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**Datasheet for the decision
of 20 September 2011**

Case Number: T 1979/09 - 3.3.09

Application Number: 03000403.0

Publication Number: 1300084

IPC: A23L 1/30

Language of the proceedings: EN

Title of invention:

Composition for the treatment of chronic venous
insufficiencies comprising an extract of red vine leaves

Patentee:

Boehringer Ingelheim International GmbH

Opponent:

Frutarom Schweiz AG

Headword:

-

Relevant legal provisions:

EPC Art. 83, 54, 56

Relevant legal provisions (EPC 1973):

-

Keyword:

"Inventive step (no - main and auxiliary requests)"

Decisions cited:

T 1416/07

Catchword:

-



Case Number: T 1979/09 - 3.3.09

D E C I S I O N
of the Technical Board of Appeal 3.3.09
of 20 September 2011

Appellant:
(Opponent)

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Representative:

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Respondent:
(Patent Proprietor)

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Representative:

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Decision under appeal:

**Interlocutory decision of the Opposition
Division of the European Patent Office posted
14 July 2009 concerning maintenance of European
patent No. 1300084 in amended form.**

Composition of the Board:

Chairman: W. Sieber
Members: J. Jardón Álvarez
F. Blumer

Summary of Facts and Submissions

I. The mention of the grant of European patent No. 1 300 084, in respect of European patent application No. 03000403.0, in the name of Boehringer Ingelheim International GmbH, filed on 19 October 2000 as a divisional application of the earlier European patent application no. 00974420.2, was published on 19 April 2006 (Bulletin 2006/16). The granted patent contained 10 claims, whereby claim 1 read as follows:

"1. A composition in a form suitable for oral administration which consists of an active principle being capable of preventing or treating the discomfort associated with mild-to-moderate chronic venous insufficiency of the lower extremities and a pharmaceutically, cosmetically or dietetically acceptable carrier, the improvement wherein is that said active principle consists of an aqueous extract of red vine leaves containing 2 to 20% flavonoids, wherein said aqueous extract of red vine leaves is obtainable by a method comprising the steps of:

- (a) collecting red vine leaves at a point of time when the content in flavonoids has reached an optimum;
- (b) drying and crushing the leaves;
- (c) cutting the leaves to pieces;
- (d) extracting the leaves with water at temperatures from 60 to 80°C for 6 to 10 hours in an exhaustive percolation;
- (e) optionally concentrating the obtained extract;

characterized in that said composition contains an amount of said aqueous extract of red vine leaves,

which corresponds to a daily dosage of 300-800 mg of the extract."

Claims 2 to 10 were dependent claims.

- II. A notice of opposition was filed by Frutarom Schweiz AG on 29 December 2006 requesting the revocation of the patent in its entirety on the grounds of Articles 100(a) (lack of novelty and lack of inventive step), (b) and (c) EPC.

During the opposition proceedings, *inter alia*, the following documents were cited:

- D1: Ministère des Affaires Sociales et de la Solidarité, Bulletin Officiel, No 90/22 bis, "Médicaments à base de plantes", 1990, pages 24, 25, 36 and 37;
- D4: Monographies de la 10^e édition de la Pharmacopée Française et du Formulaire National (FN) en vigueur à la date du 1^{er} janvier 1996, Extrait de vigne rouge (sec) (altogether 4 pages);
- D5: Rote Liste 1998, Venentherapeutika, 83 048 and 83 084; "Antistax®";
- D6: H. Beck, "Rotes Weinlaub von A bis Z", PTA heute, Nr. 8, August 1997, pages 792-796; and
- D28: Frutarom Switzerland LTD, Versuchsprotokoll VENT, dated 11 July 2005 (6 pages).

III. By its interlocutory decision announced orally on 17 June 2009 and issued in writing on 14 July 2009, the opposition division held that the grounds for opposition did not prejudice the maintenance of the patent in amended form on the basis of claims 1 to 9 according to auxiliary request 1.

