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D E C I S I O N
of 27 January 2005

Case Number: T 0543/04 - 3.3.4

Application Number: 98917372.9

Publication Number: 0973534

IPC: A61K 35/78

Language of the proceedings: EN

Title of invention:

Pharmaceutical compositions having appetite suppressant activity

Applicant:

CSIR

Opponent:

-

Headword:

Appetite suppressant/CSIR

Relevant legal provisions:

EPC Art. 56

Keyword:

"Inventive step - (yes) "

Decisions cited:

G 0001/03, G 0002/03

Catchword:

-



Case Number: T 0543/04 - 3.3.4

D E C I S I O N
of the Technical Board of Appeal 3.3.4
of 27 January 2005

Appellant:
(Applicant)

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Decision under appeal:

Decision of the Examining Division of the
European Patent Office posted 3 December 2003
refusing European application No. 98917372.9
pursuant to Article 97(1) EPC.

Composition of the Board:

Chairwoman: U. Kinkeldey
Members: M. Wieser
R. Moufang

Summary of Facts and Submissions

- I. The appeal was lodged by the Applicants (Appellants) against the decision of the Examining Division to refuse under Article 97(1) EPC the patent application EP 98 917 372.9, publication number EP-A-0 973 534 (international publication number WO-A-98/46 243). The patent application has the title: "Pharmaceutical compositions having appetite suppressant activity".
- II. The Examining Division decided that the claims of a first and a second auxiliary request before them were not novel (Article 54 EPC) or not inventive (Article 56 EPC), respectively. The main request had been withdrawn by the Applicants.

Moreover, the Examining Division decided that the claims of the third auxiliary request before them did not involve an inventive step (Article 56 EPC) in the light of document

(1) Bot.Jahrb.Syst., vol. 115, no. 2, 1993, pages 145 to 270.

- III. Claim 1 of the third auxiliary request read:

"Use of a composition comprising as an active ingredient an extract from a plant of the genus *Trichocaulon* or the genus *Hoodia*, which extract comprises an appetite suppressant agent for the manufacture of a pharmaceutical composition for preventing, treating and combating obesity."

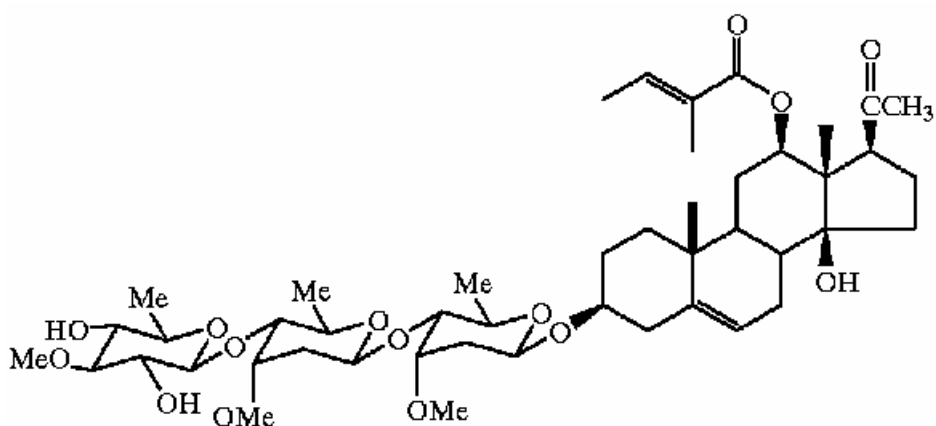
IV. The Board has issued a communication on 9 August 2004.

Oral proceedings were held on 27 January 2005 during which an amended main request was filed.

V. The Appellants requested that the decision under appeal be set aside and a patent be granted on the basis of the amended main request consisting of claims 1 to 25 filed at the oral proceedings.

