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D E C I S I O N
of 23 June 1999

Case Number: T 0445/94 - 3.3.2

Application Number: 90906500.5

Publication Number: 0463117

IPC: A61K 7/18

Language of the proceedings: EN

Title of invention:
Fluoride containing mouth rinses, dentifrices, Gels, and chewable tablets

Applicant:
AMERICAN DENTAL ASSOCIATION HEALTH FOUNDATION

Opponent:
-

Headword:
Complex Fluoride/AMERICAN DENTAL

Relevant legal provisions:
EPC Art. 54, 56

Keyword:
"Novelty: (no) - Main and first auxiliary requests"
"Inventive Activity: (no) - second auxiliary request"

Decisions cited:
-

Catchword:
-

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Case Number: T 0445/94 - 3.3.2

D E C I S I O N
of the Technical Board of Appeal 3.3.2
of 23 June 1999

Appellant: AMERICAN DENTAL ASSOCIATION HEALTH FOUNDATION
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Decision under appeal: **Decision of the Examining Division of the European Patent Office posted 26 November 1993 refusing European patent application No. 90 906 500.5 pursuant to Article 97(1) EPC.**

Composition of the Board:

Chairman: P. A. M. Lançon
Members: C. Germinario
J. H. van Moer

Summary of facts and submissions

I. European patent application No. 90 906 500.5 (international publication No. WO 90/10435) was refused by the examining division under Article 97 (1) EPC on the grounds of inadmissible extension of the content of the application as filed and lack of inventive step of the claimed subject-matter. The decision was taken on the basis of a set of 20 claims.

The text of claim 1 filed with letter dated 2 September 1993 and refused by the examining division reads as follows:

"The use of stable, non-toxic readily hydrolysable complex fluoride compound for the manufacture of an agent for use in a method for fluoridating teeth comprising: mixing in an aqueous environment and in the present (sic) of a buffer a stable, non-toxic soluble calcium salt with a stable non-toxic readily hydrolysable complex fluoride compound whereby the complex fluoride compound is hydrolysed and calcium fluoride is precipitated; and promptly applying the resultant mixture to tooth surface."

The subject-matter of claim 10 was a tooth care package comprising at least two separate compartments containing the two components cited in claim 1.

II. The following documents cited during the examination procedure are relevant for the present decision:

(1) FR-A-2 170 018,
(2) EP-A-0 263 638,

(3) FR-A-2 329 292

During the appeal proceedings, the appellant submitted the following late published document:

(4) Caries Res. Vol. 25, 1991, pp 397 to 401.

In compliance with Article 114 (1) EPC, the Board, of its own motion, additionally introduced in the appeal proceedings the following document assigned to the patentee and cited as background of the invention in the application under consideration:

(5) US-A-4 556 561.

III. Having recognised the novelty of the claimed subject-matter, the examining division identified in document (2) the closest prior art. This document disclosed the use of sodium fluoride and calcium chloride in a treatment for preventing tooth caries. Since the fluoridating agent cited in this prior document, ie sodium fluoride, was apparently considered by the examining division as being comprised in the scope of claim 1 of the application in suit, the use of a buffer was recognised as the unique novelty-imparting feature of the independent use claim. However, this feature was not regarded as able to endow the claimed subject-matter with an inventive activity.

As to the product claims, which had been amended during the examination procedure, the examining division held that not all the features of the claimed subject-matter were disclosed in the filed application. Therefore, the claims were not admissible pursuant to Article 123(2)

EPC.

IV. The appellant lodged an appeal against this decision and submitted, with the statement setting out the grounds of appeal, the results of a comparative test carried out to compare the turbidity caused by the system according to document (2) and that according to the present invention. Additionally he produced the late published document (4), which showed the amount of fluoride deposition on the tooth surface after treatment according to the invention compared to the treatment according to the prior art.

V. Oral proceedings were held before the Board on 23 June 1999. A new main request and two auxiliary requests were then filed.

VI. During the debate, the appellant maintained that the claimed subject-matter was novel over the teaching in document (5) since the fluoridating and mineralizing method therein described was carried out at acid pH values. Such a pH would have prevented the quick hydrolysis of the fluoride complex compound and the release of available fluoride ions with the result that no precipitation of calcium fluoride on the tooth surface would have occurred within the intended application time, as provided by claim 1 of the main request, or within a time of four minutes or less, as provided by claim 1 of the first auxiliary request.

