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File Number: T 349/89 - 3.3.2

Application No.: 83 106 963.8

Publication No.: 0 100 915

Title of invention: Hair grower composition

Classification: A61K 7/06

DECISION  
of 14 November 1990

Applicant: Eisai Co. Ltd.

Proprietor of the patent:

Opponent:

Headword: Hair grower compositions/EISAI

EPC Article 56

Keyword: "Inventive step (no); expected improvement resulting  
from an obvious combination of active compounds"

Headnote



Europäisches  
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Beschwerdekammern

Boards of Appeal

Chambres de recours

Case Number : T 349/89 - 3.3.2

**D E C I S I O N**  
**of the Technical Board of Appeal 3.3.2**  
**of 14 November 1990**

**Appellant :** Eisai Co. Ltd.  
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Tokyo  
JP

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**Decision under appeal :** Decision of Examining Division 001 of the European  
Patent Office dated 29 December 1988 refusing  
European patent application No. 83 106 963.8  
pursuant to Article 97(1) EPC

**Composition of the Board :**

**Chairman :** P.A.M. Lançon

**Members :** P. Krasa

L. Mancini



(3) BE-A-669 472 (DAIICHI SEIYAKU COMP.).

It was held that the available data were not appropriate to support a synergistic effect of the composition claimed.

- III. The Applicant lodged an appeal against this decision with payment of the prescribed fee. A Statement of Grounds was filed in due time.
- IV. In a communication the Board, inter alia, requested supplementing information on the performance of the tests relied on by the Appellant and expressed some doubt whether these tests were appropriate to support the alleged synergism. Oral proceedings were held on 14 November 1990.
- V. In his written submissions and at the oral proceedings the Appellant argued as follows:

The effects achieved with a composition according to Claim 1 and comprising both 1% by weight of coenzyme Q<sub>10</sub> are higher than the sum of those obtained with compositions containing only 1% by weight of carpronium chloride and 0.5% of coenzyme Q<sub>10</sub> respectively. This supra-additive effect was said to prove the unexpected synergistic effect of the claimed composition. At the oral proceedings the Appellant referred also to the following document:

(5) DE-C-835 038.

- VI. The Appellant requested that the impugned decision be set aside and that a patent be granted either on the basis of six claims (main request), Claim 1 of which being identical with that given above, or on the basis of five claims (auxiliary request), Claim 1 of which differs from that of the main request by replacing "a skin peripheral vasodilator drug" by "one or more of a skin peripheral

vasodilator drug selected from (3-carboxymethyl-propyl) trimethyl-ammonium-chloride, vitamin E nicotinate and benzyl nicotinate".

#### Reasons for the Decision

1. The appeal is admissible.
2. All the claims of the main request and of the auxiliary request are supported by the application documents as originally filed and, therefore, they are admissible under Article 123(2).
3. The application in suit is concerned with hair grower compositions comprising 0.01 to 2% by weight of ubiquinone and 0.1 to 2% a skin peripheral vasodilator drug.
  - 3.1 In the Appellant's opinion - as stated in the oral proceedings - both the documents (3) and (5) are equally close to the subject-matter of the application because they are both concerned with hair-lotions comprising a vasodilator. The Board, however, on the basis of the active ingredient's structure and the particular use, considers (3) to be the closest state of the art: it is the only document available which discloses a hair growing effect - without quantification, however - for the vasodilator (3-carboxymethyl-propyl) trimethyl-ammonium chloride (= carpronium chloride); see (3), page 2, line 30.  
~~Example 1 of (3) discloses a composition comprising 1 part by by weight of carpronium chloride and 87 parts by weight of ethanol. Therefore, a composition is already state of the art with low vasodilator contents.~~

- 3.2 In the light of this closest prior art the technical problem underlying the patent application may be seen in providing hair growing preparations having improved efficacy. According to Claim 1 of the main request, this technical problem is solved by combining a ubiquinone with the skin peripheral vasodilator drug.

In view of the Examples given in the application and having considered the supplemental information regarding the actual amounts of the compositions used in the Examples (see Appellant's letter of 26 March 1990, No. 2.1), the Board is satisfied that the above-defined technical problem is plausibly solved.

