

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No. PCT/EP2019/052069	International filing date (day/month/year) 29.01.2019	Priority date (day/month/year) 29.01.2018
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International Patent Classification (IPC) or both national classification and IPC
INV. C07C37/72 C07C37/00 C07C39/23 C07C39/19 C07C51/48 C07C65/19 C07D311/80 B01D11/02 B01D11/04 B01D15/18

Applicant
PHYTOPLANT RESEARCH S.L

1. This opinion contains indications relating to the following items:
- ☒ Box No. I Basis of the opinion
 - ☐ 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 Rule 43bis.1(a)(i) 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

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA:  European Patent Office P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Fax: +31 70 340 - 3016	Date of completion of this opinion see form PCT/ISA/210	Authorized Officer Kardinal, Siegmarr Telephone No. +31 70 340-0 
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Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:
 - ☒ 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)).
2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))
3. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:
 - a. ☐ forming part of the international application as filed:
 - ☐ in the form of an Annex C/ST.25 text file.
 - ☐ on paper or in the form of an image file.
 - b. ☐ furnished together with the international application under PCT Rule 13ter.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
 - c. ☐ furnished subsequent to the international filing date for the purposes of international search only:
 - ☐ in the form of an Annex C/ST.25 text file (Rule 13ter.1(a)).
 - ☐ on paper or in the form of an image file (Rule 13ter.1(b) and Administrative Instructions, Section 713).
4. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	<u>2-5, 7-9, 14-18, 22-25, 27</u>
	No: Claims	<u>1, 6, 10-13, 19-21, 26</u>
Inventive step (IS)	Yes: Claims	
	No: Claims	<u>1-27</u>
Industrial applicability (IA)	Yes: Claims	<u>1-27</u>
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

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

Re Item V

Reference is made to the following documents:

- D1 US 2018/000879 A1 (NADAL ROURA XAVIER) 4 January 2018
- D2 WO 2016/187679 A1 (POBELCH - GLE OOD) 1 December 2016
- D3 WO 2016/135346 A1 (BIONORICA ETHICS GMBH) 1 September 2016
(cited in the application)

1 Novelty (Article 33(2) PCT)

- 1.1 Claim 1 is worded as a "method consisting essentially of the following steps: (a) [...], (b) [...]; and (c) [...]." The intended limitation as to the presence of further steps is not clear (see Item VIII, 1). In this situation, the claim scope is construed broadly such that further steps such as concentrating the liquid and purifying the product before liquid-liquid chromatography (c) are deemed to be encompassed.

- 1.2 D1 discloses (cf. examples 1, 10; paragraph [0062]) a method for purifying one or more cannabinoids from a plant material, including a step of countercurrent chromatography.

Example 1 of D1 is a method of isolating and purifying CBGA from Cannabis sativa L including incubating plant material with hexane and countercurrent chromatography using a two-phase system Hexane:Ethanol:Water (20:12:8).

The fact that the volume of hexane is reduced in the method of D1 from the original 750 ml to about 100 ml before the liquid-liquid chromatography and the solvent mixture is thereby purified by crystallization is covered by the scope of the present claims (see e.g. claims 11 and 12, and Item VIII, 1). It is not a differentiating feature. In any, case, the process of present claim 1 can start from any plant material including plant extracts.

Example 10 of D1 discloses an analogous process which includes a step of decarboxylating the the product such as to obtain CBG.

These processes of D1 fall within the scope of at least present claims 1, 6, 10-13, 19-21 and 26. The subject-matter of at least these claims is not novel.

2 Inventive step (Article 33(3) PCT)

- 2.1 Dependent claims 2-5, 7-9, 14-18, 22-25 and 27 do not appear to contain any additional features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step, the reasons being as follows:

Starting from document D1 as closest prior art, the features of these dependent claims may be considered to be the differentiating features. For none of these differentiating features a particular technical effect has been substantiated by means of suitable comparative examples. In each case, the objective technical problem can only be formulated as the provision of an alternative method for purifying one or more cannabinoids.

- 2.2 The use of countercurrent chromatography and centrifugal partitioning chromatography for the purification of cannabinoids is known to the skilled person from the prior art, e.g. D1 (cf. [0058] and the examples), D2 and D3 (cf. the passages indicated in the search report). Solvent systems including hexane, ethanol, acetonitrile, ethyl acetate, water and similar solvents are known (cf. D1, [0061]; D2, examples and D3, cf. the claims). It appears routine work for the person skilled in the art to choose suitable solvents for isolating THC-type extracts or CBD-type extracts. When doing so, the skilled person would consider using pentane (the lower homolog of hexane) in case of concerns about the toxicity of hexane and according to the circumstances. The skilled person would thereby routinely arrive at solvent systems according to present claims 2 to 5, 25 and 27 in the expectation to provide an alternative purification method.
- 2.3 Concerning claims 7 to 9, Chemotypes I to IV of *Cannabis sativa* L and their main cannabinoids are known (see e.g. D1, [0045]). The skilled person would use them as starting materials depending on desired products.
- 2.4 The precipitation of unwanted components after extraction using suitable solvents and temperatures according to dependent claim 14 appears to be routine work when extracting plant material.
- 2.5 Concerning dependent claims 15, 16, 22, 23 the skilled person would routinely choose suitable known equipment and conditions according to the circumstances.
- 2.6 Concerning claims 17, 18 and 24, it is routine work of the skilled artisan to perform suitable further purification steps, including chromatographic purification (e.g. HPLC) or crystallisation in order to enhance the purity of the target compounds if desired and according to the circumstances.

Re Item VII

- 1 The description contains statements concerning the incorporation of priority or prior art documents by reference (see e.g. [1], [144]).
- 2 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in D1 is not mentioned in the description, nor is this document identified therein.
- 3 The list of "Aspects" expressed on pages 27 to 38 constitutes superfluous content and should be removed.

Re Item VIII

Clarity and support (Article 6 PCT)

- 1 The scope of claim 1 is not clear. The wording of claim 1 is a method "consisting essentially of" steps (a), (b) and (c). However, different additional steps such as reducing the solvent volume/drying (see claim 11), purification (see claims 12, 14) and chemical modification (see claim 13) are subject of the dependent claims. It appears thus that at least such additional steps can be present in the process of claim 1. It is not clear how the term "consisting essentially of" is to be construed. In this regard, the also definition given in the description (cf. [143]) as including "any other elements, limitations, steps and/or features that do not materially affect the basic and novel characteristic(s) of the claimed subject matter" is not particularly helpful.
- 2 The terms "Quantum CPC", "CPC PRO" and "CPC 1000 PRO" employed in the claims and appearing to be a registered trade marks have no precise meaning as they do not appear to be internationally accepted as a standard descriptive terms, thereby rendering the definition of the subject-matter of the claims unclear.
- 3 For the sake of clarity of the claims, the acronyms THC, THCV, THCA, CBD, CBDV, CBDA, CBGV, CBG, CBGA expressed in the claims should be defined at least once in the claims using the chemical name, e.g. tetrahydrocannabinol (THC) etc, see paragraph [27] of the description. This includes expressions like "CBG-type" which should at least once be written as "cannabigerol-type (CBG-type)" as indicated in paragraph [55] of the description.

- 4 The vague and imprecise statements in the description in paragraphs [136], [137], [139] implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity (Article 6 PCT) when used to interpret them.