

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 P40206WO	FOR FURTHER ACTION		See Form PCT/IPEA/416
International application No. PCT/EP2016/051388	International filing date (day/month/year) 22.01.2016	Priority date (day/month/year) 22.01.2015	
International Patent Classification (IPC) or national classification and IPC INV. A61K36/185			
Applicant Phytoplant Research S.L.			
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>8</u> sheets, including this cover sheet. 3. This report is also accompanied by ANNEXES, comprising: a. ☒ (sent to the applicant and to the International Bureau) a total of <u>14</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which have been amended and/or sheets containing rectifications authorized by this Authority, unless those sheets were superseded or cancelled, and any accompanying letters (see Rules 46.5, 66.8, 70.16, 91.2, and Section 607 of the Administrative Instructions).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 ☒ superseded sheets and any accompanying letters, where this Authority either considers that the superseding sheets contain an amendment that goes beyond the disclosure in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. ☐ (sent to the International Bureau only) 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 conclusion under Article 35(2) with regard to novelty, inventive step or 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 14.11.2016		Date of completion of this report 11.04.2017	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Fax: +49 89 2399 - 4465		Authorized officer Friederich, Martin Telephone No. +49 89 2399-7860	



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 (under Rules 12.3(a) and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4(a))
 - ☐ international preliminary examination (under 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*):

Description, Pages

1-59 as originally filed

Claims, Numbers

1-25 as originally filed

Drawings, Sheets

1/3-3/3 as originally filed

- ☐ 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.
 - ☐ 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. 1-13
 - ☐ 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)).

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/EP2016/051388

6. ☒ With regard to top-up searches (Rules 66.1 *ter* and 70.2(f)):
- ☒ A top-up search was carried out by this Authority on 13.12.2016 (all discovered documents are listed in the Supplemental Box Relating to Top-up Search).
 - ☐ 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 or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	
	No: Claims	<u>1-25</u>
Inventive step (IS)	Yes: Claims	
	No: Claims	<u>1-25</u>
Industrial applicability (IA)	Yes: Claims	<u>1-25</u>
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

With letter of 09.02.2017 the applicant has filed amended **claims 1-13** together with further explanations, which have been taken into account.

Added matter

In amended **claim 6** the Applicant has now introduced a "third solvent" mixture without indicating a basis for this amendments in the application as filed. In addition, this third solvent mixture should be the same as in step d) - again without indicating a basis for this amendments in the application as filed. The paragraphs 50 and 52 which have been cited by the applicant in this context are silent about such further steps.

This report has therefore been established as if the amendments filed with letter of 14.11.2016 and of 09.02.2017 had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c) PCT).

Additional remarks

Clarity

The term "consisting essentially of" used in independent **claims 1 and 6** is still considered as problematic for process claims.

It remains unclear from the wording of **claims 1 and 6**, which further steps are "essential" to the invention and which are not. A claim has however to be clear per se. The wording "consisting essentially of" can be at best interpreted as "comprising".

In any case it is noted that the claims are not considered to exclude chromatography.

Novelty and inventive step

With letter of 09.02.2017 the Applicant again referred to the submissions of 14.11.2016. This argumentation (see the letter of 14.11.2016, page 3, paragraph 5) seems however to be based on the fact only that the solvents of the two extraction steps a) and d) are the same - which is the case for present claim 1, but not for claim 6 (of 09.02.2017).

The claims filed with letter of 09.02.2017 do not exclude further steps as chromatography. As mentioned above, the solvents of steps a) and d) in claim 6 can be different. The objections would therefore still be relevant even if the amendments could be allowed.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

- D1 EP 2 044 935 A1 (VIVACELL BIOTECHNOLOGY ESPANA [ES]) 8 April 2009 (2009-04-08) cited in the application
- D2 WO 2004/026857 A2 (GW PHARMA LTD [GB]; FLOCKHART IAN [GB]; WHEATLEY GARY WILLIAM [GB]; DR) 1 April 2004 (2004-04-01)
- D3 GB 2 393 182 A (GW PHARMA LTD [GB]) 24 March 2004 (2004-03-24)

If not indicated otherwise, the relevant passages are those mentioned in the International search report.

Claims 22-25 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 39.1(iv)/67.1(iv) PCT. The patentability can be dependent upon the formulation of the claims. The EPO, for example, does not recognize as patentable claims to the use of a compound in medical treatment, but may allow claims to a product, in particular substances or compositions for use in a first or further medical treatment.

Patentability, in particular novelty and inventive step, of **claims 22-25** has been assessed on the basis of a purpose-limited product claim taking into account the alleged effects of the compound/composition.

Art. 33(2)

The present application does not meet the requirements of Article 33(2) PCT, because the subject-matter of **claims 1-25** does not appear to be new in the sense of Article 33(2) PCT.

With respect to product by process claims (see present **claim 20**) it is noted that a product is not rendered novel merely by the fact that it is produced by means of a new process.

The wording of present **claim 21** ("comprising") includes raw extracts as well.

