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**Datasheet for the decision
of 24 March 2015**

Case Number: T 0190/12 - 3.3.10

Application Number: 03812156.2

Publication Number: 1567474

IPC: C07C69/00, C07C67/48, C07C67/58

Language of the proceedings: EN

Title of invention:
PROCESS FOR PURIFYING DIACEREIN

Patent Proprietor:
Synteco S.p.A.

Opponents:
LABORATORIE MEDIDOM S.A.
STRAWMAN LIMITED
SUPRA CHEMICALS LTD
SANOFI AVENTIS FRANCE

Headword:

Relevant legal provisions:
EPC Art. 56

Keyword:
Inventive step - (no) - main and auxiliary request

Decisions cited:

Catchword:



**Beschwerdekammern
Boards of Appeal
Chambres de recours**

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Case Number: T 0190/12 - 3.3.10

D E C I S I O N
of Technical Board of Appeal 3.3.10
of 24 March 2015

Appellant: Synteco S.p.A.
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Decision under appeal: **Decision of the Opposition Division of the
European Patent Office posted on 28 November
2011 revoking European patent No. 1567474
pursuant to Article 101(3) (b) EPC.**

Composition of the Board:

Chairman P. Gryczka
Members: R. Pérez Carlón
 C. Schmidt

Summary of Facts and Submissions

- I. The appellant (patent proprietor) lodged an appeal against the decision of the opposition division to revoke European patent No. 1 567 474.
- II. Three notices of opposition and an intervention by an assumed infringer (opponent 4) were filed, on the grounds of sufficiency of disclosure (Article 100(b) EPC) and lack of novelty and inventive step (Article 100(a) EPC).

Opponents 2, 3 and 4 withdrew their oppositions during these appeal proceedings.

- III. The following documents were part of the opposition proceedings:

D1: US 5,391,775 A
D4: WO 96/24572 A1
D5: EP 0 928 781 A1
D6: WO 96/30034 A1

- IV. Claim 1 of the main request in this appeal proceedings, which was the first auxiliary request in opposition proceedings, reads as follows:

"A process for obtaining diacerein with a content of aloe-emodine (sic) and mono-, di- and tri-acetyl derivatives thereof ranging from 0 to 5 parts per million wherein an aqueous-organic solution of a diacerein salt with a weak base is extracted with a water immiscible or sparingly water-miscible solvent characterised in that said water immiscible or sparingly water-miscible solvent is toluene."

Claim 1 of the auxiliary request contains the same preamble as claim 1 of the main request, and its characterising portion reads as follows:

"characterised in that said water immiscible or sparingly water-miscible solvent is toluene and in that the extraction is carried out discontinuously."

- V. With respect to the then pending first auxiliary request, now the main request, the opposition division considered document D1 to be the closest prior art. The technical problem underlying the claimed invention was to provide an alternative process involving liquid/liquid extraction and the proposed solution, which was characterised by using toluene as extracting solvent, was obvious in view of the solubility of aloe-emodine in toluene. The subject-matter of the then pending first auxiliary request was thus not inventive.
- VI. The arguments of the appellant relevant for the present decision were the following:

Document D4, which disclosed the preparation of diacerein with a content of impurities below the detection limit by precipitation of its potassium salt, which was obtained from a triethylammonium salt solution, was the closest prior art. The problem underlying the claimed invention was to provide a process for the purification of diacerein which allowed high yields, extremely high purity and which was industrially exploitable. The solution was a process characterised by a discontinuous extraction with toluene, and such a process was not obvious in the light of the available prior art. Document D1, which was the sole document on file which related to the extraction of aloe-emodin from diacerein, disclosed a

continuous process which was carried out with butanone and thus taught away from the claimed solution. The subject-matter of claim 1 of the auxiliary request was for this reason inventive.

VII. The arguments of the respondent (opponent 1) and the former opponents relevant for the present decision were as follows:

Some of the former opponents argued that document D1 was the closest prior art. If, nevertheless, document D4 was considered closer, the objective technical problem was to provide an alternative purification to that of D4 and the solution, which was a process characterised by an aqueous-organic discontinuous extraction with toluene, was obvious since a discontinuous process was an obvious design choice within the skills of the person of the art and it was known for example from documents D5 and D6 that aloemodin was soluble in toluene and that toluene was poorly soluble in water. Claim 1 of the auxiliary request and, for the same reasons, claim 1 of the main request were not inventive.

VIII. The parties informed the board that they would not be attending the oral proceedings, which took place on 24 March 2015.

IX. The final requests of the parties were the following:

- The appellant (patent proprietor) requested in writing that the decision under appeal be set aside and that the patent be maintained on the basis of the main request or the auxiliary request, both requests filed with letter dated

28 March 2012.

- Respondent 1 (opponent 1) requested that the appeal be dismissed.

X. At the end of the oral proceedings, the decision was announced.

Reasons for the Decision

1. The appeal is admissible.

Inventive step, auxiliary request:

2. Claim 1 of the auxiliary request is directed to a process for obtaining diacerein with a content of aloe-emodin and mono-, di- or tri-acetyl derivatives thereof between 0 and 5 ppm which requires a discontinuous extraction, using toluene, of an aqueous-organic solution of a diacerein salt of a weak base.

