hydroxybenzoyl hexyl benzoate,
ethylhexyl triazone, avobenzene, octocrylene or mixtures thereof.

[Claim 16] Use of the nanostructured lipid carrier as defined in one of claims 1 to 15
characterized by being an ultraviolet filter booster.

[Claim 17] The use of the nanostructured lipid carrier as defined in one of claims 1 to
15 characterized by being for the preparation of a photoprotective
composition.

[Claim 18] A photoprotective composition characterized by comprising:

- (i) nanostructured lipid nanocarrier as defined in any of claims 1 to 15;
- (ii) at least one free ultraviolet filter;
- (iii) acceptable cosmeceutical excipients.

[Claim 19] The photoprotective composition, according to claim 18, characterized by
comprising:

- (i) 10% to 30% of a nanostructured lipid nanocarrier as defined in one of claims 1 to
18 based on the total weight of the photoprotective composition;
- (ii) 70% to 90% of a free filter based on the total weight of the photoprotective
composition;
- (iii) acceptable cosmeceutical excipients.

[Claim 20] The photoprotective composition, according to claim 19, characterized by
the free ultraviolet filter is selected from inorganic or organic ultraviolet
filters.

[Claim 21] The photoprotective composition, according to claim 20, characterized by the inorganic ultraviolet filter is selected from at least one of titanium dioxide, zinc oxide, colloidal silicon dioxide and derivatives thereof.

[Claim 22] The photoprotective composition, according to claim 20, characterized by the organic ultraviolet filter is selected from camphor benzalkonium methosulfate, terephthalylidene dicamphor sulfonic acid, methoxydibenzoylmethane, benzylidene camphor sulfonic acid, octocrylene, cinoxate, menthyl anthranilate, tea-salicylate phenylbenzimidazole sulfonic acid, ethylhexyl methoxycinnamate, benzophenone-3, benzophenone-4, benzophenone-5, paba, homosalate, polyacrylamidomethyl benzylidene camphor, peg-25 paba, ethylhexyl dimethyl paba, ethylhexyl salicylate, isoamyl p-methoxycinnamate, 4-methyl benzylidene camphor, 3-benzylidene camphor, ethylhexyl triazone, drometrizole trisiloxane, diethylhexyl butamido triazone, methylene bis-benzotriazolyl tetramethylbutylphenol, disodium phenyl dibenzimidazole tetrasulfonate, bis-ethylhexyloxyphenol methoxyphenyl triazine, polysilicone-15, diethylamino hydroxybenzoyl hexyl benzoate, tris-biphenyl triazine, bis-ethylhexyloxyphenol methoxyphenyl triazine, diethylamino hydroxybenzoyl hexyl benzoate, ethylhexyl triazone, avobenzene, octocrylene or mixtures thereof.

[Claim 23] A method for skin photoprotection characterized by comprising apply to the skin a photoprotective composition as defined in any of claims 18 to 22.

**ANNEX – AMENDED SET OF CLAIMS (MARKED-UP
VERSION)**

Claims

[Claim 1] A nanostructured lipid carrier comprising a solid and a liquid portion characterized by comprising:

- (i) from 6% to 10% of at least one solid lipid selected from a refined vegetal butter comprising a melting point between 50 and 70°C, palmitic acid between 50 and 70%, and oleic acid between 15 and 30%, wherein the at least one solid lipid is selected from butter of: Bacuri (*Gen. Platonina*), Cacao (*Gen. Theobroma*), Cupuaçu (*Gen. Theobroma*), Murumuru (*Gen. Astrocaryum*), Ucuuba (*Gen. Virola*), Tucumã (*Gen. Astrocaryum*), Karité (*Gen. Butyrospermum*) or mixtures thereof.
- (ii) from 2% to 4% of at least one liquid lipid selected from a refined vegetal oil comprising high levels of polyunsaturated and low levels of saturated fat, wherein the at least one liquid lipid is selected from Brazil nut oil (*Gen. Bertholletia*), Hemp seed oil (*Gen. Cannabis*), corn oil (*Gen. Zea*), cotton seed oil (*Gen. Gossypieae*), grape seed oil (*Gen. Vitis*), peanut oil (*Gen. Arachis*), sesame oil, soybean oil (*Gen. Glycine*), walnut oil (*Gen. Juglans*), sunflower oil (*Gen. Helianthus*), raspberry seed oil (*Gen. Rubus*) or mixtures thereof; and
- (iii) from 2% to 15% of at least one surfactant.