D1 discloses the isolation of CBG and/or CBD from non-polar *Cannabis* extracts by recrystallization from hexane. THC is present in very low amounts. The use of specific chemovars is mentioned. The same solvents are used (see the references to D1 in examples 6-9, 14 and 19-25 of the present application).

The subject-matter of **claims 1-25** is therefore not considered to be new (Article 33(2) PCT).

D2 discloses a purification process for cannabinoids from plant extracts based on a combination of solvent extraction, chromatography and re-crystallisation steps from hexane. Extraction of specific cannabis chemovars rich in CBD/CBG and a low THC content are mentioned. CBD/CBG can be separated from THC by chromatography.

The subject-matter of **claims 1-25** is therefore not considered to be new (Article 33(2) PCT).

D3 discloses the purification of CBD from plant material, comprising an extract of the plant material, and crystallization from non-polar solvents as hexane. The resulting extract is low in THC. Decarboxylating and chromatographic steps are mentioned as well as the use of specific chemovars.

The subject-matter of **claims 1-25** is therefore not considered to be new (Article 33(2) PCT).

Art. 33(3)

With respect to the subject-matter of **claims 1-25** the applicant's attention is drawn to the fact that even if novelty could be established over the above-cited prior art it is at present not clear wherein an inventive step may reside.

With respect to inventive step the following is to be noted:

The problem to be solved is defined in paragraph 8 of the present application as to provide compositions having a low THC content, but which are enriched in CBD/CBG. For such a separation a chromatographic step (see paragraph 66 and example 15) or an extraction starting from specific chemovars (see paragraph 45) seems however to be needed. Both features are missing in present independent claims 1 and 11. Both features are however well-known from the prior art (see D1, D2 or D3).

At present it is therefore not clear, wherein the contribution of the present application to the prior art might reside.

With respect to the argumentation on inventive step filed with applicants letter of 14.11.2016 it is further noted that the effect mentioned by the applicant has never been mentioned in the application as filed and is therefore not plausible.

Furthermore, the examples of the present application do not show any advantage which could be due to the use of the same solvent.

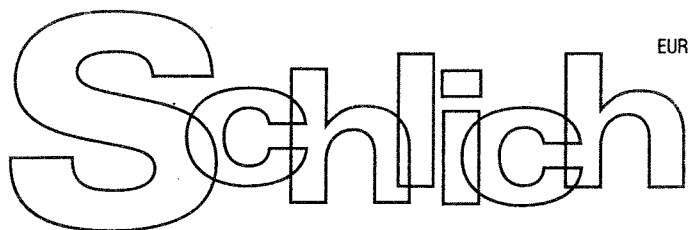
The second use of the solvent is a simple recrystallisation step, which belongs to the basic knowledge of a person skilled in the art.

Re Item VIII

Certain observations on the international application

The application does not meet the requirements of Article 6 PCT, because **claims 1-25** are not clear.

Independent **claims 1 and 11** do not meet the requirements of Article 6 PCT because the matter for which protection is sought is not clearly defined. The claims attempt to define the subject-matter in terms of the result to be achieved ("in a manner that concentrates/crystallizes", "wherein the second solvent mixture dissolves at least 50% of", "wherein the plant material is treated to decarboxylate one or more cannabinoids"), which merely amounts to a statement of the underlying problem, without providing the technical features necessary for achieving this result.



European Patent Office
Bob-van-Benthem-Platz 1
80469 Munich
Germany

Via online filing

My ref: P40206WO

Date: 14 November 2016

Dear Sirs

International Patent Application No. PCT/EP2016/051388

**"METHODS OF PURIFYING CANNABINOIDS, COMPOSITIONS AND KITS
THEREOF"**

In the name of PhytoPlant Research S.L

We request International Preliminary Examination of the above International patent application and enclose herewith:-

- Demand Form
- Fee payment
- Amended claims – we confirm these are the claims that are to be subject to examination

We request issue of a substantive examination report with an opportunity to submit a detailed response should the report initially find any claim not patentable.

In the event of overpayment or underpayment of fees we ask that the sum be credited or debited to EPO deposit account no. 2805.0546.

Our observations in response to the Written Opinion of the International Searching Authority dated 22 April 2016 are set out below.

Amendments

We file herewith an amended set of claims which is provided in both clean and marked-up versions to assist the Examiner.

In the amended claims, claims 1 and 11 have been limited to recite a method consisting essentially of the recited steps (rather than comprising the recited steps). In particular, the recited steps for purifying a cannabinoid from a plant material

involve the use of a non-polar solvent selected from petroleum ether, pentane and hexane, where the non-polar solvent is the same in the first and second extraction. Basis for this amendment can be found, for example, in paragraph 24 of the original application, which discloses the use of the specific solvents recited in the amended claims and further specifies that the solvent can be used in "any or all" of the extractions steps.

