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**Datasheet for the decision
of 5 November 2018**

Case Number: T 2202/14 - 3.3.01

Application Number: 06829580.7

Publication Number: 1962877

IPC: A61K36/48, A23L1/305, A23L1/30

Language of the proceedings: EN

Title of invention:
ETHANOL-PRECIPILATED PHASEOLUS VULGARIS EXTRACTS, THEIR USE
AND FORMULATIONS

Applicant:
Indena S.p.A.

Headword:
Phaseolus vulgaris extracts as appetite suppressants

Relevant legal provisions:
EPC Art. 56

Keyword:
Inventive step - non-obvious alternative

Decisions cited:
T 0184/82, T 0386/89

Catchword:



Beschwerdekammern
Boards of Appeal
Chambres de recours

Boards of Appeal of the
European Patent Office
Richard-Reitzner-Allee 8
85540 Haar
GERMANY
Tel. +49 (0)89 2399-0
Fax +49 (0)89 2399-4465

Case Number: T 2202/14 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 5 November 2018

Appellant: Indena S.p.A.
(Applicant) Via Ortles, 12
20139 Milano (IT)

Representative: Minoja, Fabrizio
Bianchetti Bracco Minoja S.r.l.
Via Plinio, 63
20129 Milano (IT)

Decision under appeal: **Decision of the Examining Division of the
European Patent Office posted on 20 June 2014
refusing European patent application No.
06829580.7 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman A. Lindner
Members: G. Seufert
P. de Heij

Summary of Facts and Submissions

- I. The applicant (appellant) lodged an appeal against the decision of the examining division refusing European patent application No. 06 829 580.7.

The present decision refers to the following documents:

- D1 F. M. Lajolo, F. F. Finardi, *Ciãnc. Tecnol. Aliment.*, 1984, vol. 4, no. 1, pages 1 to 11
D2 J. R. Powers, J. R. Whitacker, *Journal of Food Biochemistry*, 1977, vol. 1, pages 217 to 238
D4 V. Le Berre-Anton *et al.*, *Biochimica et Biophysica Acta*, 1997, vol. 1343, pages 31 to 40
D12 M. A. Tormo *et al.*, *British Journal of Nutrition*, 2004, vol. 92, pages 785 to 790
D13 J. C. Rodhouse *et al.*, *Epidemiol. Infest.*, 1990, vol. 105, pages 485 to 491

- II. The decision under appeal is based on the set of claims submitted with letter dated 28 April 2014.

The examining division held that the subject-matter of claims 1, 4 and 5 (product and use claims) lacked an inventive step in view of document D12. According to the examining division, the problem to be solved was considered to be the provision of an alternative extract. The provision of an alternative and less pure product was considered as a straightforward measure for the skilled person. The subject-matter of claims 2 and 3 (method claims) were held to be obvious in view of documents D1 or D2.

- III. With the statement of grounds of appeal, the appellant resubmitted the set of claims underlying the decision under appeal as its sole request.

Independent claims 1, 2 4 and 5 read as follows:

"1. Extract obtainable by extraction from *Phaseolus vulgaris* seeds with mixtures of ethanol and water, characterised by an α -amylase inhibitor content in between 1,000 and 1,600 USP/mg (HPLC titre between 6 and 14% w/w) and a phytohaemagglutinin content in between 8,000 and 30,000 HAU/g."

"2. Process for the preparation of the extract claimed in claim 1, which comprises:

- a) Extraction of *Phaseolus vulgaris* seeds with aqueous buffers having a pH ranging between 3 and 6.5, and subsequent separation of the extract from the biomass, which can be further extracted with the buffer if required until the α -amylase inhibitors and phytohaemagglutinins are exhausted;
- b) Filtration or centrifugation of the combined extracts, and concentration to a volume corresponding to approx. 10% of the weight of the extract after centrifugation;
- c) Differential precipitation of the concentrated aqueous extract with diluted ethanol, at a final alcohol concentration of between 60 and 70% v/v;
- d) Separation of precipitate and re-precipitation from demineralised water with 60% ethanol, or diafiltration through a membrane with a 10,000 Da cut-off, and drying of precipitation residue."

"4. Use of the extracts claimed in claim 1 to prepare a composition useful as appetite suppressants."

