PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.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.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IB2018/055866	03.08.2018	04.08.2017

International Patent Classification (IPC) or both national classification and IPC
INV. A61K36/00 A61P1/04

Applicant
NEILOS S.R.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 43*bis*.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 notifed the International Bureau under Rule 66.1*bis*(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:	Date of completion of this opinion	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Fax: +49 89 2399 - 4465	see form PCT/ISA/210	Zellner, Eveline Telephone No. +49 89 2399-0

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/IB2018/055866

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 43*bis*.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 13*ter*.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 13*ter*.1(a)).

      ☐ on paper or in the form of an image file (Rule 13*ter*.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 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-10
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-10
Industrial applicability (IA)	Yes:	Claims	1-10
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 Reference is made to the following documents and the passages identified in the International Search Report; the numbering will be adhered to in the rest of the procedure:

D1 DATABASE EMBASE [Online]
ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL; 1964,
SANYAL A K ET AL: "Studies on peptic ulceration. I. Role of banana in fhenylbutazone induced ulcers",
XP002780537,
Database accession no. EMB-0008618024 ; &
ARCH.INT.PHARMACODYN. 1964,
vol. 149, no. 3, 1964, pages 393-400,

D2 BEST R ET AL: "THE ANTI ULCEROGENIC ACTIVITY OF THE UNRIPE PLANTAIN BANANA MUSA-SPP",
BRITISH JOURNAL OF PHARMACO, WILEY-BLACKWELL, UK,
vol. 82, no. 1, 1 January 1984 (1984-01-01), pages 107-116,
XP009150633,
ISSN: 0007-1188

D3 MOHAN KUMAR ET AL: "Healing effects of Musa sapientum var. paradisiaca in diabetic rats with co-occurring gastric ulcer: cytokines and growth factor by PCR amplification",
BMC COMPLEMENTARY AND ALTERNATIVE MEDICINE, BIOMED CENTRAL LTD., LONDON, GB,
vol. 13, no. 1, 5 November 2013 (2013-11-05), page 305, XP021166136,
ISSN: 1472-6882, DOI: 10.1186/1472-6882-13-305

D4 EP 3 124 048 A1 (NEILOS S R L [IT]) 1 February 2017 (2017-02-01)

D5 CA 2 656 220 A1 (LYCORED LTD [IL]) 3 January 2008 (2008-01-03)

D6 EP 2 208 500 A1 (BIONAP S R L [IT]) 21 July 2010 (2010-07-21)

D7 WO 99/03486 A1 (WARNER LAMBERT CO [US]) 28 January 1999 (1999-01-28)

D1 refers to the effect of sun-dried unripe banana powder as studied in the prevention and healing of PBZ-induced gastric ulcers in guinea pigs.

D2 refers to results showing that various preparations of dried powdered unripe plantain banana possess anti-ulcerogenic activity against aspirin-induced gastric ulceration in the rat; Modern studies on the anti-ulcerogenic activity of banana were stimulated by the discovery that the ripe fruit banana contains high levels of 5-HT; banana emulsions introduced directly into the stomach reduced gastric secretion and ulceration induced by repeated injections of histamine;

D3 refers to extract of Musa sapientum fruit (MSE) showing better gastric ulcer healing effects.

D4 refers to a composition comprising a mixture of a salt of an alginate with an alkali metal; a salt of a carbonate with an alkaline earth metal; a salt of a bicarbonate with an alkali metal; a digestive enzyme; and liquorice (Glycyrrhiza glabra) in the form of a liquid extract or dry extract for use in gastoesophageal reflux;

D5 refers to extract is from a species of Conyza Less and antacid hydroxide or bicarbonate for use in the treatment of Gastro Esophageal Reflux Disease.

D6 refers to compositions comprising Opuntia ficus indicacladodes extract in combination with antacid agents (e.g. bicarbonate) useful in the therapy of the upper gastrointestinal tract.

D7 refers to a composition extracted from papaya, comprising one or more proteolytic enzymes, including but not limited to, papain, chymopapain and papaya proteinase for reducing gastric acidity further comprising an antacid such as calcium carbonate and magnesium hydroxide;

2 Novelty - Art. 33 (2) PCT

The present claims 1 - 10 are novel in view of the cited documents, as none of said documents describes a combination of an extract of fruit of a plant of the genus Musa i.e. banana in combination with an antacid and a protease.

3 Inventive step - Art. 33 (3) PCT

D1, D2 or D3 represent the closest prior art documents both teaching that banana fruit extract is used for the treatment of gastric disease by reducing gastric acid secretion.

The essential feature distinguishing the subject-matter of the present set of claims from D1, D2 or D3 is that antacid and protease digestive enzyme is added to the fruit extract of Musa in the present application.

No effects have been demonstrated in the present application. In the examples merely lists of compounds are given without showing a true effect or synergistic effect.

Therefore the problem is defined as the provision of a further composition for use in the treatment of gastric diseases.

The use of fruit extracts of Musa in combination with antacid and digestive enzyme is arbitrary as no result has been shown. Thus the solution is considered obvious in view of D1, D2 or D3 in combination with D4 to D7 already teaching the combination of plant extracts, antacids and digestive enzymes for use in the treatment of gastric acid disease.

Therefore the subject-matter of Claims 1-10 does not involve an inventive step.