Claim 11 further includes an initial extraction step using the solvents listed in paragraph 52. Additional basis can be found in paragraph 204, which defines the transitional phrase "consisting essentially of". The closed-ended transitional phrase "consisting essentially of" limits the scope of a claim to the expressly recited elements, limitations, steps and/or features and any other elements, limitations and/or features that do not materially affect the basic and novel characteristic(s) of the claimed subject matter. In the case of the present invention, the basic and novel characteristics are two-fold: first, the use of one of petroleum ether, pentane and hexane, and second, the requirement that the same solvent be used in the first and second extractions steps.

Claims 2, 3 and 5 have been amended to recite "recovery" or "recovered" rather than "purify" or "purified", with basis for example at paragraph 190.

Claims 3, 5 and 13 have been amended to recite collection of a crystalline product, with basis at paragraphs 31 and 37, which describe filtration of the crystallized material to form a mother liquid. Additional basis is found at paragraph 11 and in the examples.

Claims 20 – 25 have been deleted and new claims 20 – 23 have been added. New claims 20 and 21 have basis at paragraphs 24, 119, 135 and 152. New claims 22 and 23 have basis at paragraph 23, which discusses filtration of the second solvent solution.

Additional minor amendments have been made in the claims to address the clarity objections raised by the Examiner.

As noted above, the present amendments have basis in the original application and do not add matter.

Excluded Subject Matter

The Examiner has alleged that claims 22 – 25 relate to excluded subject matter. However, the claims in question have been deleted and the objection is therefore moot.

Novelty

The Examiner has alleged that claims 1 – 25 lack novelty over each of documents D1 – D3.

Claims 22 – 25 have been deleted and the objection, insofar as it applies to those claims, is moot. With regards to the remaining claims, we maintain that the subject matter of these claims is novel over the cited prior art for the reasons set out below.

D1 discloses a composition of at least one non-psychoactive cannabinoid compound and/or at least one phenolic or flavonoid compound and/or the 1,4-phenanthrenequinone Denbinobin and is used for prevention and treatment of gastrointestinal inflammatory disease and/or cancer diseases. The composition is obtained by extracting decarboxylated plant material with acetone, which is evaporated and then partitioned between hexane and aqueous methanol, or dissolved in methanol and further fractionated by column chromatography (see paragraphs 40 – 46 of D1).

D2 describes methods of preparing “substantially pure” forms of cannabinoids from plant material. The method of D2 includes obtaining a plant extract, partially purifying the plant extract using chromatography, then further purifying the cannabinoids for dissolving in a first and then a second solvent, where the first and second solvents are different (see D2 page 5, lines 9 – 29). The product may be further purified by flash column chromatography. Preferably, the first solvent is CO₂ and the second solvent is an ethanolic precipitation (see D2 page 11, lines 33 – 39).

D3, the priority document of D2, describes methods of preparing “substantially pure” forms of cannabinoids from plant material. The method includes obtaining a plant extract, dissolving the extract in a solvent, removing the insoluble material (preferably by filtration), and evaporating the solvent from the solution (see D3 page 3, lines 25 – 31).

The claims of the present application, as amended, are distinguished from all three cited references, as the claims are directed to the material steps of the method using the transitional phrase “consisting essentially of”. For example, the claimed non-polar solvent is either hexane, pentane or petroleum ether, and is the same for both the first and second extraction, and the extraction steps are followed by crystallization of the solvent solutions to obtain the cannabinoid. Dependent claims include non-material steps such as filtration and liquid:liquid chromatography. It is evident that the amended claims are directed to features not disclosed in any of D1 – D3 and hence the Examiner’s objections should be withdrawn and novelty of all claims should be acknowledged.

Inventive Step

The Examiner has objected that claims 1 – 25 lack an inventive step over the disclosure of documents D1 – D3.

We do not agree with the Examiner’s conclusion and we note the subject matter of the amended claims is distinct from the disclosure of the cited prior art (as noted above under novelty).

The present invention addresses the problem of providing cost effective methods of making compositions having a low THC content, which are enriched in CBD/CBG. The claimed methods are cost effective and use the same solvent in two or more extraction and crystallisation steps that enrich for either CBD or CBG. Thus, the claimed methods solve this problem in a manner that is neither disclosed in nor obvious in light of the cited prior art.

Accordingly, the subject matter of the amended claims is inventive over documents D1 – D3.

Clarity

The Examiner has alleged that claims 1 and 11 lack clarity because they contain desiderata such as “in a manner that concentrates/crystallizes”.

Without agreeing with the Examiner’s findings, the applicant has amended the claims to address the Examiner’s concerns by removing the alleged desiderata.

Accordingly, the amended claims are clear.

We look forward to receiving a favourable IPRP in due course. However, if the Examiner is minded to issue an unfavourable report, a further written opinion is requested.