Claim 1 of auxiliary request 1 was based on granted claim 1 (see point I above) wherein the expression "A composition" had been amended to read "A dietary supplement composition" based on granted claim 8.

In view of the experimental results filed by the opponent (cf. D28), the opposition division was convinced beyond reasonable doubt that the method of D4 provided an extract which was indistinguishable from the extract obtained by carrying out steps (a)-(d) of claim 1, even if D4 did not specify the extraction temperature and the flavonoid content of the extract. Notwithstanding the above, the opposition division acknowledged novelty because D4 neither disclosed a material being suitable for use as dietary supplement nor a carrier that was pharmaceutically, cosmetically or dietetically acceptable.

The opposition division considered D5 or D6 to represent the closest state of the art, because the Antistax[®] products disclosed in these documents were intended for the same purpose as the claimed product. The problem underlying the patent in suit was to provide an alternative product for oral administration being suitable for treating chronic venal insufficiency. The claimed solution using the extract according to claim 1 was seen as involving an inventive step because

the skilled person would have regarded the presence of esculin in the Antistax[®] products of D5 and D6 as essential so that he would not have contemplated the exclusion of said component from the known products.

IV. On 14 September 2009 the opponent (appellant) lodged an appeal against the interlocutory decision of the opposition division. The appeal fee was paid on the same day.

The statement of grounds of appeal was filed on 12 November 2009 together with the following further documents:

D30: P.H. List and P.C. Schmidt, "Technologie pflanzlicher Arzneizubereitungen", Wissenschaftliche Verlagsgesellschaft mbH Stuttgart, 1984, altogether 29 pages;

D31: R.O.B. Wijesekera, Ed., "The Medicinal Plant Industry", CRC Press, Inc, 1991, Chapter 7, pages 85-88, 93-96 and 111;

D32: Les médicaments à base de plantes (Septembre 1997), Agence du Médicament, Paris, 1998; pages 3-9, 54-57, 60 and 61; and

D33: Copy of the minutes of the oral proceedings of 22 September 2009 in appeal case T 1416/07-3309.

The appellant requested that the decision under appeal be set aside and the patent be revoked in its entirety because the claimed subject-matter lacked novelty and inventive step, and was insufficiently disclosed. The

appellant further requested that the point of law, which had been the subject in G 3/06, be again referred to the Enlarged Board of Appeal, because the referral proceedings in G 3/06 had been terminated following the withdrawal of the remaining appeals in the referring decision.

- V. With its reply dated 28 May 2010 the patent proprietor (respondent) disputed all the arguments submitted by the appellant and requested that the appeal be dismissed.

It also filed the following fresh evidence:

D34: E. Schneider, "Gutachterliche Darstellung zur Aussagekraft von Leitsubstanzen als alleiniger Parameter zur Charakterisierung und zum Vergleich von Pflanzenextrakten unter Betrachtung der Phytoäquivalenz", dated 18 February 2008, 22 pages;

D35: M. Veit, "Stellungnahme zur Vergleichbarkeit pflanzlicher Extrakte *sui generis* und Gutachten zur Einordnung und Vergleichbarkeit von unterschiedlichen Weinlaubextrakten", dated 18 February 2008, 14 pages; and

D36: Pharmaton GmbH, Fachinformationen relating to Antistax[®] Kapseln, Januar 1996.

- VI. On 1 April 2011 the board dispatched a summons to attend oral proceedings. In the attached communication the board drew the attention of the parties to the points to be discussed during the oral proceedings.

VII. On 19 August 2011 both the appellant and the respondent filed further arguments in support of their requests.

The respondent also filed a set of seven claims for an auxiliary request marked "Auxiliary Request I- Appeal" and the following two further documents:

D37: PLANTA-SUBTIL Arzneimittel GmbH, "Zusammenfassung der pharmakologischen, toxikologischen und klinischen Untersuchungen zur Wirksamkeit von ANTISTAX Liquidum bei Venenerkrankungen (Chronisch Venöser Insuffizienz)"; a non-dated internal document; and

D38: C. Diehm, "Comparison of leg compression stocking and oral horse-chestnut seed extract therapy in patients with chronic venous insufficiency" THE LANCET, vol. 347, February 1996, pages 292-294.