[Claim 2] The nanostructured lipid carrier according to claim 1 characterized by (i) the solid lipid is selected from bacuri butter.

[Claim 3] The nanostructured lipid carrier according to claim 1 characterized by (ii) the liquid lipid comprises oleic acid (5-35%), linoleic acid (40-65%), linolenic acid (20-35%).

[Claim 4] The nanostructured lipid carrier according to claim 1 characterized by (ii) the liquid lipid is selected from raspberry seed oil.

[Claim 5] The nanostructured lipid carrier according to claim 1 characterized by the vegetable oil has photoprotective activity or potentiates photoprotective activity, or combinations thereof.

[Claim 6] The nanostructured lipid carrier according to claim 1 characterized by all vegetable sources have anti-inflammatory, antioxidant and moisturizing activity or potentiates anti-inflammatory, antioxidant and moisturizing activity, or combinations thereof.

- [Claim 7] The nanostructured lipid carrier according to claim 1 characterized by the (iii) surfactant is selected from triblock copolymer of polyethylene oxide-polypropylene oxide-polyethylene oxide, copolymer of ethylene oxide and propylene oxide blocks, steareth, polysorbate 20, polysorbate 40, polysorbate 60, polysorbate 80, sodium lauryl sulfate, polyglycerol oleate, lauryl glucoside, polyoxyl-35 castor oil, polyoxyl 40 hydrogenated castor oil, lecithin and derivatives thereof, phospholipids and derivatives thereof, sorbitan monostearate and/or C₈₋₁₀ mono- and di-glycerides.
- [Claim 8] The nanostructured lipid carrier according to claim 7 characterized by (iii) the surfactant is selected from polyglycerol oleate, polysorbate 60 and/or copolymer of ethylene oxide and propylene oxide blocks.
- [Claim 9] The nanostructured lipid carrier according to any of claims 1 to 8, characterized by the carrier has a particle size in a range from about 100 nm to about 300nm.
- [Claim 10] The nanostructured lipid carrier according to any of claims 1 to 8, characterized by the carrier has a polydispersion index in a range from about 0.001 to about 0.5.
- [Claim 11] The nanostructured lipid carrier according to any of claims 1 to 10, characterized by the carrier has a surface potential in a range from about -50mV to about +30mV.
- [Claim 12] The nanostructured lipid carrier according to any of claims 1 to 11, characterized by the carrier has an encapsulation efficiency greater or equal than 70%.
- [Claim 13] The nanostructured lipid carrier according to any of claims 1 to 12 characterized by further comprising at least one inorganic or organic ultraviolet filter.
- [Claim 14] The nanostructured lipid carrier according to claim 13 characterized by the inorganic ultraviolet filter is selected from at least one of titanium dioxide, zinc oxide, colloidal silicon dioxide and derivatives thereof.
- [Claim 15] The nanostructured lipid carrier according to claim 13 characterized by the organic ultraviolet filter is selected from camphor benzalkonium methosulfate, terephthalylidene dicamphor sulfonic acid, methoxydibenzoylmethane, benzylidene camphor sulfonic acid,