Yours faithfully,



CLEMENTS; Andrew Russell Niel

/kld

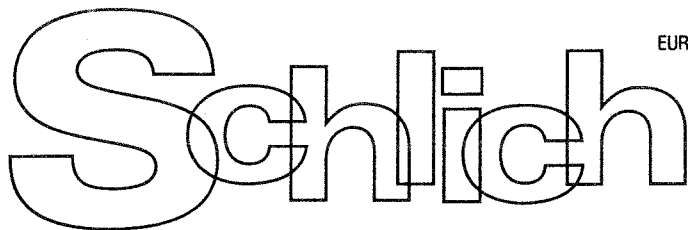
Enc. As listed above

CLAIMS

1. A method of purifying one or more cannabinoids from a plant material, the method consisting essentially of the following steps:
 - a) incubating the plant material with a non-polar solvent selected from the group consisting of petroleum ether, pentane and hexane to form a first solvent mixture which extracts the one or more cannabinoids from a plant material;
 - b) reducing the volume of the first solvent mixture to about 50% or less of the original volume of the first solvent mixture in step (a) thereby concentrating the one or more cannabinoids;
 - c) incubating the reduced first solvent mixture at a temperature range of between about -70°C to about 40°C to crystalize the one or more cannabinoids;
 - d) incubating the one or more crystalized cannabinoids with the non-polar solvent, wherein the non-polar solvent is the same non-polar solvent as in step (a) to form a second solvent mixture, thereby dissolving at least 50% of the one or more crystalized cannabinoids; and
 - e) incubating the second solvent mixture at a temperature range of between about -70°C to about 40°C to crystalize the one or more cannabinoids, thereby resulting in the purification of one or more cannabinoids.
2. The method according to claim 1, wherein the one or more crystalized cannabinoids of step (c) is recovered prior to step (d).
3. The method according to claim 2, wherein the recovery is performed using filtration that results in collection of a crystalline product and a mother liquor.
4. The method according to claim 3, further comprising incubating the mother liquor at a temperature range of between about -70°C to about 40°C to crystalize the one or more cannabinoids.
5. The method according to claim 4, further comprising
 - f) recovering the one or more crystalized cannabinoids using filtration that results in collection of a crystalline product and a mother liquor; and
 - g) incubating the mother liquor at a temperature range of between about -70°C to about 40°C in a manner that crystalizes the one or more cannabinoids.
6. The method according to claim 5, wherein steps (f) and (g) are repeated at least once.
7. The method according to any one of claims 1-6, wherein steps (d) and (e) or steps (b) and (c) are repeated at least once.
8. The method according to any one of claims 1-7, wherein the first solvent mixture of step (a) is purified prior to step (b) or (c).

9. The method according to any one of claims 1-8, wherein prior to step (a), the one or more cannabinoids present in the plant material are decarboxylated.
10. The method according to any one of claims 1-9, further comprising performing liquid:liquid chromatography after one or more of steps (b) or (d).
11. A method of purifying a cannabinoid from a plant material, the method consisting essentially of the following steps:
 - a) incubating the plant material with a solvent selected from the group consisting of pentane, hexane, heptane, cyclohexane, petroleum ethers, dicloromethane, trichloromethane, tetrahydrofurane, diethyl ether, ethanol, methanol, isopropanol, acetone, acetonitrile, ethyl acetate, butane, propane, refrigerant gas 1,1,1,2-Tetrafluoroethane (R134a), liquid CO₂, subcritical CO₂ or supercritical CO₂ or mixes of these solvents to form a first solvent mixture which extracts the one or more cannabinoids from a plant material;
 - b) filtering, decanting or centrifuging the first solvent mixture;
 - c) reducing the volume of the first solvent mixture to dryness thereby concentrating the one or more cannabinoids in a first extract;
 - d) incubating the first extract with a non-polar solvent selected from the group consisting of petroleum ether, pentane and hexane to form a second solvent mixture which extracts the one or more cannabinoids from the first extract;
 - e) filtering, decanting or centrifuging the second solvent mixture;
 - f) incubating the second solvent mixture at a temperature range of between about -70°C to about 40°C to crystallize the one or more cannabinoids;
 - g) collecting the one or more crystalized cannabinoids in step (d) using filtration that results in a collection of a crystalline product and a mother liquor;
 - h) incubating the one or more crystalized cannabinoids with the non-polar solvent wherein the non-polar solvent is the same non-polar solvent as in step (d) to form a third solvent mixture, wherein the third solvent mixture dissolves at least 50% of the one or more crystalized cannabinoids;
 - i) incubating the third solvent mixture at a temperature range of between about -70°C to about 40°C to crystallize the one or more cannabinoids; and
 - j) collecting the one or more crystalized cannabinoids of step (i) using filtration that results in a collection of a crystalline product and a mother liquor, thereby resulting in the purification of one or more cannabinoids
12. The method according to claim 11, wherein the mother liquor of step (g) and/or step (j) is incubated at a temperature range of between about -70°C to about 40°C to crystallize the one or more cannabinoids.