4. After having examined all the documents cited in the Search Report the Board has reached the conclusion that the subject-matter of the disputed patent is novel. Since novelty was acknowledged by the Examining Division there is no need to consider this matter in detail.
5. It still remains to be examined whether the requirement of inventive step is met by the claimed subject-matter.
- 5.1 From (2) the use of a ubiquinone in hair tonics was known. Thus, it has to be investigated whether or not it was obvious for the skilled person to combine a ubiquinone with a skin peripheral vasodilator drug as known from (3) in a hair growing composition. While the Board could have understood that hair tonics are not necessarily the same as hair growing compositions, the Appellant explained at the oral proceedings that all measures which are directed to taking care of hair would also advance the growth of hair. Thus, a skilled person would expect from a hair tonic and a compound used therein a beneficial effect on the growing of hair.

For establishing inventive step it is necessary to make credible - on the balance of probability - the existence of a true supra additive synergism if, as in the present case, the combination of two known active compounds was prima facie obvious in view of their known properties.

- 5.2 In the application, experiments are disclosed demonstrating the influence of compositions comprising either (a) 0.5% by weight of ubiquinone-10 or (b) 1.0% by weight of carpronium chloride or (c) a combination of 0.5% by weight of ubiquinone-10 and 1% by weight of carpronium chloride. Tables I, II and III on pages 10 and 11 of the application give the reduction in hair fallout achieved by treating ten panels each with the three compositions (a), (b) and (c), respectively.

It can be accepted to the benefit of the Appellant that these tables support the Appellant's interpretation of the experiments even when an objective quantification of effects seems to be difficult on the basis of a rating scale with the steps no effect (-), slightly good effect ( $\pm$ ), good effect (+) and remarkably good effect (++) as used in the application: from the said tables I to III an additional effect can be deduced for composition (c) when compared with the sum of the effects to be achieved, with (a) and (b), the latter being a composition within the scope of (3) and resembling that of example 1 of (3). Nevertheless, the data available is not appropriate to infer the existence of synergism between ubiquinone-10 and the vasodilator drug carpronium chloride: it is common general knowledge that synergism does not necessarily derive from the finding that the effect observed for the combination does not correlate with that obtained by the addition of the single doses. Such an additional effect may result from the normal non-linearity of dose-effect-

relationships. No evidence has been submitted for comparison of same amounts on the one hand for the single ingredients and, on the other hand, of their mixture.

Appellant's submission that hair grower compositions should not be treated as pharmaceuticals in this respect is not convincing. In both cases, biological systems are the object of the investigations and neither can the Board see any reason why the said general principle should not be applicable to hair grower compositions, nor were such reasons advanced by the Appellant. Hence, the Board concurs with the Examining Division's finding that the available data is not sufficient in the present case to make plausible a supra additive synergism for the compositions of Claim 1.

This opinion is supported by the Appellant's admission that the Examining Division's statement was probably true that increased effects were to be expected for compositions (a) and (b) as soon as the respective single active compounds were used in a concentration of 1.5% by weight. This shows the justification of the Examining Division's doubts regarding the conclusiveness of the experiments disclosed in the application as far as synergism is concerned.

- 5.3 It remains that the compositions of the application have an improved hair growing effect when compared with a composition comprising 1% by weight of carpronium chloride, i.e. composition (b) accepted by the Board as illustrating the closest state of the art. This, however, is not sufficient to infer that the claimed subject-matter involves an inventive step:

A skilled person aiming at an improvement of the hair growing effect of the compositions known from (3) would immediately increase the amount of active compound. For

such purpose he could either use the same active ingredient or turn to other active compounds for which a hair growing effect was to be expected (see No. 5.1 hereinabove) and he would add such a compound, as are the ubiquinones of Claim 1 of the main request, to the known compositions. The improvement of the known compositions, thus, results from measures which were obvious for the skilled person in respect to the effect aimed at, and cannot create inventiveness, even when the extent of the improvement was not predictable.

Hence, the Board holds that Claim 1 of the main request lacks inventive step.

- 5.4 Dependent Claims 2 and 3 and Claims 4 to 6 of the main request, the latter claims covering methods of preparation of the compositions of Claim 1 by mixing the ingredients, fall together with Claim 1 of this request.
- 5.5 One of the three skin peripheral vasodilator drugs specified in Claim 1 of the auxiliary request is carpronium chloride (see No. VI hereinabove). This is the compound of the experiments disclosed in the application - compare No. 5.2. Hence, all the considerations set forth under No. 5.3 apply also to Claim 1 of the auxiliary request. Thus, the Board holds that the subject-matter of Claim 1 of the auxiliary request lacks also inventive step. Claims 2 to 4 fall together with Claim 1.

**Order**

For these reasons, it is decided that:

The appeal is rejected.

The Registrar:

The Chairman:

M. Beer

P. Lançon