octocrylene, cinoxate, menthyl anthranilate, tea-salicylate
 phenylbenzimidazole sulfonic acid, ethylhexyl methoxycinnamate,
 benzophenone-3, benzophenone-4, benzophenone-5, paba,
 homosalate, polyacrylamidomethyl benzylidene camphor, peg-25 paba,
 ethylhexyl dimethyl paba, ethylhexyl salicylate, isoamyl p-
 methoxycinnamate, 4-methyl benzylidene camphor, 3-benzylidene
 camphor, ethylhexyl triazone, drometrizole trisiloxane, diethylhexyl
 butamido triazone, methylene bis-benzotriazolyl tetramethylbutylphenol,
 disodium phenyl dibenzimidazole tetrasulfonate, bis-ethylhexyloxyphenol
 methoxyphenyl triazine, polysilicone-15, diethylamino hydroxybenzoyl
 hexyl benzoate, tris-biphenyl triazine, bis -ethylhexyloxyphenol
 methoxyphenyl triazine, diethylamino hydroxybenzoyl hexyl benzoate,
 ethylhexyl triazone, avobenzene, octocrylene or mixtures thereof.

[Claim 16] Use of the nanostructured lipid carrier as defined in one of claims 1 to 15 characterized by being an ultraviolet filter booster.

[Claim 17] The use of the nanostructured lipid carrier as defined in one of claims 1 to 15 characterized by being for the preparation of a photoprotective composition.

[Claim 18] A photoprotective composition characterized by comprising:

- (i) nanostructured lipid nanocarrier as defined in any of claims 1 to 15;
- (ii) at least one free ultraviolet filter;
- (iii) acceptable cosmeceutical excipients.

[Claim 19] The photoprotective composition, according to claim 18, characterized by comprising:

- (i) 10% to 30% of a nanostructured lipid nanocarrier as defined in one of claims 1 to 18 based on the total weight of the photoprotective composition;
- (ii) 70% to 90% of a free filter based on the total weight of the photoprotective composition;
- (iii) acceptable cosmeceutical excipients.

[Claim 20] The photoprotective composition, according to claim 19, characterized by the free ultraviolet filter is selected from inorganic or organic ultraviolet filters.

[Claim 21] The photoprotective composition, according to claim 20, characterized by the inorganic ultraviolet filter is selected from at least one of titanium dioxide, zinc oxide, colloidal silicon dioxide and derivatives thereof.

[Claim 22] The photoprotective composition, according to claim 20, characterized by the organic ultraviolet filter is selected from camphor benzalkonium methosulfate, terephthalylidene dicamphor sulfonic acid, methoxydibenzoylmethane, benzylidene camphor sulfonic acid, octocrylene, cinoxate, menthyl anthranilate, tea-salicylate phenylbenzimidazole sulfonic acid, ethylhexyl methoxycinnamate, benzophenone-3, benzophenone-4, benzophenone-5, paba, homosalate, polyacrylamidomethyl benzylidene camphor, peg-25 paba, ethylhexyl dimethyl paba, ethylhexyl salicylate, isoamyl p-methoxycinnamate, 4-methyl benzylidene camphor, 3-benzylidene camphor, ethylhexyl triazone, drometrizole trisiloxane, diethylhexyl butamido triazone, methylene bis-benzotriazolyl tetramethylbutylphenol, disodium phenyl dibenzimidazole tetrasulfonate, bis-ethylhexyloxyphenol methoxyphenyl triazine, polysilicone-15, diethylamino hydroxybenzoyl hexyl benzoate, tris-biphenyl triazine, bis-ethylhexylolxyphenol methoxyphenyl triazine, diethylamino hydroxybenzoyl hexyl benzoate, ethylhexyl triazone, avobenzene, octocrylene or mixtures thereof.

[Claim 23] A method for skin photoprotection characterized by comprising apply to the skin a photoprotective composition as defined in any of claims 18 to 22.

ANNEX – AMENDED SET OF CLAIMS (CLEAN VERSION)

Claims

[Claim 1] A nanostructured lipid carrier comprising a solid and a liquid portion characterized by comprising:

(i) from 6% to 10% of at least one solid lipid selected from a refined vegetal butter comprising a melting point between 50 and 70°C, palmitic acid between 50 and 70%, and oleic acid between 15 and 30%, wherein the at least one solid lipid is selected from butter of: Bacuri (*Gen. Platonina*), Cacao (*Gen. Theobroma*), Cupuaçu (*Gen. Theobroma*), Murumuru (*Gen. Astrocaryum*), Ucuuba (*Gen. Virola*), Tucumã (*Gen. Astrocaryum*), Karité (*Gen. Butyrospermum*) or mixtures thereof.