"5. Pharmaceutical and diet formulations comprising as active ingredient the extracts claimed in claim 1 at

doses ranging between 50 and 1.000 mg and physiologically acceptable adjuvant(s) and/or carrier(s)."

- IV. In a communication issued in preparation for oral proceedings the board expressed its preliminary opinion and indicated the issues that may require discussion, in particular whether the synergistic effect relied on by the appellant had been sufficiently demonstrated.
- V. The appellant's arguments as far as they relate to the decisive issues of the present decision can be summarised as follows:

Although phytohaemagglutinin was a potentially harmful compound, the claimed extracts with phytohaemagglutinin amounts within the specified range were safe to administer. None of the animals which had been treated with the claimed extract showed any sign of being sick, in particular too sick to eat or drink. The reduced intake of water was associated with a reduced need of fluids due to the decreased food intake associated with the treatment.

Document D12 was a suitable starting point for the assessment of inventive step. The difference between D12 and the presently claimed subject-matter was the α -amylase content and the phytohaemagglutinin content, expressed in terms of titre and/or activity. Phytohaemagglutinin was not present in the extract of D12. The problem to be solved was the provision of an improved extract. As apparent from the experimental evidence provided with letter dated 27 September 2010, phytohaemagglutinin acted in a synergistic manner with α -amylase. The effect on food intake reduction obtained by administering the same amount of an extract

containing both α -amylase and phytohaemagglutinin was higher than the sum of the effects obtained by administering separately the same amount of an extract with either α -amylase or phytohaemagglutinin alone. This functional interaction was surprising, as phytohaemagglutinin was known to be an undesired impurity, which was usually eliminated. Moreover, a comparison of examples A) and B) of the aforementioned experimental evidence clearly showed an improvement in the food intake reduction with the claimed extract. This effect could be taken into account in the formulation of the problem to be solved. According to the jurisprudence of the boards of appeal, the applicant may be allowed to put forward a modified version of the problem, in particular if, as was presently the case, new prior art existed, which came closer to the invention than that considered in the application. Reference was made to T 184/82 and T 386/89.

Even if the problem were to be considered as the provision of an alternative, the claimed solution would not have been obvious for the person skilled in the art. There was no pointer in the prior art to the presently claimed extracts. The presence of phytohaemagglutinin in an α -amylase extract was undesirable. It was removed and discarded. The prior art therefore taught away from the claimed extract, which was not only sufficiently active, but also safe to administer.

- VI. The appellant requested that the decision under appeal be set aside and a patent be granted on the basis of the set of claims filed with the statement of the grounds of appeal.

Reasons for the Decision

1. The appeal is admissible.

Sole request

2. The examining division had no objections under Article 123(2) and 54 EPC. The board has no reason to deviate from the examining division's findings. The examining division's initial clarity objection against the units USP/mg and HAU/g has not been maintained in view of the evidence provided filed with the applicant's letter dated 28 April 2014.
3. Inventive step (Article 56 EPC)
 - 3.1 Claim 1 of the sole request is directed to an extract from *Phaseolus vulgaris* seeds with a certain α -amylase inhibitor and phytohaemagglutinin content. Claims 2, 4 and 5 are directed to a method for the preparation of such an extract, its use in the preparation of a composition suitable as appetite suppressant and pharmaceutical and diet formulations comprising the extracts according to claim 1 as active ingredient (see point III above).

According to page 1, lines 4 to 8 of the description, the extract reduces absorption of glucose originating from starches in the diet and reduces appetite after repeated administration. Therefore, it is useful in preventing and treating undesired body weight gains and disorders related thereto.

- 3.2 In the decision under appeal, the examining division has selected document D12 as the closest prior art. The

board has no reason to deviate from the examining division's choice. It was also not contested by the appellant.

Document D12 describes the extraction and purification of an α -amylase inhibitor from *Phaseolus vulgaris* seeds (see page 785, right-hand column, line 6 to page 786, left-hand column, line 20) resulting in an α -amylase inhibitor without any detectable amounts of phytohaemagglutinin (kidney bean lectin, see page 788, right-hand column, lines 1 to 5). Document D12 also discloses a significant reduction in daily food intake (appetite suppressing) after administration of the purified α -amylase inhibitor extract, thereby confirming the long known anorexogenic effect (see table 1 on page 788 and page 788, right-hand column, last paragraph to page 789, line 10).

