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Datasheet for the decision of 13 June 2007

Case Number: T 0288/04 - 3.3.07

Application Number: 93308476.6

Publication Number: 0595576

IPC: A61K 7/16

Language of the proceedings: EN

Title of invention:
Stabilized sorbic acid or salt thereof

Applicant:
McNeil-PPC, Inc.

Headword:
-

Relevant legal provisions:
EPC Art. 56

Relevant legal provisions (EPC 1973):
-

Keyword:
"Inventive step - problem and solution (yes)"

Decisions cited:
-

Catchword:
-

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0288/04 - 3.3.07

D E C I S I O N
of the Technical Board of Appeal 3.3.07
of 13 June 2007

Appellant: McNeil-PPC, Inc.
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Decision under appeal: **Decision of the Examining Division of the European Patent Office posted 28 July 2003 refusing European application No. 93308476.6 pursuant to Article 97(1) EPC.**

Composition of the Board:

Chairman: S. Perryman
Members: F. Rousseau
B. Struif

Summary of Facts and Submissions

I. The appeal lodged on 07 October 2003 lies from the decision of the Examining Division posted on 28 July 2003 refusing European application No. 93308476.6, published under No. 0 595 576. The application as filed comprised eight claims, claims 1 and 4 reading as follows:

"1. A stabilized aqueous solution containing sorbic acid or salt thereof in an antimicrobial proportion, and further containing from 0.1 to about 5 parts, by weight, per million parts of solution of manganous ion, said manganous ion being in an amount sufficient to inhibit oxidation of said sorbic acid or salt thereof to acetaldehyde.

4. The solution of any preceding claim further containing sucralose."

II. The decision of the examining division was based on claims 1 to 17 according to the main, first and second auxiliary requests, respectively filed on 12 May 2003, 22 April 2003 and 12 May 2003. The application was refused on the ground that none of these requests met the requirements of article 123(2) EPC. According to that decision claim 1 of each request defined the combined use of a pH range of at least 3 together with an amount of from 0.1 to 0.475 ppm for the manganous ions, for which the application as originally filed did not provide any basis. The decision under appeal also referred *inter alia* to the following documents:

(1) US-A-3 404 987,

(2) Acta Chemica Scandinavica, vol. 26 (1972), No. 6, pages 2367-2371,
(3) Suomen Kemistilehti B vol. 40 (1967), No. 2, pages 54-58,
(9) J. Agric. Food Chem., 1980, vol. 28, No. 6, pages 1246-1249, and
(10 J. Phys. Chemistry, 58(7), 1954, pages 537-541.

III. With the statement setting out the grounds of appeal filed on 5 December 2003, the Appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of the claims of the main request or, alternatively on the basis of the claims of the auxiliary request, both sets submitted with the letter of appeal dated 7 October 2003.

IV. In reply to a communication of the Board sent as an annex to the summons for oral proceedings, the appellant filed a main and seven auxiliary requests. The oral proceedings were held on 13 June 2007, in the course of which all previous requests were replaced by a sole request consisting of Claim 1, which reads:

"1. An aqueous liquid concentrate of sucralose comprising:

from 3 to 35 weight percent sucralose;
a preservative system including sorbic acid or a salt thereof, said sorbic acid or salt thereof being present in an amount within the range of from 0.005% to 5% by weight;
a buffering system to maintain a pH of 4 to 5.5;
water, and

from 0.1 to 5 parts by weight per million parts of solution of Mn^{2+} ion.

V. The arguments of the appellants, as far as they are relevant to the present decision, can be summarised as follows:

(a) The present claim is based essentially on page 4, lines 22 to 33 of the application as filed, referring to aqueous liquid concentrates containing from 3 to 35 weight percent sucralose, a preservative system including sorbic acid or a salt thereof, a buffering system to maintain a pH of 4 to 5.5, and from 0.1 to 5 parts by weight per million parts of solution of Mn^{2+} ion, and on the sentence bridging pages 3 and 4 mentioning that the aqueous solutions of the invention contain sorbic acid or a salt thereof in an antimicrobial proportion usually within the range of about 0.005% to 5% by weight.