VIII. Oral proceedings were held before the board on 20 September 2011 during which the appellant withdrew its request for a referral to the Enlarged Board of Appeal (see above point IV). The appellant requested that documents D37 and D38 not be admitted into the proceedings because they were *prima facie* not relevant and/or not published before the filing date of the patent in suit. During the oral proceedings the appellant's main and auxiliary requests were discussed.

The claims of the main request are the claims of auxiliary request 1 found allowable by the opposition division (see point III above).

The claims of the auxiliary request are the claims filed on 19 August 2011 as "Auxiliary Request I - Appeal". Claim 1 of the auxiliary request reads as follows:

"1. A dietary supplement composition for use in the prevention or alleviation of the discomfort associated with mild-to-moderate chronic venous insufficiency of the lower extremities in a form suitable for oral administration which consists of an active principle being capable of preventing or treating the discomfort associated with mild-to-moderate chronic venous insufficiency of the lower extremities and a pharmaceutically, cosmetically or dietetically acceptable carrier, the improvement wherein is that said active principle consists of an aqueous extract of red vine leaves containing 2 to 20% flavonoids, wherein said aqueous extract of red vine leaves is obtainable by a method comprising the steps of

- (a) collecting red vine leaves at a point of time when the content in flavonoids has reached an optimum;
- (b) drying and crushing the leaves;
- (c) cutting the leaves to pieces;
- (d) extracting the leaves with water at temperatures from 60 to 80°C for 6 to 10 hours in an exhaustive percolation;
- (e) optionally concentrating the obtained extract;

characterized in that said composition contains an amount of said aqueous extract of red vine leaves, which corresponds to a daily dosage of 300-800 mg of the extract, and the composition is administered in a

daily dose of 300-800 mg of the extract in 1 to 3 capsules or tablets taken once daily."

IX. The arguments presented by the appellant in its written submissions and at the oral proceedings insofar as they are relevant for the present decision may be summarized as follows:

- The requirements of Article 83 EPC were not fulfilled, essentially because the specification did not describe a method for analyzing the complete group of flavonoids.
- The claimed subject-matter lacked novelty in view of D4. D4 disclosed the use of an auxiliary substance which could not be distinguished from a carrier.
- Concerning inventive step of both requests, the appellant pointed out that the situation in the present appeal case was the same situation as in the parent patent, which had been revoked for lack of inventive step (T 1416/07). The reasons given in that decision equally applied to the now claimed subject-matter.

X. The arguments of the respondent may be summarized as follows:

- The subject-matter of claim 1 was novel over the disclosure of D4 at least because there was no disclosure of a carrier as claimed. Additionally, the process of D4 did not result in the same extract as the one obtained when carrying out steps (a) to (e) of claim 1.

- Regarding inventive step the respondent saw the disclosure of Antistax[®], D5, as the closest prior art document. The subject-matter of claim 1 differed from this prior art in that the composition did not include esculin; the red vine leaves extract was specified to contain 2 to 20% flavonoids; and in that the method of preparation of the extract was specified. It pointed out that the experiments of the appellant, D28, did not show any prior art extract and that it was the task of the appellant to prove that the extraction conditions mentioned in D4 would inevitably result in an extract being identical to the claimed extract. The respondent stressed that there was no suggestion in the prior art that the red vine leaves extract alone would be sufficiently active. The fact that this extract would have the same efficiency as the known product Antistax[®] was an unexpected result. To affirm the contrary could only be done with knowledge of the invention (*ex post facto*).

- The auxiliary request involved an inventive step because there was no hint in the available documents as to the claimed dosage regime. On the contrary, the prior art's constant teaching (D5, D36) was towards an intake two or three times daily, actually teaching away from the invention. In the respondent's opinion it was quite unexpected that good results in treating chronic venous insufficiency could be obtained by using a different red vine leaves extract, eliminating the esculin from the Antistax[®] composition and administering it only once daily. Moreover, a single daily

administration dosage regime was more likely to be complied with by the patients.