Phytohaemagglutinin is an undesirable and potentially harmful substance. A high content has been associated with incidents of kidney bean poisoning in the UK (see D13).

- 3.3 At the oral proceedings before the board, the appellant formulated the problem to be solved as the provision of an improved α -amylase inhibitor extract. The proposed solution was the claimed extract with its particular content of α -amylase inhibitor and phytohaemagglutinin.
- 3.4 The board doubts whether the alleged improvement has been conclusively demonstrated. However, since the board comes to the conclusion that the less ambitious problem, that is the provision of a further appetite suppressing extract which can safely be administered, is plausibly solved (see point 3.5 below) and that the extract according to claim 1 of the appellant's sole

request is not obviously derivable from the prior art (see points 3.6 to 3.9 below), there is no need to further consider whether the alleged improvement has been plausibly demonstrated.

3.5 The appellant has provided experimental evidence that an extract according to the invention reduces the food intake (see example A) of the appellant's experimental evidence). Furthermore, there is no conclusive evidence that the claimed extract with a phytohaemagglutinin content of 18,600 HAU/g is harmful or toxic. According to the appellant, the observed reduction in water intake, which was not observed in D12, was attributed to the reduced need of fluids due to the decreased food intake. It was not an indication that the extract was in any way unsafe. None of the treated rats had shown any signs of sickness, when treated with the extract according to example 2 of the invention. The appellant also confirmed that additional experiments showed that safe administration was possible, if the phytohaemagglutinin content was kept within the claimed range. In the absence of any conclusive evidence to the contrary, the board is not in a position to contest the appellant's assertion and therefore considers that the aforementioned technical problem (see point 3.4 above) is solved.

3.6 It remains to be examined whether the proposed solution is obvious.

According to the examining division, the provision of an alternative, less pure extract was a straightforward measurement. The skilled person could simply leave out the ion exchange column and use the crude extract as an appetite suppressant.

- 3.7 The board is not convinced. It cannot be denied that a less pure extract could be obtained by simply leaving out the purification step(s) via ion exchange column (i.e. the chromatographic step(s)) in the process according to D12. The board, however, sees no motivation for the person skilled in the art to omit this/these step/steps. As mentioned before (see point 3.2 above) phytohaemagglutinin is an undesired impurity. As a potentially harmful substance, it is conventionally eliminated from the extract (see for example D1, D2 and D12). Moreover, crude extracts of *Phaseolus vulgaris* seeds were known to be unsuccessful as appetite suppressants due to their low inhibitor content and the presence of undesired impurities (see D12, page 785, left-hand column, lines 9 to 15; D4, page 31, right-hand column, lines 9 to page 32, left-hand column, line 4). Hence, starting from D12 and faced with the technical problem as formulated in point 3.4 above, the skilled person, who has at his disposal an effective and highly pure α -amylase extract, which can safely be administered, would not be motivated to omit the chromatographic step(s).
- 3.8 Document D1 and D2 also disclose the preparation of α -amylase extracts. Like in D12 the focus lies on the preparation of a purified extract, from which the undesirable phytohaemagglutinin and other unwanted impurities are eliminated. Similar to document D12, the extract preparation according to D1 and D2 includes chromatographic steps and the steps preceding these steps are different compared to the preparation of the presently claimed extract. The board is therefore of the opinion that, similar to point 3.7 above, none of documents D1 and D2 provides the skilled person with a motivation to omit the chromatographic step(s).

3.9 For the aforementioned reasons, the board concludes that the subject-matter of claim 1 of the sole request complies with the requirement of Article 56 EPC. The same applied to claims 2, 4 and 5 directed the preparation of the abstract, its use as appetite suppressant and formulations comprising the extract (claims 2, 4 and 5).

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The case is remitted to the examining division with the order to grant a patent in the following version:

Description: pages 1-7 as originally filed;

Claims: claims 1-5 as filed with the statement of the grounds of appeal.

The Registrar:

The Chairman:



M. Schalow

A. Lindner

Decision electronically authenticated