The appellant further indicated document (2) as the closest prior art, and emphasised that the treatment according to the present invention produced a strong increase in fluoride deposition compared with the

deposition obtained in (2), and that this improvement could not be predicted in the light of the teaching in (5) or in any other cited document.

Although conceding that the fine mechanism of fluoride deposition according to the invention was not sufficiently elucidated, the appellant stressed that the treatment according to the invention did not envisage the preliminary formation of dicalcium phosphate dihydrate (DCPD) onto the tooth surface, and the subsequent fixation of fluoride in the form of hydroxyapatite, as disclosed in document (5). This prior document established, so the appellant argued, a fixed indissoluble link between the use of a fluoride complex and the concomitant formation of DCPD. For this reason, the skilled person would not have found in (5) any incentive to use a fluoride complex in a different treatment.

VII. The texts of claims 1 according to the main request and first and second auxiliary requests, all filed during the oral proceedings on 23 June 1999, read as follows:

Main request

"The use of a two-component system for the preparation of a composition for fluorinating teeth, comprising

a) a first component comprising a stable, non-toxic, soluble calcium salt, and

b) a second component comprising a stable, non-toxic, readily hydrolysable complex fluoride compound,

which upon application is mixed in an aqueous environment resulting in the hydrolysis of the fluoride compound and precipitation of calcium fluoride on the tooth surface which occurs within the intended application time."

First auxiliary request

"The use of a two-component system for the preparation of a composition for fluorinating teeth, comprising

a) a first component comprising a stable, non-toxic, soluble calcium salt, and

b) a second component comprising a stable, non-toxic, readily hydrolysable complex fluoride compound,

which upon application is mixed in an aqueous environment resulting in the hydrolysis of the fluoride compound and precipitation of calcium fluoride on the tooth surface within a time of four minutes or less."

Second auxiliary request

"The use of a two-component rinse or dentifrice system for the preparation of a composition for fluorinating teeth, comprising

a) a first component comprising a stable, non-toxic, soluble calcium salt, and

b) a second component comprising a stable, non-toxic, readily hydrolysable complex fluoride compound,

which upon application is mixed in an aqueous environment resulting in the hydrolysis of the fluoride compound and precipitation of calcium fluoride on the tooth surface which occurs within the intended application time and wherein the first component, the second component or both contain a buffer to maintain the pH above 5."

VIII. The appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of the main or auxiliary requests I or II filed during the oral proceedings.

Reasons for the decision

1. The appeal is admissible.

2. *Article 123(2) EPC*

The independent claims of all the valid requests were amended during the appeal proceedings. After evaluation of all the amendments, the Board concludes that the newly filed claims comply with the requirements of Articles 123(2) and 84 EPC.

3. *Article 54 EPC*

Main Request and First Auxiliary Request

3.1 The novelty of the claimed subject-matter over the documents considered by the examining division, namely documents (1), (2) and (3), was not a point at issue in

the decision under appeal. The Board shares the opinion that these three prior documents are not prejudicial to the novelty of any of the claims according to the present main request and first and second auxiliary requests.

3.2 However, novelty has also to be evaluated with respect to document (5), which was considered for the first time during the appeal proceedings.

This document describes a method for topically fluoridating and/or mineralising dental tissue comprising two essential steps which can be carried out either successively, in a two-step treatment, or concomitantly in a single-step treatment.

3.2.1 The first step is treating the tooth surface with a non-aqueous composition comprising calcium phosphates, which upon mixing with an aqueous solvent, the saliva, gives rise to a solution in which dicalcium phosphate dihydrate (DCPD), ie $CaHPO_4 2H_2O$, is formed. Since the solution, which has pH 4.3 or less, contains DCPD approaching the saturation concentration, this latter precipitates onto the tooth surface (see claim 1).

The above-mentioned solution, which is said "DCPD-forming solution", comprises soluble calcium salts such as dicalcium phosphate anhydrous (DCPA), monocalcium phosphate monohydrate (MCPM) or monocalcium phosphate anhydrous (MCPA) and necessarily the freshly formed DCPD (see column 4, lines 22 to 40 and examples 1 and 2). All these salts are non-toxic, since used in vivo, are soluble, within the meaning of "soluble" given in the application in suit, ie at least 0.008 grams of Ca

in 100 grams of water (page 5, lines 20) and, at least in the case of DCPD, are stable.