13. The method according to claim 12, further comprising
 - i) collecting the one or more crystalized cannabinoids using filtration that results in collection of crystals and a mother liquor; and
 - j) incubating the mother liquor at a temperature range of between about -70°C to about 40°C to crystalize the one or more cannabinoids.
14. The method according to claim 13, wherein steps (i) and (j) are repeated at least once.
15. The method according to any one of claims 11-14, wherein steps (h) and (i) are repeated at least once.
16. The method according to any one of claims 11-14, wherein steps (h) (i) and (j) are repeated at least once.
17. The method according to any one of claims 11-16, wherein the first solvent mixture of step (a) is purified prior to step (b).
18. The method according to any one of claims 11-17, wherein prior to step (a), the one or more cannabinoids present in the plant material are decarboxylated.
19. The method according to any one of claims 11-18, further comprising performing liquid:liquid chromatography after one or more of steps (c) (g) or (j).
20. The method of claims 1 or 11, wherein the non-polar solvent is petroleum ether or pentane and the cannabinoid is CBD.
21. The method of claims 1 or 11, wherein the non-polar solvent is hexane and the cannabinoid is CBG or CBGA.
22. The method of claim 1, wherein the second solvent mixture of step (d) is filtered or decanted after the crystals are dissolved, to remove insoluble material.
23. The method of claim 11, wherein the second solvent mixture of step (f) is filtered or decanted after the crystals are dissolved, to remove insoluble material.



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Via Online Filing

My ref: P40206WO
Date: 9 February 2017

Dear Sirs

International Patent Application No. PCT/EP2016/051388
"METHODS OF PURIFYING CANNABINOID,
COMPOSITIONS AND KITS THEREOF"
In the name of PhytoPlant Research S.L

We refer to the second Written Opinion of the International Preliminary Examining Authority dated 20 December 2016.

We file herewith an amended set of claims which is provided in both clean and marked-up versions to assist the Examiner. In view of the Examiner's refusal to enter the amendments filed on 14 November 2016, the marked-up version of the claims shows the changes relative to the originally-filed claims.

In the amended claims, claims 1 and 11 have been limited to recite a method consisting essentially of the recited steps (rather than comprising the recited steps). In particular, the recited steps for purifying a cannabinoid from a plant material involve the use of a non-polar solvent selected from petroleum ether, pentane and hexane, where the non-polar solvent is the same in the first and second extraction. Basis for this amendment can be found, for example, in paragraph 24 of the original application, which discloses the use of the specific solvents recited in the amended claims and further specifies that the solvent can be used in "any or all" of the extraction steps.

Claim 11 further includes an initial extraction step using the solvents listed in paragraph 52. Additional basis can be found in paragraph 204, which defines the transitional phrase "consisting essentially of". The closed-ended transitional phrase "consisting essentially of" limits the scope of a claim to the expressly recited elements, limitations, steps and/or features and any other elements, limitations and/or features that do not materially affect the basic and novel characteristic(s) of the claimed subject matter. In the case of the present invention, the basic and novel characteristics are two-fold: first, the use of one of petroleum ether, pentane and hexane, and second, the requirement that the same solvent be used in the first and second extraction steps.

Claim 3 has been amended to recite collection of a crystalline product, with basis at paragraphs 31 and 37, which describe filtration of the crystalized material to form a mother liquid. Additional basis is found at paragraph 11 and in the examples.

Claims 5, 6, 8-10, 13, 14 and 17-25 have been deleted and the remaining claims have been renumbered accordingly. New claims 10-13 have been added. New claims 20 and 21 have basis at paragraphs 24, 119, 135 and 152. New claims 22 and 23 have basis at paragraph 23, which discusses filtration of the second solvent solution.

As noted above, the present amendments have basis in the original application and do not add matter.

Clarity

The Examiner's objections in respect of clarity were raised in respect of the amendments filed on 14 November 2016, which were not entered. The following observations explain why these objections do not apply to the amendments filed herewith, and thus there is no impediment to the entry of these amendments.

The Examiner has alleged that the term "consisting essentially of" used in the independent claims (i.e. amended claims 1 and 6) is vague and unclear and leaves the reader in doubt as to the meaning of the technical feature to which it refers. However, we believe the Examiner is mistaken. In particular, we note that paragraph 204 of the original application defines the transitional phrase "consisting essentially of", which limits the scope of a claim to the expressly recited elements, limitations, steps and/or features and any other elements, limitations and/or features that do not materially affect the basic and novel characteristic(s) of the claimed subject matter. In the case of the present invention the basic and novel characteristics are two-fold, first the use of one of petroleum ether, pentane and hexane, and second, the requirement that the same solvent be used in the first and second extraction steps. Accordingly, contrary to the Examiner's allegation, there is no need for the skilled person to identify "which further steps are "essential" to the invention and which are not" – the transitional language in the independent claims is clear in terms of the materiality of the claimed steps. For example, claimed steps can be repeated, and steps before and after the process may be added, but the novel and inventive characteristics of the claimed subject matter rest in the sequence of steps recited in claims 1 and 6. These include the advantageous ease and cost effectiveness of the recited purification methods.