3. Closest prior art:

Document D4 discloses a process for preparing diacerein with a content of aloe-emodin below the detection limit (see example 1), whereas the process of document D1 achieves a lower degree of purity (20 ppm, column 5, line 51). Already for this reason the board agrees with the appellant that document D4 is closer to the claimed invention than document D1.

D4 discloses a process for purifying diacerein by forming, as in the claimed process, a salt thereof with a weak base (diacerein triethylammonium salt) in an aqueous acetone solution. Such a solution is treated with potassium acetate to form diacerein potassium

salt, insoluble, which is filtered and washed. This potassium salt is dissolved in water and the solution obtained is subsequently acidified so that diacerein precipitates in the form of its free base, which is recovered from the suspension.

4. Technical problem underlying the invention:

The technical problem underlying the claimed invention is seen as to provide an alternative process to that of the closest prior art for producing diacerein with a low content of aloe-emodin and its acetyl derivatives, in high yield and which is industrially applicable.

5. Solution:

The claimed solution is a process involving an aqueous-organic solution of diacerein triethylammonium salt, which is characterised by its discontinuous extraction with toluene.

6. Success:

In the light of the data provided in Example 3 of the application, it is considered that the problem mentioned under point 5. above has been credibly solved by the process according to claim 1 of the auxiliary request.

7. Lastly, it remains to be decided whether or not the proposed solution to the objective problem underlying the patent in suit is obvious in view of the state of the art.

7.1 It is not disputed that liquid-liquid extraction is a well-known separation method in organic chemistry. Oil-

water extraction is suitable for separating water-soluble salts from non-polar organic compounds by dissolving them, respectively, in an aqueous phase and in an organic phase scarcely soluble in water.

The separation required by claim 1 of the auxiliary request is carried out over an aqueous solution as disclosed in D4 (Example 1, page 5, last paragraph), containing a compound which is in the form of a salt (diacerein triethylammonium salt) and apolar impurities (aloe-emodin and its acetyl derivatives).

The skilled person would immediately recognise that these components can be separated by oil-water extraction, since diacerein triethylammonium salt is soluble in water (D4, page 5, last paragraph) whereas aloe-emodin and its acetyl derivatives are soluble in organic solvents.

The simplest set-up for an extraction is an extraction funnel performing a discontinuous separation.

For these reasons, a process for preparing diacerein including a step of discontinuous extraction of the aqueous acetone solution of diacerein triethylammonium salt disclosed in D4 is obvious for the person skilled in the art in the light of his common general knowledge in the field of organic chemistry.

- 7.2 It remains to be examined whether the choice of the specific solvent required by claim 1, namely toluene, could, nevertheless, be inventive.

It is well known that toluene, which is scarcely miscible with water, is a solvent suitable for oil-water extraction.

Document D6 discloses the selective extraction with toluene of aloe-emodin from a complex mixture by means of a Soxhlet extraction unit (page 30, lines 2-15). Although Soxhlet extraction is a process different from an oil-water extraction, it relies like the latter on the solubility of aloe-emodin in toluene.

Document D5 discloses the recrystallisation of aloe-emodin in toluene [37]. A compound can only be recrystallised from a solvent in which it is soluble.

Thus, both D5 and D6 teach that toluene is a suitable solvent for aloe-emodin, which is the impurity to be removed in the present case.

The choice of toluene as solvent for the obvious oil-water extraction step required by claim 1 of the auxiliary request is thus also obvious for the person skilled in the art.

- 7.3 The skilled person would thus purify a water-acetone solution of diacerein triethylammonium salt containing aloe-emodin, like that disclosed in document D4, by discontinuously extracting said solution with toluene, since he would immediately recognise that such a mixture can be separated by oil-water extraction, discontinuous extraction techniques fall within the normal skills of the organic chemist and toluene is not only a suitable solvent for oil-water extraction but also a particularly suitable solvent for aloe-emodin.

The process subject-matter of the auxiliary request is thus not inventive as required by Article 56 EPC.

7.4 The appellant considered that document D1 (column 7, step e), which disclosed a continuous extraction of diacerein with a different solvent (butanone), taught away from the present invention for the following reasons:

7.4.1 D1 relied on a continuous process. Such a process would not have been carried out unless a successful, discontinuous extraction required multiple extraction steps. For this reason, D1 taught away from a discontinuous extraction.

However, the patent in suit disclosed reducing the level of aloe-emodin to the limit required by claim 1 only after five extractions with toluene (Example 3), and claim 1 is not limited to performing only one extraction step. This argument is, therefore, not convincing.

7.4.2 The appellant further argued that the difference between the solvent used in D1 (butanone) and toluene, in particular in terms of its water solubility, would teach away from the specific choice of solvent in the claimed invention.

However, for the reasons explained already, the solubility of aloe-emodin in toluene is known from documents D5 and D6 and it is well known to the skilled person that toluene is a solvent suitable for oil-water extraction. This appellant's argument is also unconvincing.

Inventive step, main request:

8. Claim 1 of the main request differs from claim 1 of the auxiliary request only in that it does not require that

the extraction with toluene be carried out discontinuously. The subject-matter of claim 1 of the main request is thus broader than that of the auxiliary request, while containing all the subject-matter of the latter. Its subject-matter is thus not inventive for the reasons explained with respect to the auxiliary request (see point 7.2 above).

9. None of the requests on file is allowable.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairman:



C. Rodríguez Rodríguez

P. Gryczka

Decision electronically authenticated