(b) The sole cited prior art document disclosing a sucralose-containing aqueous liquid concentrate is document (6), which, however, does not disclose the presence of manganous ions.

(c) The problem to be solved over the closest prior art represented by document (6) is to stabilise sorbic acid or sorbate against oxidation in a buffered aqueous sucralose solution. The problem has indeed been solved, as shown by the results in Figures 1 to 3 relating to Example 1 of the application. Whereas for low concentrations of manganous ions an undesirably high level of

acetaldehyde is observed, with high concentrations of manganous ions other decomposition products of the sorbate, as indicated by a colour development, are obtained. The selection of the concentration range operated in the present application is therefore not arbitrary. There is no suggestion in the prior art documents cited that the rate of oxidation of sorbate might depend on the ratio of manganous ion to sorbate, rather than on the concentration of metal ion. The prior art documents cited do not suggest that the amount of manganous ions as defined in the claim would provide stabilisation of sorbic acid or sorbate against oxidation at a pH of from 4.0 to 5.5, nor that at higher concentrations of manganous ions, sorbate would be degraded and colour be developed. Thus, the subject-matter of the claim of the sole request is inventive.

VI. The appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of the claim of the sole request submitted at the oral proceedings on 13 June 2007.

VII. At the end of the oral proceedings the decision of the Board was given orally.

Reasons for the Decision

1. The appeal is admissible.

2. *Amendments*

The application as filed, according to its claim 1, relates to a stabilized aqueous solution containing sorbic acid or salt thereof in an antimicrobial proportion, and further containing from 0.1 to about 5 parts, by weight, per million parts of solution of manganous ion, said manganous ion being in an amount sufficient to inhibit oxidation of said sorbic acid or salt thereof to acetaldehyde.

Present claim 1 is now directed to a preferred composition, namely a stabilized aqueous liquid concentrate of sucralose, as disclosed page 4, lines 25-30 of the application as originally filed, wherein the antimicrobial amount of sorbic acid or salt thereof has been specified to be within the range of from 0.005% to 5% by weight. This range, according to the sentence bridging pages 3 and 4 of the application as originally filed, represents the antimicrobial concentration of sorbic acid or a salt thereof to be used according to the invention for the purpose of preservation of aqueous solutions in general, and thus also of the concentrates of sucralose, as disclosed on page 4, lines 25-30 of the application as filed.

Moreover, in view of the tests carried out in example 1 of the application as filed, the use of 0.1 to 5 parts by weight per million parts of solution of manganous ion is sufficient to inhibit oxidation of sorbic acid

or salt thereof to acetaldehyde in a solution as presently claimed (see point 4.2.3 below). Thus, the purposive feature "said manganous ion being in an amount sufficient to inhibit oxidation of said sorbic acid or salt thereof to acetaldehyde" originally present in claim 1 as filed has been replaced by a quantification based on the original text, and shown to be effective.

Consequently, the claim of the sole request meets the requirements of Article 123(2) EPC.

3. *Novelty*

Document (6) is the sole prior art document on file disclosing sucralose-containing aqueous liquid concentrates. They comprise (i) sucralose which can be present in an amount of from 3.0% to 35% by weight of the total composition, with a preferred range of from 20.0% to 28.0% by weight (claim 1, page 2, lines 51-52), (ii) a preservative system in an amount of from 0.05% to 3.0% by weight of the total composition, preferably a mixture of potassium sorbate and sodium benzoate in a 1:1 ratio (claims 1 and 8, paragraph bridging pages 2 and 3) and (iii) a buffering system to maintain the pH preferably in the desired range of 4.0 to 5.5 (claims 1 and 2, page 3, lines 8 to 10) and water (claim 3, page 2, line 54, page 3, lines 37-40). Specific compositions are disclosed in examples I-III, VI, IX-XII. The sucralose-containing aqueous liquid concentrates of document (6), however, do not contain manganous ions. Hence, novelty of the presently claimed subject-matter can be acknowledged (Article 54 EPC).