The Examiner has further alleged that some of the dependent claims had further steps, rendering the scope of those dependent claims broader than the scope of the independent claim they refer to. We do not agree with the Examiner on this point but, to advance the prosecution of this application, claims 5, 6, 8-10, 13, 14 and 17-19 have been deleted. The remaining dependent claims give rise to no difficulties in interpreting the independent claims to which they refer and the scope of the remaining dependent claims is entirely commensurate with the requirement that any further steps do not materially affect the basic and novel characteristics set out in the independent claims.

Accordingly, the Examiner's objections in respect of clarity do not apply to the presently amended claims.

Added Matter

Again, the Examiner's objections in respect of added matter concern the amendments filed on 14 November 2016, which were not entered. The following observations will confirm that these objections do not apply to the presently amended claims.

With regard to claims 1 and 11 filed on 14 November 2016, the Examiner has alleged that the feature that the solvents in step a) and d) should be the same "has never been disclosed in the application as filed". We do not agree with this finding.

In particular, paragraph 24 of the original application explicitly provides for the use of hexane in any one of or all of the extraction steps. Similarly, paragraph 24 explicitly provides for the use of pentane or petroleum ether as a solvent in one or more of the extraction and/or purification steps. Accordingly, there is no selection of solvent, and consequently no double selection of solvent, and using the same solvents in both steps, as alleged by the Examiner. Rather, the original application explicitly provides for using petroleum ether, pentane or hexane as the solvent in both step a) and step d) of independent claims 1 and 6 as presently amended.

Next, the Examiner has objected to the wording "reducing the volume of the first solvent to dryness" in claim 11 filed on 14 November 2016. The Examiner will note that this wording does not appear in independent claim 6 of the presently amended claim set. Rather, claim 6 includes the wording "reducing the volume of the first solvent mixture to about 50% or less of the original volume of the first solvent mixture", thereby using the same form of wording as was used in the originally-filed claims.

Next, the Examiner has alleged that the initial extraction step a) of claim 11 has only been mentioned for cannabinoid acids and only together with the use of acidified solvents. The Examiner has referred specifically to paragraph 52 of the specification.

We believe the Examiner is mistaken and that this objection is not applicable to presently amended claim 6. Closer reading of paragraph 52 will demonstrate that the use of acidified solvents is optional: "In embodiments wherein the method is to be used for the isolation of cannabinoid acids and acidified extraction solvent to prepare the initial extract may optionally be used to ensure the extraction of high levels of cannabinoid acids. Moreover, paragraph 50 of the specification discloses the use of the solvents recited in claim 6 step a) without limitation to embodiments in which the method is used to isolate cannabinoid acids (rather paragraph 50 merely refers to cannabinoids of interest, giving CBG, CBGA or CBD as examples). Thus, the initial extraction step of claim 6 is disclosed in the general context of purifying a cannabinoid from a plant material, and is not exclusively disclosed for the extraction of cannabinoid acids with the use of acidified solvents. Accordingly, this objection does not apply to amended claim 6.

The Examiner has further alleged that paragraph 190 discloses very specific conditions of an example and has alleged that claims 2, 3 and 5 filed on 14 November 2016 represent an unacceptable generalisation. Whilst we do not agree with this objection, the Examiner will note that claims 2 and 3 of the presently amended

claims use the original "purified" or "purification" language and that claim 5 has been deleted. Accordingly, this objection does not apply to the presently amended claims.

Finally, in respect of added matter, the Examiner has alleged that claims 22 and 23 filed on 14 November 2016 do not have adequate basis in paragraph 23 of the application. Whilst we do not agree with this allegation, the Examiner will note that claims 12 and 13 of the presently amended claim set refer only to filtering, not decanting, and therefore have explicit basis in paragraph 23 of the original application.

Accordingly, the added matter objections raised in the second Written Opinion do not apply to the presently amended claims.

Excluded Subject Matter

The Examiner's objection in respect of original claims 22-25 is moot in view of the deletion of those claims.

Novelty and Inventive Step

The applicant's submissions in respect of novelty and inventive step filed on 14 November 2016 apply equally to the presently amended claims, which are both novel and inventive over the cited prior art.

We would add that the Examiner is incorrect in making the further observation that "the effect mentioned by the applicant has never been mentioned in the application as filed and is therefore not plausible". The need for a simple and less expensive process that selectively purifies and concentrates medically beneficial cannabinoids from THC, thereby lowering THC content as a percentage of the cannabinoid mix is disclosed in paragraph 8 of the original application. Paragraph 41 confirms that the disclosed methods can achieve substantially pure preparations of one or more cannabinoids without the use of chromatographic steps and this is confirmed elsewhere in the original application (see e.g. paragraph 50). The examples also confirm that the methods of the invention permit the preparation of compositions having a low THC content and which are enriched in CBD/CBG. Thus, the advantages arising from the claimed methods are mentioned in the application as filed and are plausible.

Accordingly, novelty and inventive step should be acknowledged for all claims.

We look forward to receiving a favourable IPRP in due course.