The Board therefore concludes that this solution meets all the conditions stated for the "first component" in claim 1 of all the main and auxiliary requests. On the other hand, no argument or evidence has been produced by the appellant to convince the Board that any novel feature of the present invention over document (5) was entailed in the use of the specific calcium salts.

3.2.2 The second step of the treatment according to document (5) comprises applying a fluoridation agent capable of releasing fluoride ions which are then fixed by DPCD to the tooth surface in the form of fluorapatite.

As illustrated in column 3, lines 27 to 36, the method of document (5) can also be performed as a one-step treatment. In this case, a fluoride complex compound is used as fluoridation agent. Such complex compound is selected from fluorosilicate, fluoroborate, fluorophosphate and other, as reported in column 3, lines 31 to 45, column 5, lines 35 to 58 and column 8, lines 30 to 46 and in table II.

Since the fluoride complex compounds used in (5) are the same as those used in the present invention, they necessarily meet all the conditions stated for this "second component" in claim 1 of the main and auxiliary requests.

3.2.3 Finally, document (5) provides that all the reagents necessary to perform the fluoridating treatment be incorporated into a ready-for-use composition in the

form of a toothpaste, chewing gum or mouthrinse which upon contact with saliva, **thus upon application**, forms the aqueous solution or gel which is the environment in which the fluoridation occurs (see column 7, lines 33 to 34 and lines 49 to 51, column 9, lines 45 to 51 and column 10, lines 10 to 13).

Considering the application forms envisaged in (5), specifically toothpaste or mouthrinse, the Board is convinced that in the one-step treatment the mixing of the different substances, the hydrolysis of the fluoride complex and the precipitation of CaF2 must necessarily happen upon application and within the intended application time, as stated by claim 1 of the main request. Moreover, when the application consists in brushing the teeth with a toothpaste or rinsing the mouth with a mouthrinse this "intended application time" is actually a matter of a few minutes, that is in practice tantamount to the "four minutes or less" defined by claim 1 of the first auxiliary request.

In the Board's view, therefore, the sequence of reactions and times characterising the treatment according to document (5) is identical to the sequence steps and times stated in claim 1 of the main request and first auxiliary request.

3.3 The appellant contested this conclusion and argued that the acid pH characterising the treatment according to document (5) would have prevented the hydrolysis of the fluoride complex compound and the necessary release of available fluoride ions with the result that no precipitation of CaF2 could have occurred within the intended application time.

These arguments are however in contradiction with the experimental results reported in (5). In fact, example 2, which describes a one-step treatment, unambiguously proves that the content of fluoride incorporated onto the tooth enamel after a treatment of a few minutes is significantly higher than the fluoride content in the control, in spite of a pH value of 2.1. In particular, as illustrated in table II, using calcium fluorosilicate the fluoride content in the enamel increases by about 2.5 times or even more. These results thus prove that the hydrolysis of the fluoride complex, which releases fluoride ions, though probably showing optimum pH of 5 or higher as asserted by the appellant, still occurs significantly at pH 4.3 or less.

3.4 Finally, the Board wishes to emphasise that the present case is not comparable to the case of decision T 290/86 (OJ EPO 1992, 414) in which the novelty of a second therapeutic application of a known medicament over a previously known similar treatment of the human body for the same therapeutic purpose was accepted by the then competent Board on the basis of a technical effect not previously recognised. In the present instance (as also clarified under point 4.7.3 below) the treatment according to the prior document (5) implies the formation and precipitation of CaF_2 as an essential step for the achievement of the final therapeutic effect, as also implied by the invention in suit. On this point, it should moreover be noted that the fine mechanism of tooth fluoridation after CaF_2 precipitation according to the present invention was not sufficiently elucidated, as admitted by the appellant at the oral proceedings, which means that a mechanism identical to the one of

(5) cannot be excluded. In fact the wording of claim 1 according to the main and first auxiliary requests does not even exclude that DCPD be used or that the fluoridation effect be achieved through the same DCPD intermediate of document (5).

In view of the foregoing, the Board's judgement is that the subject-matter of claim 1 according to the main request and first auxiliary request lacks novelty.

Second Auxiliary Request

3.5 Claim 1 of the second auxiliary request is further characterised by the presence of a buffer in either components of the system, or both, to maintain the pH above 5.

The Board recognises that neither the documents considered by the examining division nor document (5) disclose the use of a two-component system additionally comprising a buffer. The subject-matter of claim 1 is therefore novel.