4. *Inventive step*

4.1 *Closest state of the art*

The closest prior art for the purpose of objectively assessing inventive step is normally a prior art document disclosing 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 EPO, 5th edition 2006, I.D.3.1).

The present application relates to aqueous liquid concentrates of sucralose comprising sorbic acid or a salt thereof as preservative agent and a buffering system to maintain a pH of 4 to 5.5. They find utility as a sweetener, for example in beverages, jellies, pharmaceuticals, tonics, cough medications (page 4, lines 23-25, paragraph bridging pages 4 and 5).

Document (6) also relates to aqueous liquid concentrates of sucralose comprising a preservative system including sorbic acid or salt thereof and a buffering system to maintain the pH preferably in the desired range of 4.0 to 5.5 (see point 3 above), which also are conceived for a sweetener finding utility in beverages, jellies, pharmaceuticals, tonics or cough medications (page 3, lines 33-37). As indicated in point 3 above, the presently claimed aqueous liquid concentrates are with the exception of the presence of manganous ions the same as those disclosed in document

(6). In view of the above, document (6) represents the closest state of the art.

4.2 *Problem and solution*

4.2.1 Sorbic acid and salts thereof are prone to oxidation in aqueous liquid concentrates of sucralose (see example 1, control experiment, figures 3, 10 and 11 of the present application). This oxidation produces products such as aldehydes (see control experiment, figure 3) which can cause development of undesired flavours or odours and undesired colour due to the development of polymers of aldehydes (page 1, lines 15-18 and control experiment, figure 10). Moreover, the oxidation of sorbic acid or of a salt thereof can result in the loss of sufficient sorbate ion to impair the desired antimicrobial effect (page 1, lines 16-20, example 1, control experiment, figure 11). Improvement of the above mentioned properties is, however, particularly desirable in view of the use of the aqueous liquid concentrates of sucralose of document (6) for the production of pharmaceuticals or food products (see point 4.1 above). The technical problem underlying the present application is therefore to reduce the amount of acetaldehyde and coloured oxidation products of sorbic acid and salts thereof in the aqueous liquid concentrates of sucralose of the closest prior art, while maintaining the concentration of sorbic acid for not impairing the desired antimicrobial effect.

4.2.2 As the solution to this problem, the present application proposes to add 0.1 to 5 parts by weight per million parts of solution of manganous ions (page 2, lines 13-16, page 4, lines 23-32).

4.2.3 In example 1 of the present application, various amounts of manganous ions were added to the sucralose-containing aqueous liquid concentrate disclosed in example I of document (6), namely an aqueous solution consisting of 25% by weight of sucralose, 0.22% by weight of a preservative system which is a mixture of potassium sorbate and sodium benzoate in a 1:1 ratio, 0.272% by weight of anhydrous citric acid and 0.258% by weight of sodium citrate dihydrate acting as a buffering system to obtain a pH of 4.4 and the rest water.

The stability of the solution according to document (6) and those containing various amounts of manganous ions was tested, by measuring (i) the amount of acetaldehyde of the solutions freshly prepared and after storage at 50°C for 5 and 10 days and (ii) the percentage of original sorbate remaining and the colour development after 59 days at 50°C.

As can be gathered from Figure 3, the samples containing at least 0.2 ppm manganous ions contained no detectable acetaldehyde after 10 days, whereas the control composition according to example I of document (6) and compositions containing an amount of manganous ions below 0.1 ppm exhibited after 10 days undesired level of acetaldehyde.

It can also be deduced from the results shown in Figure 11 that the amount of sorbate remaining after 59 days of storage at 50°C is at its maximum when between 0.1 and 5 ppm of manganous ions are added to the sucralose concentrate. The results summarized in

Figure 10 also show that the colour development is at its lowest within this range.