XI. The appellant (opponent) requested that the decision under appeal be set aside and that the European patent No. 1 300 084 be revoked.

The respondent (patent proprietor) requested that the appeal be dismissed (main request) or, subsidiarily, that the patent be maintained on the basis of "Auxiliary Request I - Appeal" as filed with letter dated 19 August 2011.

Reasons for the Decision

1. The appeal is admissible.
2. *Procedural matters*
 - 2.1 The respondent filed documents D37 and D38 with letter dated 20 August 2010. The reason given for the late filing was that it had managed to get access to the unpublished study on Antistax[®] (D37) only during the preparation of its latest submission. D38 was necessary to properly understand the effects presented in D37.
 - 2.2 The appellant requested not admitting these documents into the proceedings because they were *prima facie* not relevant and/or not published before the filing date of the patent in suit.
 - 2.3 In the present appeal proceedings both parties filed new documents, namely D30 to D38. There is no evidence

that the filing of these new documents by the respective parties amounts to a tactical abuse of the proceedings. The submissions were made at an early stage of the appeal proceedings or at the moment the documents were made available to the party. Moreover, the documents were filed in support of previous arguments and/or to establish the skilled person's general knowledge. Finally, the other party had enough time to take them into consideration. As regards the fact that D37 was not pre-published, the board notes that this document was merely used as a witness document to provide evidence for the effect allegedly achieved by the claimed subject-matter.

- 2.4 Thus the board saw no reasons not to admit the newly filed documents, and in particular D37 and D38 into the appeal proceedings (Article 114(2) EPC).

MAIN REQUEST

3. *Interpretation of Claim 1*

- 3.1 Claim 1 is directed to a dietary supplement composition with the following features:

- (α) a dietary supplement composition
- (β) in a form suitable for oral administration which consists of
- (γ) an active principle being capable of preventing or treating the discomfort associated with chronic venous insufficiency
- ($\gamma 1$) the active principle consists of an aqueous extract of red vine leaves obtainable by a method comprising the steps of collecting red vine leaves,

drying and crushing the leaves, cutting them to pieces and extracting with water under certain conditions, and

(δ) a pharmaceutically, cosmetically or dietetically acceptable carrier wherein

(ε) said composition contains an amount of aqueous extract of red vine leaves, which corresponds to a daily dosage of 300-800 mg of the extract.

3.2 Concerning feature (ε), it is noted that the expression "daily dosage" is a feature relating to the use of the composition, namely the amount to be taken per day, not to the composition itself. This feature is therefore not a limiting feature of the claimed composition. It is interpreted as indicating that the composition must be suitable for administering a daily dosage of 300-800 mg of the aqueous extract.

3.3 This interpretation of the claim is in conformity with the respondent's own interpretation (page 2 of its letter dated 19 August 2011).

4. *Sufficiency of disclosure*

4.1 The appellant has maintained during the appeal proceedings the objection that the requirements of Article 83 EPC are not satisfied because of the absence of a method for analyzing the complete group of flavonoids in the specification of the patent in suit.

4.2 In fact, the same objection has been raised in the appeal proceedings dealing with the parent application/patent, namely T 1416/07. As set out in point 3.5 of the reasons of this decision, "... it is

well known which flavonoids are present in red vine leaves ... and that methods for analysing them, for instance high pressure liquid chromatography, are also well known and available to the skilled person without undue burden.... In these circumstances, the fact that it may be difficult and time consuming to identify and quantify all of the flavonoid species contained in the red vine leaves extract is not a matter to be criticised under the aspect of sufficiency." These reasons apply *mutatis mutandis* to the present case, in particular because the appellant has not provided any evidence whatsoever which could challenge the finding in T 1416/07.

4.3 Consequently the board is satisfied that the patent discloses the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.