VI. Claims 1 and 14 of the amended main request read as follows:

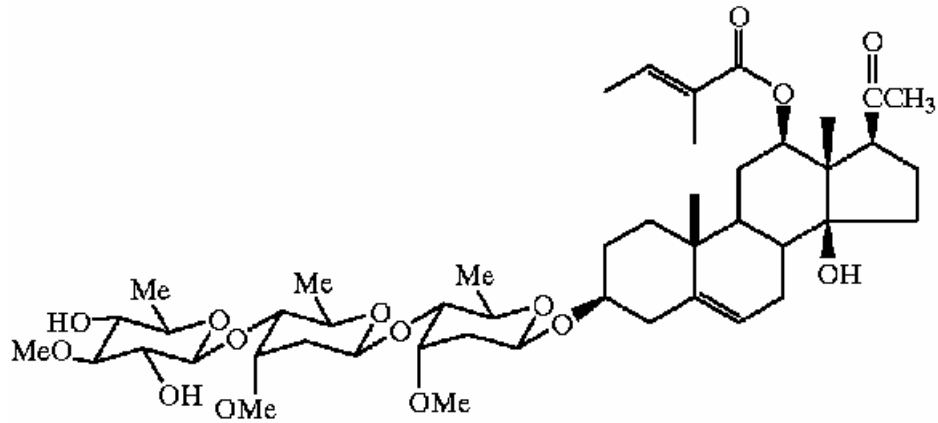
1. Use, in the manufacture of a medicament having appetite-suppressant activity for treating, preventing or combating obesity of a human or animal, of an extract from a plant of the genus *Trichocaulon* or the genus *Hoodia*, which extract contains an effective amount of an appetite-suppressant steroidal glycoside from said plant, wherein the steroidal glycoside has the formula



(1)

14. A non-therapeutic method of reducing total calorific intake of a human or animal, the method comprising administering to the said human or animal a

foodstuff or beverage comprising an extract from a plant of the genus *Trichocaulon* or the genus *Hoodia*, which extract contains an effective amount of an appetite-suppressant steroidal glycoside from said plant, wherein the steroidal glycoside has the formula



(1)

VII. Besides document (1), mentioned in section (II) above, the following documents are referred to in this decision:

(4) E.v.Koenen, Heil-, Gift- und eßbare Pflanzen in Namibia, vol.2; 1996, Klaus Hess Verlag, page 131

(8) White & Sloane, The Stapelieae, vol.III, 2nd ed., 1937, The Abbey San Eucino Press, pages 1000-1002

(11) Affidavit, Dr Rees, 21 April 2004

(12) Affidavit, Dr Horak, 25 November 2004.

VIII. The submissions made by the Appellants may be summarised as follows:

The closest prior art document for the assessment of an inventive step following the problem and solution approach should be a document aiming at the same objective as the claimed invention. In the present case this would be a document describing an appetite-suppressing medicament, foodstuff or beverage. Prior art compositions serving this purpose and containing Fenfluramine as active moiety were known at the filing date. Fenfluramine was used in the patent application as reference standard. The problem to be solved was seen in the provision of alternative appetite-suppressants having improved activity.

The succulents of the genera *Trichocaulon* and *Hoodia* had been known for a long-time as traditional foodstuff of original inhabitants of the Kalahari desert. However, the disclosure in document (8), wherein the author reported that eating such plant "removed the pangs of hunger so efficiently that I could not eat anything for a day after having reached the camp" did not allow to conclude that an extract from *Trichocolon* or *Hoodia* could be used in the manufacture of a medicament according to claim 1 or in the method of claim 14.

Reasons for the Decision

Amendments and Clarity - Articles 123(2) and 84 EPC

1. Claim 1 of Appellants' amended main request is based on claims 13 and 25, page 4, lines 22 to 28, and page 116, lines 14 to 23 of the application as published.

Independent claim 14 is based on claims 15 and 25, page 47, lines 5 to 9 and page 116, lines 14 to 23 as published. In order to disclaim subject-matter which, under Article 52(4) EPC, is excluded from patentability for non-technical reasons, the method of claim 14 has been defined as being a "non-therapeutic" method. Such disclaimer, although not having a basis in the application as published, is allowable and does not contravene the requirements of Article 123(2) EPC according to decisions G 1/03 und G 2/03 of the Enlarged Board of Appeal, OJ EPO 2004, 413 and 448; point (2.4).

Dependent claims 2 to 13 and 15 to 25 are based on original claims 1 to 8, 12 and 16.

2. Consequently, claims 1 to 25 meet the requirements of Article 123(2) EPC. The claims are clear and supported by the description and do not give rise to an objection under Article 84 EPC.

Novelty - Article 54 EPC

3. The subject-matter of independent claim 1, namely the use of an extract of a plant of the genus *Trichocaulon* or the genus *Hoodia* for the manufacture of a medicament having appetite-suppressant activity, is not disclosed in the prior art documents on file.

The same applies to the subject-matter of independent claim 14, referring to a non-therapeutic method of reducing total calorific intake of a human or animal by administering a foodstuff or beverage comprising said extract.

Accordingly, claims 1 and 14, as well as claims 2 to 13 and 15 to 25 dependent thereon are novel and meet the requirements of Article 54 EPC.