Furthermore, the results summarized in Figures 10 and 11 show that the presence of at least 63 ppm of manganous ions, although it reduces the colour development, results in a higher loss of sorbate ions.

4.2.4 The above result clearly demonstrate that both crucial objectives, namely reduction of the colour development and reduction of the loss of sorbate ions, cannot be achieved by the mere addition of an arbitrary amount of manganous ions, but only by selecting a value for the amount of manganous ions in a specific range, namely that claimed. The addition of between 0.1 and 5 ppm of manganous ions to the sorbic acid or salts thereof present in the aqueous liquid concentrates of sucralose of document (6) reduces the amount of acetaldehyde and coloured oxidation products of sorbic acid and salts thereof, while maintaining the level of sorbic acid required for the desired antimicrobial effect. The Board is therefore satisfied that the claimed subject-matter solves the problem.

4.3 *Obviousness*

4.3.1 It remains to decide whether or not the proposed solution is obvious in view of the state of the art. When looking for a solution to the above problem, the skilled person would have reason only to refer to documents which relate to the lack of stability of sorbic acid or salt thereof, such as documents (1), (2), (3), (9) or (10) in these proceedings.

4.3.2 Document (1) relates to food preservative compositions containing a preserving agent, selected from the group consisting of propionic acid, sorbic acid, benzoic acid, methyl and ethyl esters of benzoic acid and edible salts of these acid and a potentiating agent in the form of an edible mineral salt selected from the group consisting of salts of iron, manganese, zinc, tin, and silver (column 2, lines 33 to 43). The combination of preserving agent and potentiating agent brings about an increase of the antimicrobial effectiveness and of the life-span of the antimicrobial activity (column 1, lines 59 to 62). Document (1), however, is not concerned with the problem of avoiding the formation of acetaldehyde or coloured oxidation products of sorbic acid. As a particular example of a salt stabilizing the preserving activity of sorbic acid, document (1) discloses manganese chloride (column 3, lines 18-20). In Example II the antimicrobial effectiveness of an aqueous solution containing solely sorbic acid (0.1% by weight) and 0.001% of $MnSO_4$, corresponding to about 3 ppm of manganous ions is also tested. This example would at most indicate that the antimicrobial effectiveness of sorbic acid is higher in the presence of manganous ions. It does not provide any indication of the amount of sorbic acid remaining, nor does it suggest that the content of acetaldehyde or coloured oxidation products will be reduced with the quantity of manganous ions employed. It can be furthermore deduced from document (1), based on the proportions of edible salt and preservative substance recommended and the amount of food preservative contained in the food product (claim 5, column 4, lines 16 to 20, column 6, lines 26-36), that the food products taught in document (1) can contain manganous ions in much larger

amounts. Table III (column 7) discloses for example an amount of manganous ions of 436 ppm. As document (1) does not provide any information on the influence of the concentration of manganous ions on the antimicrobial effectiveness and life-span of the antimicrobial activity of the preservative composition, the skilled person would not derive from it any suggestion that an amount of manganous ions comprised between 0.1 and 5 ppm should be selected for a food composition. Thus, document (1) does not lead the skilled person towards the claimed solution.

4.3.3 Document (2) describes the influence of metal acetates on the oxidation of sorbic acid by molecular oxygen in acetic acid. In the presence of manganese acetate in concentration of 10^{-5}, 10^{-4}, 10^{-3} or 10^{-2} mol/l (corresponding to concentrations of 0.55 to 555 ppm), the percentage of oxidized sorbic acid, when initially present at a concentration of 0.07 M (7.8% by weight), is reported to be at most 6% during the first 6 hours at 80°C (page 2368, paragraph below figure 1). Although document (2) mentions amounts of manganese acetate of at least 0.55 ppm in order to retard the autoxidation reaction of sorbic acid, the skilled person looking for effectively improving the long term stability of sorbic acid in aqueous liquid concentrates of sucralose (test conditions used in the examples are up to 59 days at 50°C), would not further consider document (2) which already provides up to 6% oxidation after only 6 hours at a temperature of 80°C. Furthermore, document (2) does not suggest that the stability of sorbic acid may vary within the range of concentration of manganous ions employed. It cannot *a fortiori* suggest that the loss of sorbate ions is at its minimum within the range