(ii) from 2% to 4% of at least one liquid lipid selected from a refined vegetal oil comprising high levels of polyunsaturated and low levels of saturated fat, wherein the at least one liquid lipid is selected from Brazil nut oil (*Gen. Bertholletia*), Hemp seed oil (*Gen. Cannabis*), corn oil (*Gen. Zea*), cotton seed oil (*Gen. Gossypieae*), grape seed oil (*Gen. Vitis*), peanut oil (*Gen. Arachis*), sesame oil, soybean oil (*Gen. Glycine*), walnut oil (*Gen. Juglans*), sunflower oil (*Gen. Helianthus*), raspberry seed oil (*Gen. Rubus*) or mixtures thereof; and

(iii) from 2% to 15% of at least one surfactant.

[Claim 2] The nanostructured lipid carrier according to claim 1 characterized by (i) the solid lipid is selected from bacuri butter.

[Claim 3] The nanostructured lipid carrier according to claim 1 characterized by (ii) the liquid lipid comprises oleic acid (5-35%), linoleic acid (40-65%), linolenic acid (20-35%).

[Claim 4] The nanostructured lipid carrier according to claim 1 characterized by (ii) the liquid lipid is selected from raspberry seed oil.

[Claim 5] The nanostructured lipid carrier according to claim 1 characterized by the vegetable oil has photoprotective activity or potentiates photoprotective activity, or combinations thereof.

[Claim 6] The nanostructured lipid carrier according to claim 1 characterized by all vegetable sources have anti-inflammatory, antioxidant and moisturizing activity or potentiates anti-inflammatory, antioxidant and moisturizing activity, or combinations thereof.

- [Claim 7] The nanostructured lipid carrier according to claim 1 characterized by the (iii) surfactant is selected from triblock copolymer of polyethylene oxide-polypropylene oxide-polyethylene oxide, copolymer of ethylene oxide and propylene oxide blocks, steareth, polysorbate 20, polysorbate 40, polysorbate 60, polysorbate 80, sodium lauryl sulfate, polyglycerol oleate, lauryl glucoside, polyoxyl-35 castor oil, polyoxyl 40 hydrogenated castor oil, lecithin and derivatives thereof, phospholipids and derivatives thereof, sorbitan monostearate and/or C₈₋₁₀ mono- and di-glycerides.
- [Claim 8] The nanostructured lipid carrier according to claim 7 characterized by (iii) the surfactant is selected from polyglycerol oleate, polysorbate 60 and/or copolymer of ethylene oxide and propylene oxide blocks.
- [Claim 9] The nanostructured lipid carrier according to any of claims 1 to 8, characterized by the carrier has a particle size in a range from about 100 nm to about 300nm.
- [Claim 10] The nanostructured lipid carrier according to any of claims 1 to 8, characterized by the carrier has a polydispersion index in a range from about 0.001 to about 0.5.
- [Claim 11] The nanostructured lipid carrier according to any of claims 1 to 10, characterized by the carrier has a surface potential in a range from about -50mV to about +30mV.
- [Claim 12] The nanostructured lipid carrier according to any of claims 1 to 11, characterized by the carrier has an encapsulation efficiency greater or equal than 70%.
- [Claim 13] The nanostructured lipid carrier according to any of claims 1 to 12 characterized by further comprising at least one inorganic or organic ultraviolet filter.
- [Claim 14] The nanostructured lipid carrier according to claim 13 characterized by the inorganic ultraviolet filter is selected from at least one of titanium dioxide, zinc oxide, colloidal silicon dioxide and derivatives thereof.
- [Claim 15] The nanostructured lipid carrier according to claim 13 characterized by the organic ultraviolet filter is selected from camphor benzalkonium methosulfate, terephthalylidene dicamphor sulfonic acid, methoxydibenzoylmethane, benzylidene camphor sulfonic acid,