5. *Novelty (Article 54 EPC)*

5.1 The novelty of Claim 1 was contested by the appellant having regard to the disclosure of D4.

5.1.1 Document D4 discloses a method of preparation of a dry extract of red vine leaves (see under "Extrait de vigne rouge (sec), lines 1-10). According to D4, appropriate auxiliary substances can be incorporated, if necessary, before the drying step (lines 5-6).

5.1.2 However, the generic disclosure of "auxiliary substances" in D4 cannot take away the novelty of the specific carriers (pharmaceutically, cosmetically or dietetically acceptable carriers) now required in

claim 1, in particular because D4 does not disclose any use of the extract for a pharmaceutical, cosmetic or dietetic application.

5.1.3 For this reason alone the subject-matter of claim 1 of the main request is novel.

6. *Inventive step (Article 56 EPC)*

6.1 The present invention relates to a dietary supplement composition having as active principle an extract of red vine leaves, for preventing or alleviating the discomfort associated with mild-to-moderate chronic venous insufficiency of the lower extremities.

6.2 Closest prior art

6.2.1 The board considers, in agreement with the decision under appeal and the parties, that the closest prior art is represented by the orally administered Antistax[®], a commercially available product disclosed in D5, D6 and D36. Antistax[®] contains as active principle a mixture of an extract of red vine leaves (98,4%) and esculin (1,6%) and is also used for the treatment of venous insufficiency of the lower extremities (cf. D5, product 83 048; D6, abstract and pages 795-796, last section of the article; and D36 whole document).

Document D5 is silent about the composition of the red vine leaves extract used. In D6 and D36 it is stated that the main components of the extract are flavonoids (D6, page 793, right column, first full paragraph and D36 middle column under "1. Weinlaub-Extrakt") and that the properties of the flavonoids are significant for

its use in the treatment of venous insufficiency (D6, page 794 section "*Venenleiden und Bioflavonoide*", in particular last paragraph and D36 middle column under "1. Weinlaub-Extrakt").

6.2.2 However, none of these documents disclose how the red vine leaves extract used in Antistax[®] is prepared. Thus, the composition of claim 1 differs from Antistax[®] as disclosed in these documents in that:

- it does not include esculin; and
- it is specified how the red vine leaves extract with a content of 2 to 20% flavonoids is prepared.

6.3 The problem to be solved and its solution

6.3.1 The compositions of claim 1 have the same use as the product Antistax[®], namely the treatment of chronic venous insufficiency of the lower extremities. There is no evidence on file of any unexpected effect of the claimed compositions when compared with Antistax[®]. In fact, even the respondent saw the technical problem to be solved by the patent in suit in the provision of alternative compositions which are also useful for the treatment of venous insufficiency of the lower extremities.

6.3.2 This problem is solved by using the compositions defined in claim 1, wherein the active principle consists of an aqueous extract of red vine leaves containing 2 to 20% flavonoids and the extract is obtainable under specific extraction conditions.

In the light of the results of the study described in the patent specification the board is satisfied that

the above-defined problem has been credibly solved.
This finding was not challenged by the appellant.

6.4 Obviousness

6.4.1 It remains to be decided whether the suggested solution is obvious from the prior art. In this context it has to be analysed as to whether or not (i) the specific method of preparing the extract and (ii) the use of the red vine leaves extract alone can contribute to inventive step.

6.4.2 The respondent has maintained during the proceedings that the method of preparation of the red vine leaves extract results in an extract having very specific properties. It pointed out that plant extracts are complex mixtures defined by their method of preparation. The claimed extracts being characterized by a content of 2 to 20% flavonoids, mandatorily included 98 to 80% of other ingredients which were defined by the method of extraction. The respondent supported this affirmation by the two expert opinions, D34 and D35, indicating that two extracts were phytoequivalent, if their pharmaceutical equivalence and their therapeutical equivalence were demonstrated. As this evidence had not been provided by the appellant, it should be recognized that a different extract was used in the claims.

6.4.3 It is true that the method of preparation of the red vine leaves extract is not specified in the prior art, and thus a comparison of the claimed extracts with the extract used in Antistax[®] is not possible. In the absence of this information it has to be assumed, as

pointed out by the appellant, that the prior art extract has been prepared according to the general knowledge of the skilled person using standard methods like the one disclosed in D4.