4. *Article 56 EPC*

4.1 The examining division and the appellant have both indicated document (2) as the closest prior art. The Board accepts this opinion.

This document describes an oral composition in the form of toothpaste or mouthwash for inhibiting caries through the deposition of particles of a fluoride ion-releasing material in the mouth and onto the tooth surface, the particles being freshly precipitated

calcium fluoride particles.

The invention in (2) implies the combined use of two compositions comprising, the former, an aqueous solution containing calcium ions, the latter, an aqueous solution containing fluoride ions, and being such that when mixed directly in the mouth or immediately before use rapid precipitation of calcium fluoride occurs. Calcium chloride and sodium fluoride are used as preferred embodiments of the invention (see claims 1 to 6, experiments 1 and 2 and examples 1 and 2). A specific effect sought by the treatment of (2) is the **rapid** precipitation of CaF2 (see page 3, lines 1 to 19).

4.2 The technical problem to be solved by the present invention in relation to document (2) is that of **providing means for improving the deposition and/or retention of fluoride on the oral and tooth surfaces**. In fact, as discussed in the application under consideration, page 2, lines 17 to 32, it was estimated that the known fluoridation treatments yielded deposition of less than 0.5% of the available fluoride contained in a mouthrinse or dentifrice.

4.3 The solution proposed by the invention is to replace the sodium fluoride used in (2) as source of fluoride ions with a stable, non-toxic, readily hydrolysable complex fluoride compound and to maintain the pH above 5 with a buffer.

4.4 As explained in the application in suit, when the two components of the system are brought in contact just prior to application, a controlled reaction

precipitates extremely fine particles of calcium fluoride continuously within the application period. This relatively prolonged precipitation deposits significantly more fluoride in the mouth than the currently used formulations containing comparable amounts of fluoride. These arguments have been confirmed by two pieces of proof, namely a spectrophotometric graph and the late published document (4), enclosed in the statement setting out the grounds of appeal.

On the basis of these results the Board is convinced that the technical problem is actually solved by the proposed solution.

4.5 The recognition of the drawback of a low yield in fluoride deposition upon treatment with the known conventional fluoridating agents was not a contribution of the present invention since it had already been recognised in document (5).

In fact, the treatment disclosed in (5), regardless of whether in one or two steps, always implies the fresh formation of CaF_2, not as a side-effect to be minimized or avoided, but rather as a desired effect which can improve the effectiveness of the treatment in its entirety, as evident from the passage in column 3, lines 8 to 10.

The document, however, explains (see column 3, lines 30 to 42) that in the one-step treatment, which involves direct mixing of the DCPD-forming solution with the fluoridation agent, it is not possible to add the simple fluoride compounds present in conventional

fluoridation agents into the DCPD-forming solution without causing massive precipitation of calcium fluoride, CaF_2. This precipitation not only removes calcium from the solution, but it also reduces the fluoride concentration of the solution to a negligible amount. The result is a drastic reduction in remineralisation and fluoridation capacity. Thus the teaching in (5) makes plain that a quick, excessive precipitation of CaF_2 reduces the yield of the fluoridation treatment.

4.6 To avoid the drawback of a drastic reduction in fluoridation capacity, document (5) teaches to replace the conventional fluoridation agents, which are eg SnF_2, NaF or TiF_4 (see column 7, line 46), with a complex fluoride compound that does not immediately release free fluoride ions into the aqueous solution or gel upon dissolution. Thus, large quantities of free fluoride ions are not released and there is minimal precipitation of calcium fluoride (see column 5, lines 35 to 41).

Thus document (5) unambiguously teaches that, in order to improve the fluoridation yield in a fluoridation treatment carried out in a single step, as claimed in the application in suit, the conventional fluoridating agents such as the NaF used according to the closest prior art, document (2), have to be replaced by complex fluoride compounds.

4.7 Claim 1 of the second auxiliary request is further defined by the presence of a buffer to maintain the pH of the aqueous environment above 5. Thus, the question has to be considered whether the pH factor endows the

claimed subject-matter with an inventive merit.

4.7.1 The first reason to add a buffer is explained in the filed application, on page 7, lines 25 to 30, where it is stated that "since hydrolysis of the complex fluoride produces free fluoride as well as hydrogen ions, to maintain the pH of dentifrice or rinse constant above approximately 5, pH buffer may be added..".