octocrylene, cinoxate, menthyl anthranilate, tea-salicylate
 phenylbenzimidazole sulfonic acid, ethylhexyl methoxycinnamate,
 benzophenone-3, benzophenone-4, benzophenone-5, paba,
 homosalate, polyacrylamidomethyl benzylidene camphor, peg-25 paba,
 ethylhexyl dimethyl paba, ethylhexyl salicylate, isoamyl p-
 methoxycinnamate, 4-methyl benzylidene camphor, 3-benzylidene
 camphor, ethylhexyl triazone, drometrizole trisiloxane, diethylhexyl
 butamido triazone, methylene bis-benzotriazolyl tetramethylbutylphenol,
 disodium phenyl dibenzimidazole tetrasulfonate, bis-ethylhexyloxyphenol
 methoxyphenyl triazine, polysilicone-15, diethylamino hydroxybenzoyl
 hexyl benzoate, tris-biphenyl triazine, bis -ethylhexyloxyphenol
 methoxyphenyl triazine, diethylamino hydroxybenzoyl hexyl benzoate,
 ethylhexyl triazone, avobenzene, octocrylene or mixtures thereof.

[Claim 16] Use of the nanostructured lipid carrier as defined in one of claims 1 to 15 characterized by being an ultraviolet filter booster.

[Claim 17] The use of the nanostructured lipid carrier as defined in one of claims 1 to 15 characterized by being for the preparation of a photoprotective composition.

[Claim 18] A photoprotective composition characterized by comprising:

- (i) nanostructured lipid nanocarrier as defined in any of claims 1 to 15;
- (ii) at least one free ultraviolet filter;
- (iii) acceptable cosmeceutical excipients.

[Claim 19] The photoprotective composition, according to claim 18, characterized by comprising:

- (i) 10% to 30% of a nanostructured lipid nanocarrier as defined in one of claims 1 to 18 based on the total weight of the photoprotective composition;
- (ii) 70% to 90% of a free filter based on the total weight of the photoprotective composition;
- (iii) acceptable cosmeceutical excipients.

[Claim 20] The photoprotective composition, according to claim 19, characterized by the free ultraviolet filter is selected from inorganic or organic ultraviolet filters.

[Claim 21] The photoprotective composition, according to claim 20, characterized by the inorganic ultraviolet filter is selected from at least one of titanium dioxide, zinc oxide, colloidal silicon dioxide and derivatives thereof.

[Claim 22] The photoprotective composition, according to claim 20, characterized by the organic ultraviolet filter is selected from camphor benzalkonium methosulfate, terephthalylidene dicamphor sulfonic acid, methoxydibenzoylmethane, benzylidene camphor sulfonic acid, octocrylene, cinoxate, menthyl anthranilate, tea-salicylate phenylbenzimidazole sulfonic acid, ethylhexyl methoxycinnamate, benzophenone-3, benzophenone-4, benzophenone-5, paba, homosalate, polyacrylamidomethyl benzylidene camphor, peg-25 paba, ethylhexyl dimethyl paba, ethylhexyl salicylate, isoamyl p-methoxycinnamate, 4-methyl benzylidene camphor, 3-benzylidene camphor, ethylhexyl triazone, drometrizole trisiloxane, diethylhexyl butamido triazone, methylene bis-benzotriazolyl tetramethylbutylphenol, disodium phenyl dibenzimidazole tetrasulfonate, bis-ethylhexyloxyphenol methoxyphenyl triazine, polysilicone-15, diethylamino hydroxybenzoyl hexyl benzoate, tris-biphenyl triazine, bis-ethylhexylolxyphenol methoxyphenyl triazine, diethylamino hydroxybenzoyl hexyl benzoate, ethylhexyl triazone, avobenzene, octocrylene or mixtures thereof.

[Claim 23] A method for skin photoprotection characterized by comprising apply to the skin a photoprotective composition as defined in any of claims 18 to 22.