In D4 the extract is obtained by warm lixiviation of suitable, cut red vine leaves with water to complete exhaustion. The method used in D4 is described in a general way without indicating the specific conditions used in every process step.

Compared to this known process, the process of claim 1 requires:

- (a) collecting red vine leaves at a point of time when the content in flavonoids has reached an optimum;
- (b) drying and crushing the leaves;
- (c) cutting the leaves to pieces; and
- (d) extracting the leaves with water at temperatures from 60 to 80 °C for 6 to 10 hours in an exhaustive percolation.

Steps (a), (b) and (c) define in a very broad way how the leaves are handled before the extraction step. The leaves are to be collected when the content in flavonoids reaches an optimum and they are dried, crushed and cut into pieces. None of these steps are further concretized in the claim. In the absence of such further information it must be assumed that the skilled person would carry out these process steps according to the known standard technologies for the processing of medicinal plants (cf. D30 and D31) with the aim of optimizing the extraction of flavonoids, the known active components in red vine leaves. Steps (a),

(b) and (c) thus cannot contribute to essentially distinguishing the claimed extract from the prior art extracts.

6.4.4 Concerning step (d), the actual extraction step, this step is carried out at a temperature in the range of 60° to 80°C for 6 to 10 hours in an exhaustive percolation to achieve a high content in flavonoids during the extraction as indicated in paragraph [0018] of the specification. This extraction step by percolation is similar to the lixiviation to complete exhaustion disclosed in D4 as both processes aim to extract the drug until exhaustion of the soluble substances.

In this context, the appellant provided further experimental evidence (D28) that the extraction conditions had little influence on the flavonoid content of a particular sample of red vine leaves. Thus, regardless of whether the temperature was inside or outside the range required in claim 1, whether percolation or maceration or even a mixture of water and ethanol was used, the content of flavonoids extracted from said sample, that is to say the known main active ingredients of the extract used in Antistax[®], is always within the range of 2 to 20%.

Insofar as the respondent relied on the presence of compounds in the extract other than the main active ingredients, the board notes the following:

- The extract used in the patent in suit contains as main active ingredients quercetin-3-O-β-D-glucuronide and isoquercitrin ([0009]). These are

exactly the same main components present in the red vine leaves extract used in Antistax[®] according to D6 (page 793, right column, lines 25 - 29) and D36. The skilled person when preparing a red vine leaves extract for treating venous insufficiency would ensure that the components which are said to be the main active components are present in the extract in good yield.

- There is no information on file showing that the activity of the compositions could be due to other unspecified components of the extract which would not be extracted when carrying out the process of D4.

6.4.5 Thus, it is evident from the above that the extract obtained by steps (a) to (d) of claim 1 is very similar, if not identical, to the extract used in Antistax[®]. But even if there is no identity, the slight differences in the preparation leading to a slight difference in the extract, it has not been shown that slight variations in the preparation contribute to inventive step. On the contrary, all the process steps identified in claim 1 are common in this field.

The preparation of the red vine leaves extract can for these reasons not contribute to justifying an inventive step.

6.4.6 Concerning the use of the extract of red vine leaves alone, that is to say without esculin (question (ii) above), it is noted that D6 emphasizes the importance of the flavonoids present in the red vine leaves extract as the main active principle of the Antistax[®] product and being essentially responsible for its

activity in the treatment of venous insufficiency (cf. D6, page 792, last sentence of the abstract and page 794, second and third columns). It would therefore be evident to the skilled person from studying these passages of D6 that a composition containing only the red vine leaves extract and being free of esculin would also show the desired activity.

This finding is also confirmed by further documents on file indicating that the red vine leaves extract was already known for the treating of venous insufficiency (for instance, D1, page 25) and that the effect on venous insufficiency is due to the presence of flavonoids (D36, middle column, "1. Weinlaub-Extrakt"). Furthermore, it is stated in D36, right hand column that esculin and the extract of wine leaves act in the same way ("gleichsinnig"). Nothing is said of the two components working in a synergistic way.