Yours faithfully


Clements; Andrew Russell Niel
/g.m-g

Encs. Amended claims (clean and marked-up copies)

CLAIMS

1. A method of purifying one or more cannabinoids from a plant material, the method consisting essentially of the following steps:
 - a) incubating the plant material with a non-polar solvent selected from the group consisting of petroleum ether, pentane and hexane to form a first solvent mixture which extracts the one or more cannabinoids from a plant material;
 - b) reducing the volume of the first solvent mixture to about 50% or less of the original volume of the first solvent mixture in step (a) thereby concentrating the one or more cannabinoids;
 - c) incubating the reduced first solvent mixture at a temperature range of between about -70°C to about 40°C to crystalize the one or more cannabinoids;
 - d) incubating the one or more crystalized cannabinoids with the non-polar solvent, wherein the non-polar solvent is the same non-polar solvent as in step (a) to form a second solvent mixture, thereby dissolving at least 50% of the one or more crystalized cannabinoids; and
 - e) incubating the second solvent mixture at a temperature range of between about -70°C to about 40°C to crystalize the one or more cannabinoids, thereby resulting in the purification of one or more cannabinoids.
2. The method according to claim 1, wherein the one or more crystalized cannabinoids of step (c) is purified prior to step (d).
3. The method according to claim 2, wherein the purification is performed using filtration that results in collection of a crystalline product and a mother liquor.
4. The method according to claim 3, further comprising incubating the mother liquor at a temperature range of between about -70°C to about 40°C to crystalize the one or more cannabinoids.
5. The method according to any one of claims 1-4, wherein steps (d) and (e) or steps (b) and (c) are repeated at least once.
6. A method of purifying a cannabinoid from a plant material, the method consisting essentially of the following steps:
 - a) incubating the plant material with a solvent selected from the group consisting of pentane, hexane, heptane, cyclohexane, petroleum ethers, dicloromethane, tricloromethane, tetrahydrofurane, diethyl ether, ethanol, methanol, isopropanol, acetone, acetonitrile, ethyl acetate, butane, propane, refrigerant gas 1,1,1,2-Tetrafluoroethane (R134a), liquid CO₂, subcritical CO₂ or supercritical CO₂ or mixes of these solvents to form a first solvent mixture which extracts the one or more cannabinoids from a plant material;
 - b) filtering, decanting or centrifuging the first solvent mixture;
 - c) reducing the volume of the first solvent mixture to about 50% or less of the original volume of

- the first solvent mixture in step (a) thereby concentrating the one or more cannabinoids in a first extract;
- d) incubating the first extract with a non-polar solvent selected from the group consisting of petroleum ether, pentane and hexane to form a second solvent mixture which extracts the one or more cannabinoids from the first extract;
 - e) filtering, decanting or centrifuging the second solvent mixture;
 - f) incubating the second solvent mixture at a temperature range of between about -70°C to about 40°C to crystalize the one or more cannabinoids;
 - g) collecting the one or more crystalized cannabinoids in step (d) using filtration that results in a collection of a crystalline product and a mother liquor;
 - h) incubating the one or more crystalized cannabinoids with the non-polar solvent wherein the non-polar solvent is the same non-polar solvent as in step (d) to form a third solvent mixture, wherein the third solvent mixture dissolves at least 50% of the one or more crystalized cannabinoids;
 - i) incubating the third solvent mixture at a temperature range of between about -70°C to about 40°C to crystalize the one or more cannabinoids; and
 - j) collecting the one or more crystalized cannabinoids of step (i) using filtration that results in a collection of a crystalline product and a mother liquor, thereby resulting in the purification of one or more cannabinoids
7. The method according to claim 6, wherein the mother liquor of step (g) and/or step (j) is incubated at a temperature range of between about -70°C to about 40°C to crystalize the one or more cannabinoids.
 8. The method according to any one of claims 6-7, wherein steps (h) and (i) are repeated at least once.
 9. The method according to any one of claims 6-7, wherein steps (h) (i) and (j) are repeated at least once.
 10. The method of claims 1 or 6, wherein the non-polar solvent is petroleum ether or pentane and the cannabinoid is CBD.
 11. The method of claims 1 or 6, wherein the non-polar solvent is hexane and the cannabinoid is CBG or CBGA.
 12. The method of claim 1, wherein the second solvent mixture of step (d) is filtered after the crystals are dissolved, to remove insoluble material.
 13. The method of claim 6, wherein the second solvent mixture of step (f) is filtered after the crystals

are dissolved, to remove insoluble material.