Inventive step - Article 56 EPC

4. In accordance with the problem and solution approach, the Boards of Appeal have developed in their case law certain criteria for identifying the closest prior art which provides the best starting point for assessing inventive step. It has been repeatedly pointed out that this should be prior art relating to subject-matter conceived for the same purpose or aiming at the same objective as the claimed invention and having the most relevant technical features in common, i.e. requiring the minimum of structural modifications (cf Case Law of the Boards of Appeal of the European Patent Office, 4th Edition 2001, chapter I.D.3).

5. The invention according to claim 1 serves the purpose to provide an appetite-suppressant medicament for treating, preventing and combating obesity. Claim 14 refers to a non-therapeutic method for reducing calorific intake of human or animal.

In the light of the criteria elaborated by the Boards of Appeal for identifying the closest prior art, the most appropriate starting point for the objective assessment of an inventive step following the problem and solution approach is in the present case considered to be a document aiming at the same purpose as the present application, i.e. appetite-suppression for the treatment of obesity and reduction of calorific intake.

6. None of the prior art documents on file serves this purpose or objective.

Nevertheless, the application as published itself (in example 44 starting on page 91 of the description), in order to prove the superiority of the claimed subject-matter, makes use of Fenfluramine as reference standard, a substance known to the skilled person as having appetite-suppressing activity.

The Board agrees with the Appellants that treatment of obesity and reduction of calorific intake by administering appetite-suppressing substances like Fenfluramine to individuals in need thereof represents the closest state of the art.

The problem to be solved by the subject-matter of the claims is seen in the provision of other appetite-suppressants having improved activity.

7. The problem has been solved by using an extract from a plant of the genus Trichocaulon or the genus Hoodia in the manufacture of a medicament (claim 1) and by administering a foodstuff or beverage comprising said extract to a human or animal (claim 14).

According to the results shown in tables 1(b) and 3(b), food consumption and body weight of the test animals could be reduced with a much higher significance by administering the plant extract according to the invention, compared to administering the reference standard Fenfluramine (see especially groups (5), (6) and (11)).

8. The question to be answered by the Board, in order to decide if the claimed subject-matter involves an inventive step in accordance with Article 56 EPC, is whether or not the skilled person would have arrived at this solution in an obvious way.

9. The Board is aware that the traditional knowledge of the original inhabitants of the Kalahari desert, like the San people, is the subject of a large number of publications. Many thereof have been published on the Internet. However, most of these documents have been published after the filing date of the present patent application and there is no convincing evidence on file that this post-published information, about what was known before the filing date, reflects reality. Therefore, the Board will not take into account post-published documents relating to traditional knowledge allegedly available to the public before the filing date, and consider only those documents which have been published before said date and which refer to different uses of plants of the genera *Trichocaulon* and *Hoodia*.

10. These documents are:

10.1 Document (1), referring to a revision of *Hoodia* and *Lavrania*, describes in the passage bridging pages 175 and 176 different medical and non-medical uses of *Hoodia*. The stems of several species are widely known as foodstuff, while other species are more rarely eaten because of their bitter flavour. The edible species "... have a peculiar pervasively spreading sweet taste which is remarkably persistent and **is said** to quench thirst

- and hunger for extended periods" (emphases added by the Board).
- 10.2 Document (4) describes that the stems of *Hoodia currori* are eaten for their anti-diabetes activity.
- 10.3 Document (8), with a publication date in 1937, describes *Trichocaulon piliferum*, whose stems are used as a substitute for food and water. The document reports on page 1002 an effect as described by a person having eaten the plant upon advice of a native guide and who is quoted with the words: "... it saved further suffering from the pangs of hunger so efficiently that I could not eat anything for a day after having reached the camp."
11. While document (4) is concerned with a different medical use of *Hoodia*, both documents (1) and (8) mention the suppression of hunger after consumption of the plant. This information is considered to be relevant for the problem of obesity caused by increased calorific intake of a human or animal. While document (1) describes this effect only from a "hear-say" position ("... is said to ..."), document (8) refers to first-hand information obtained from a person having actually eaten the plant. For this reason, the Board considers the disclosure in document (8) to be of higher relevance.
12. The view of the Appellants, supported by their technical experts, with regard to the disclosure in the prior art documents is as follows:

- Plants of the genera *Trichocaulon* and *Hoodia* are succulents. Their stems consist for the most part of fibrous material. Due to their structure the plants are able to store large quantities of water.
 - Eating the stems of these plants, as a substitute for food and water as described in document (8), fills the stomach of the consumer and leads to the feeling of satiety for an extended period. This is so all the more in an environment as the Kalahari desert where the mean day-temperature is in excess of blood temperature for more than eight months of the year, where the average sand temperature is about 70° C, where the loss of body fluids needed for cooling down is about one litre per hour and the demand for solid food is reduced anyhow.
 - The natural consequences following from the consumption of fibrous plant material with a high water content, namely a full stomach and the feeling of satiety, is not an indication to use an extract from the plants in the manufacture of an appetite-suppressant anti-obesity medicament, foodstuff or beverage.
13. In point (6) of the decision under appeal, the Examining Division came to a different conclusion, namely that the knowledge of a hunger and thirst quenching effect caused by *Trichocaulon* and *Hoodia* plants would obviously lead the skilled person to use extracts from the plants for the claimed purpose. This was all the more so as a consumer, when chewing parts of the plant, produces an extract thereof in the mouth (cf point (11) of the reasons for the decision).

14. The Appellants have provided evidence in the form of affidavits signed by their technical experts to disprove this argument.

In document (12) it is stated that the observation that extracts of *Trichocaulon/Hoodia* succulents were able to suppress appetite in laboratory animals without apparent toxic effects, was first made by the Appellants who had screened more than 1000 species of wild South African plants known to be used as indigenous "bush foods", in order to determine which of them could be safely eaten (point (5)). The extracts of the plant material had to be provided for the sole reason that the laboratory animals used did not eat solid plant material. Suppression of appetite and loss of weight in the animals was monitored and recorded as possible sign of toxicity of the administered plant extracts. However, in the case of *Trichocaulon/Hoodia* a suppression of appetite was observed, which turned out not to be associated with toxicity (point (8)).

By using modern NMR technology, the Appellants finally succeeded to isolate the steroidal glycoside having formula (1) as the active appetite-suppressing moiety contained in the plant extracts.

15. Document (11) reports the results of a double-blind, randomised, placebo-controlled study wherein a group of nineteen overweight (BMI 28-36 kg/m²) male subjects received either an extract from *Hoodia gordonii* (codenamed PYM50027) 1800 mg b.d. or placebo b.d. for 15 days. Assessments recorded during the study included daily calorific intake, body weight and body fat

content. The "extract-group" showed statistically significant reduction in all these parameters (cf point (6)) when compared with the placebo group.

Additionally, the absorption of the steroidal glycoside having formula (I) (codenamed PYM 50057) by non-obese healthy adult male subjects was investigated after oral and buccal administration of *Hoodia gordonii* and buccal administration of a crude extract from the plant. It was shown that sucking the sap from 50 gram of fresh plant stem or eating the same quantity of material gave rise to a very low plasma concentration of the active moiety, which were close to the quantification limit of the assay.

By contrast, the plasma concentration of the active moiety observed during administration of the extract daily dosing regimen (1800 mg b.d., see point (15) above), which was proven to reduce calorific intake, body weight and body fat content, was more than 200 fold higher.

16. In the light of the evidence provided by the Appellants, the Board does not agree with the conclusion drawn by Examining Division.

A skilled person, knowing from document (8) that consumption of parts of a fibrous, water-storing plant of the genus *Trichocaulon* very efficiently "removed the pangs of hunger", could not obviously derive from this disclosure that an extract from the plant could be used for the manufacture of an appetite-suppressant, anti-obesity medicament. Appellants have shown that a consumer eating the stems of the plant or sucking the

sap of the fresh plant is not able to absorb a sufficient amount of the active moiety contained in an extract of the plant which is responsible for its appetite-suppressing activity. The Board is convinced by the evidence provided by Appellants' technical experts, that the effect disclosed in document (8), and also reported in document (1), can be explained by the stomach-filling properties of the plants in question, which had been used as "bush-food" by the original inhabitants of the Kalahari desert for a long time.

17. Thus, when trying to solve the problem underlying the present invention, namely to provide an alternative appetite-suppressant having improved activity when compared with prior art compositions comprising for instance Fenfluramine, the skilled person would not arrive at the subject-matter of claims 1 to 25 in an obvious way.

In the light of the disclosure in the prior art documents on file the skilled person would not be prompted to use an extract from a plant of the genus *Trichocaulon* or the genus *Hoodia* in the manufacture of a medicament having appetite-suppressant activity, according to claim 1, or to administer to a human or animal a foodstuff or beverage comprising said extract in order to reduce their total calorific intake, according to claim 14.

Accordingly, claims 1 to 25 involve an inventive step and meet the requirements of Article 56 EPC.

Order

For these reasons it is decided:

1. The decision under appeal is set aside.

2. The case is remitted to the first instance with the order to grant a patent on the basis of claims 1 to 25 of the amended main request filed at the oral proceedings and a description adapted thereto.

The Registrar:

The Chairwoman:

P. Cremona

U. Kinkeldey