Consequently, the exclusion of esculin from the Antistax[®] product cannot justify the presence of an inventive step.

- 6.4.7 The respondent has filed document D37 during the appeal proceedings in order to show an unexpected result of the claimed compositions. In its opinion it was an unexpected result that the activity of the claimed composition would be maintained even if one active component of Antistax[®], namely esculin, were removed. This was demonstrated when comparing the results of D37 with those of the patent in suit.

However no direct comparison of a treatment with the compositions of claim 1 with a treatment with Antistax[®]

has been made. As discussed in detail during the oral proceedings it is rather difficult, if not impossible, to compare the results presented in the patent with the results of D37. The study in D37 was conducted with patients with only one leg suffering chronic venous insufficiency and its results cannot be compared with those of the patent conducted with patients suffering from chronic venous insufficiency in both legs. The assumption made by the respondent that the results in D37 were likely to be overestimated by a factor of 2 appears rather speculative. Consequently, no conclusion can be achieved by comparing both experimental results.

- 6.5 For these reasons the subject-matter of claim 1 of the main request lacks inventive step.

AUXILIARY REQUEST

7. *Inventive step (Article 56 EPC)*

- 7.1 Claim 1 of the auxiliary request is drafted in the form of a first medical use claim ("A dietary supplement composition for use in the prevention or alleviation of the discomfort associated with mild-to-moderate chronic venous insufficiency of the lower extremities ...") which contains in addition to the features of claim 1 of the main request a dosage regime, namely that "the composition is administered in a daily dose of 300-800 mg of the extract in 1 to 3 capsules or tablets taken once daily" (point VIII above).
- 7.2 Since claim 1 of the main request already refers to "an active principle being capable of preventing or treating the discomfort associated with mild-to-

moderate chronic venous insufficiency of the lower extremities", the mere reformulation of claim 1 to a first medical use claim cannot contribute to overcoming the inventive step objection against claim 1 of the main request.

Thus, the actual difference of the subject-matter of claim 1 of the auxiliary request over claim 1 of the main request is the dosage regime.

- 7.3 The recommended dose of Antistax[®] in D5 and D36 varies from 360 mg to 540 mg taken in two or three capsules twice a day. The now claimed dosage regime uses an amount of extract covering the known amount but it requires that it is taken only once a day.
- 7.3.1 It is well known that in designing dosage regimen the two major parameters that can be adjusted are the dose itself, i.e. the quantity of drug administered, and the dosing frequency, i.e. the time interval between doses.
- 7.3.2 In the present case the amount of active ingredient remains the same as the amount used in D5 and there is no evidence on file of any unexpected technical effect caused by administering the red vine leave extract once daily. The board considers that it is within the competence of the skilled person to find out the optimal dosage regime. Consequently, the replacement of a dosage regime by another dosage regime for the same purpose is considered to be a matter of routine experimentation and cannot be seen as involving an inventive step.

7.3.3 In this respect the board cannot accept the argument of the appellant that it was unexpected that the same activity would be achieved by a change of dosage regime. In fact, a comparison of the claimed dosage regime with the dosage regime of D5/D36 has not been made. The only comparison which has been made compares the now required dosage regime with the use of compression stockings and/other oedema-reducing agents (last paragraph of the patent specification). The information given in the patent is that the red vine leave extract in a daily dose of 300-800 mg taken once daily is useful for treating chronic venous insufficiency. It has never been shown that taking a dose of 300-800 mg once daily has the same effect as taking the same dose twice daily.

Finally, insofar as the respondent relied on the fact that by changing the dosage regime from two times a day to only once a better adherence of the regime by patients is achieved, this advantage is in itself known and its exploitation in the present case cannot justify an inventive step.

7.4 Consequently, the subject-matter of claim 1 of the auxiliary request also lacks inventive step.

8. In summary, none of the requests relate to patentable subject-matter.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The patent is revoked.

The Registrar

The Chairman

D. Magliano

W. Sieber