REIVINDICACIONES

1. Un método de purificación de uno o más cannabinoides a partir de material vegetal. El método consiste esencialmente en los siguientes pasos:

a) incubar el material vegetal con un disolvente no polar seleccionado del grupo que un grupo compuesto de éter de petróleo, pentano y hexano para formar una primera mezcla disolvente que extrae uno o más cannabinoides de un material vegetal;

b) reducir el volumen de la primera mezcla disolvente a aproximadamente un 50 % o menos del volumen original de la primera mezcla disolvente en el paso (a) de manera que concentre el uno o más cannabinoides;

c) incubar la primera mezcla disolvente reducida en un rango de temperatura entre aproximadamente -70°C a aproximadamente 40°C para cristalizar el uno o más cannabinoides;

d) incubar el uno o más cannabinoides cristalizados con el disolvente no polar, en el que el disolvente no polar es el mismo disolvente no polar del paso (a) para formar una segunda mezcla de disolventes, disolviendo de este modo por lo menos el 50% del uno o más cannabinoides cristalizados; y

e) incubar la segunda mezcla disolvente en un rango de temperatura de entre aproximadamente -70 °C a aproximadamente 40 °C para cristalizar el uno o más cannabinoides, dando como resultado la purificación de uno o más cannabinoides.

2. El método conforme a la reivindicación 1, donde el uno o más cannabinoides cristalizados del paso (e) se purifica antes del paso (d).

3. El método conforme a la reivindicación 2, donde la purificación se lleva a cabo utilizando la filtración que da lugar a recolectar un producto cristalino y un licor madre.

4. El método conforme a la reivindicación 3, que comprende además la incubación del licor madre en un rango de temperaturas de entre aproximadamente -70°C a aproximadamente 40°C para cristalizar el uno o más cannabinoides.

5. EL método de acuerdo con cualquiera de las reivindicaciones 1 a 4 a 4, en donde los pasos (d) y (e) o los pasos (b) y (e) se repiten al menos una vez.

6. Un método de purificación de un cannabinoide a partir de material vegetal. El método consiste esencialmente en los siguientes pasos:

a). incubar el material vegetal con un disolvente seleccionado del grupo que consiste en pentano, hexano, heptano, ciclohexano, éteres de petróleo, diclorometano, triclorometano, tetrahidrofurano, éter dietílico, etanol, metanol, isopropanol, acetona, acetonitrilo, acetato de etilo, butano, propano , gas refrigerante 1,1,1,2-tetrafluoroetano (R134a), CO2 líquido, CO2 subcrítico o CO2 supercrítico o mezclas de estos disolventes para formar una primera mezcla disolvente la cual extrae uno o más cannabinoides de un material vegetal;

- b) filtrar, decantar o centrifugar la primera mezcla de disolventes;
 - c) reducir el volumen de la primera mezcla disolvente a aproximadamente un 50 % o menos del volumen original de la primera mezcla disolvente en el paso (a) de manera que concentre el uno o más cannabinoides;
 - d) incubar el primer extracto con un disolvente no polar seleccionado del grupo que un grupo compuesto de éter de petróleo, pentano y hexano para formar una segunda mezcla disolvente que extrae uno o más cannabinoides del primer extracto;
 - e) filtrar, decantar o centrifugar la segunda mezcla disolvente;
 - f) incubar la segunda mezcla disolvente en un rango de temperatura entre aproximadamente -70°C a aproximadamente 40°C para cristalizar el uno o más cannabinoides;
 - g) recolectar el uno o más cannabinoides cristalizados en el paso (d) usando la filtración que da lugar a recolectar un producto cristalino y un licor madre;
 - h) incubar el uno o más cannabinoides cristalizados con el disolvente no polar, en el que el disolvente no polar es el mismo disolvente no polar del paso (d) para formar una tercera mezcla de disolventes, en donde la tercera mezcla disolvente disuelve al menos 50% del uno o más cannabinoides cristalizados;
 - i) incubar la tercera mezcla disolvente en un rango de temperatura entre aproximadamente -70°C a aproximadamente para cristalizar el uno o más cannabinoides; y
 - j) recolectar el uno o más cannabinoides cristalizados del paso (i) utilizando la filtración que da lugar a recolectar un producto cristalino y un licor madre, de esto modo dando como resultado la purificación de uno o más cannabinoides.
7. El método de acuerdo con la reivindicación 6, donde el licor madre del paso (g) y/o el paso (j) se incuba en un rango de temperaturas de entre aproximadamente -70°C a aproximadamente 40°C para cristalizar el uno o más cannabinoides.
8. El método de acuerdo con cualquiera de las reivindicaciones 6 a 7, donde los pasos (h) e (i) se repiten al menos una vez.
9. El método de acuerdo con cualquiera de las reivindicaciones 6 a 7, donde los pasos (h), (i) y (j) se repiten al menos una vez.
10. El método de las reivindicaciones 1 o 6, donde el solvente no polar es éter de petróleo o pentano y el cannabinoide es CBD.
11. El método de las reivindicaciones 1 o 6, donde el solvente no polar es hexano y el cannabinoide es CBG o CBGA.
12. El método de la reivindicación 1, donde la segunda mezcla disolvente del paso (d) se filtra después de disolver los cristales para remover material insoluble.

13. El método de la reivindicación 6, donde la segunda mezcla disolvente del paso (f) se filtra después de disolver los cristales para remover material insoluble.