The Board understands from this passage that the purpose of a buffer should be that of keeping the pH around values suitable for and compatible with application on teeth and mucous membranes. It is obvious to the person skilled in the art that extremely acid values are to be avoided because they are irritant, as is self-evident, and because they facilitate the demineralisation of the tooth enamel, as is well known in itself and emphasised in document (3), page 3, lines 7 to 10. Actually, the closest prior art itself, document (2), teaches in example 2 that the pH has to be adjusted to values of 7.0-7.5.

Therefore, as long as the scope of a buffer is to guarantee the physiological compatibility of the compositions, the Board cannot recognise in this feature any inventive step.

4.7.2 During the oral proceedings, the appellant developed a further argument. Namely, the fluoridation treatment according to (5) was carried out at a pH below 4.3. This acid pH prevented, so he argued, the hydrolysis of the fluoride complex and the necessary release of fluoride ions. Therefore a pH value above 5, as stated

in claim 1, would improve the final fluoridation effect.

The Board notes that the treatments disclosed in (5), including the one-step treatment, always entail two essential reactions which, having different rates and different optimum conditions, run necessarily successively. The former is the formation of DCPD, which requires an acid pH, below 4.3, the latter is the hydrolysis of the fluoride complex which is slowed down by the acid pH. On this aspect of the treatment, document (5) is very clear. It teaches that the pH of the solution or gel (that at the beginning of the treatment is 4.3 or less) gradually increases as DCPD is formed, and that **the complex fluoride compounds hydrolyse as the pH of the solution or gel increases** (emphasis added). As the fluoride concentration slowly rises, CaF_2 may begin to precipitate out of the solution or gel (see column 5, lines 41 to 48). This passage unambiguously suggests that the pH necessary for the hydrolysis of the fluoride complex cannot be strongly acid, but on the contrary has to be increased likely above 4.3 in order that the reaction can start and prosecute. That the pH value is expected to rise during the development of the treatment is further confirmed by the absence in the system of (5) of any buffer: indeed, a buffer would prevent such an increase.

Thus, the skilled person faced with the problem of improving the fluoride deposition and/or retention obtained according to the closest prior art, and well aware that at least a part of the solution to said problem was to replace the conventional fluoridating agent of (2) with a fluoride complex compound, was

suggested on the one hand by document (5) to maintain the pH above the acid value 4.3 in order to facilitate the fluoride complex hydrolysis, and on the other, to approach as much as possible the neutral pH, as disclosed in (2), for the simple reason of physiological compatibility.

Moreover, the skilled person, in an attempt to modify the oral preparation described in document (2), had no reason at all to envisage an acid pH value, since the fluoridation treatment of (2) does not imply the previous formation of DCPD of the tooth surface.

Under this circumstance, the feature in claim 1 of a pH maintained "above 5", which in its meaning comprises neutrality as well, is considered by the Board as an obvious, arbitrary compromise equivalent to any other possible value between the pH 4.3 of (5) and the neutral pH of (2), and for this reason unable to underlie in itself an invention.

The Board wishes to emphasise that the appellant failed to produce any argument aimed to prove that the specific pH value 5 was indeed the result of a purposive selection and thus the threshold of a novel unpredictable effect able to endow the claim with an inventive merit.

4.7.3 During the oral proceedings, the appellant also expressed the opinion that document (5) established a fixed indissoluble link between the use of a fluoride complex compound and the formation of DCPD on the tooth surface. For this reason the skilled person would not have found in (5) any incentive to use a fluoride

complex in a treatment not contemplating the formation of DCPD, such as the treatment according to document (2).

The Board concedes that the formation of DCPD is a preliminary step in the treatment according to (5). Nevertheless the fluoridation treatment therein described also comprises the formation and precipitation of CaF_2 as an essential step necessary to achieve the desired final effect. This step is independent of the subsequent fate of the precipitated CaF_2, namely whether incorporated in the enamel as hydroxyapatite through the intermediate DCPD or causing in itself a parallel additional fluoridation. For this reason, the skilled person would understand from the teaching in (5) that the formation of DCPD and the precipitation of calcium fluoride upon hydrolysis of the fluoride complex, though both contributing to the final result, were not so rigidly interconnected as to dissuade him from considering the use of a fluoride complex compound independently from a DCPD-forming reagent.

In view of the foregoing, the Board judges that the subject-matter of claim 1 according to the second auxiliary request does not involve an inventive step, and that, under these circumstances, it is not necessary for the Board to evaluate the patentability of the remaining independent claims.

Order

For these reasons, it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

P. Martorana P. A. M. Lançon