of concentration selected in the present claim, when present in a sucralose composition. Nor does it even mention the existence of coloured oxidation products and *a fortiori* gives no hints how to reduce their content. Therefore, document (2) does not provide any incentive to modify the sucralose composition of document (6) in the direction of what is claimed.

4.3.4 Document (3) relates to effects of salts of heavy metals on the stability of sorbic acid in oxygenated dilute sulphuric acid solutions. According to the results summarized in table 1, page 55, concentrations of manganese sulphate of at least 10^{-3} mole/l corresponding to concentrations of manganous ions of at least 55 ppm are required to obtain a solution of sorbic acid (0.1 M, i.e. about 1 wt%; sulphuric acid 0.04 N) which exhibits a loss of sorbate of at most 1.4% after 23 hours at 25°C. Concentrations of 10^{-4} mole/l or less, corresponding to concentrations of manganous ions of 5 ppm or less, however, result in a much higher lost of sorbic acid (33.9% for 5 ppm, 62.6% for 0.55 ppm and 58.9% for 0.055 ppm; see table 1). Manganous ions are therefore reported to accelerate the oxidation of sorbic acid when present at low concentrations, but to retard the reaction in high concentrations (page 55, last paragraph). In addition, document (3) does not touch upon the formation of coloured oxidation products. Thus, the prior art document (3) gives no hints which would lead the skilled person to the solution now claimed.

4.3.5 Document (9) concerns the stability of sorbic acid in aqueous solutions. According to the authors a number of factors such as pH, temperature, trace metal ions salts,

amino acids, and other food additives such as sucrose, glycerol, acetic acid and alcohol considerably influence the stability of sorbic acid in aqueous systems, some of these factors having a prooxidant effect (page 1246, summary and page 1249, last paragraph). According to document (9) Cu^{2+}, Fe^{2+} and Mn^{2+} ions have a very pronounced stabilizing effect on the stability of sorbic acid in aqueous solution. The only amount tested was 50 ppm for which a reduction of the rate of degradation, corroborated by a reduction of the amount of glyoxal (page 1248, Tables V and VI), was observed. This document, however, does not teach the use of lower amounts of manganous ions. It is also silent on the influence of the amount of metal ions on the reduction of the loss of sorbate ions and on the development of coloured polymers of aldehydes. Therefore, document (9) would not lead the skilled person to the solution now claimed.

4.3.6 Document (10) which is a dielectric study of the autoxidation of ethyl sorbate neither indicates a way of increasing its stability, nor does it mention the possibility of using manganese ions. Thus, it would not lead the skilled person to the solution now claimed.

4.3.7 The other prior art documents cited in the proceedings are even more remote, as they do not even mention any stability problem with sorbic acid or salts thereof. Therefore, these documents would not lead the skilled person to arrive at the presently claimed solution.

4.4 The Board concludes that the skilled person who wanted to reduce in the aqueous liquid concentrates of sucralose of document (6) the amount of acetaldehyde

and coloured oxidation products of sorbic acid and salts thereof, while maintaining the level of sorbic acid required for the desired antimicrobial effect, would not have found in the available prior art any hint to add manganous ions in an amount of from 0.1 to 5 ppm. Consequently, the subject-matter of present claim 1 is considered to involve an inventive step as required by Article 56 EPC.

5. The Board notes that the description must still be adapted to the claim of the present request.

Order

For these reasons it is decided that:

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 the claim of the sole request submitted at the oral proceedings on 13 June 2007 and a description to be adapted thereto.

The Registrar: The Chairman:

C. Eickhoff S. Perryman