

The opinion in support of the decision being entered today was **not** written for publication and is **not** binding precedent of the Board.

Paper No. 19

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte PETER F. EISENHARDT and LEONARD P. SMITH

Appeal No. 1999-1216
Application No. 08/421,825

ON BRIEF

Before WILLIAM F. SMITH, ELLIS and MILLS, Administrative Patent Judges.
ELLIS, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 of the examiner's final rejection of claims 9-15 and 31-46, all the claims remaining in the application. Claims 1-8 and 16-30 have been canceled.

As a preliminary matter, we note that this appeal is related to Appeal No. 1999-1229 of Application No. 08/543,975. Thus, concurrent with the present decision, this merits panel is also rendering a decision in Appeal No. 1999-1229. However, we are not consolidating the appeals. The issues raised in each appeal have been considered only

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on the basis of the evidence provided therein and its relevancy to the claims in the involved application.

Claims 9 and 46 are illustrative of the claims in the present appeal and read as follows:

9. A process for the enzymatic hydrolysis of lactose in mammals with a solid, orally administrable composition comprising first and second active lactases, said process comprising:

hydrolyzing in the stomach environment having a first pH and a first portion of said lactose with the first, active lactase, said first, active lactase having a first optimum pH range which encompasses said first pH; and

hydrolyzing in the intestinal environment having a second pH a second portion of said lactose with the second, active lactase having a second optimum pH range which encompasses said second pH, said first pH and second pH being of a different magnitude.

46. A method for treating or controlling the symptoms of lactose intolerance comprising the oral administration prior to or concurrently with the ingestion of lactose-containing food, a solid, orally administrable composition comprising:

an amount of lactase derived from fungi selected from the group consisting of Aspergillus oryzae and Aspergillus niger equivalent to about 3000 to about 6000 FCC Lac U:

an amount of enterically coated lactase derived from Kluyvercomyces lactis equivalent to about 7000 to about 35,000 neutral lactase units; and

a solid pharmaceutically acceptable carrier.

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The references relied upon by the examiner are:

Sipos	4,079,125	Mar. 14, 1978
Kan et al. (Kan)	4,895,801	Jan. 23, 1990

Rosado, J. L. et al. (Rosado), "Enzyme Replacement Therapy for Primary Adult Lactase Deficiency", Gastroenterology, Vol. 87, pp. 1072-1082 (1984).

Gekas, V. et al. (Gekas), "Hydrolysis of Lactose: A Literature Review", Process Biochem., Vol. 20, No. 1, pp. 2-12 (Feb. 1985).

Barillas, C. et al. (Barillas), "Effective Reduction of Lactose Maldigestion in Preschool Children by Direct Addition of β -Galactosidases to Milk at Mealtime", Pediatrics, Vol. 79, No. 5, pp. 766-772 (May 1987).

Medow, M. S. et al. (Medow), " β -Galactosidase Tablets in the Treatment of Lactose Intolerance in Pediatrics, American Journal of Diseases of Children, Vol. 144, pp. 1261-1264 (Nov. 1990).

Claims 9-15 and 31-46 stand rejected under 35 U.S.C. § 103 as being unpatentable over the teachings of Barillas, Rosado, Medow, Gekas, Kan and Sipos.

We reverse.

BACKGROUND

Lactose is the sugar found in milk and whey. Specification, p. 1. Lactose is normally broken down (hydrolyzed) in the human digestive system by the enzyme lactase or β -D-galactosidase into two monosaccharides, glucose and galactose. Id. However, many individuals in the population lack the ability to hydrolyze lactose; these individuals are commonly referred to as being lactose intolerant. Id. Prior to the appellants' invention, lactose-intolerant patients were treated with tablets containing a lactase derived from A.

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oryzae, or by limiting the milk and dairy products in their diet to only those which had been pre-hydrolyzed. Specification, pp. 1-2.

As indicated by the claims, the present invention is generally directed to a method of hydrolyzing lactose in mammals which involves the use of a solid composition comprising two different lactases. The first lactase is capable of hydrolyzing lactose in the stomach at the pH range found therein; whereas, the second lactase is capable of hydrolyzing lactose in the intestines at the pH range normally found therewithin. The second lactase may be enterically coated to prevent deactivation by the gastric enzymes of the stomach environment. In addition, the invention encompasses a specific method of treating lactose-intolerance which involves the use of a solid composition comprising two specific lactases, i.e., a lactase derived from A. oryzae or A. niger, and a lactase derived from K. lactis, wherein the latter lactase is enterically coated.

DISCUSSION

The examiner's conclusion of obviousness is said to be based on the teachings of Barillas, Rosado, Medow, Gekas, Kan and Sipos.

To that end, we find that Barillas and Rosado each disclose the administration of a lactase derived either from the yeast K. lactis or from the fungus A. niger, to randomly-selected children and to healthy and lactose-intolerant adults, respectively. The authors quantified lactose absorption using a modified hydrogen breath analysis procedure.

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According to the examiner, the authors note a difference in the activity of the two enzymes, but she does not explain what the difference is, or its significance.

Answer, p. 4.

Medow discloses that the co-administration of lactose and lactase-containing tablets reduced the hydrogen breath secretion in 16 of 18 lactose-intolerant children by 89%.

Medow, p. 1263, col. 3, last para. The reduction of hydrogen breath secretion was said to be associated with a decrease in lactose-intolerant symptoms normally reported by the test group. Id.

Gekas is a review article which is

directed to the enzymatic and nonenzymatic methods of lactose hydrolysis and it contains recent information of the enzyme lactase and its immobilization techniques. Particular attention is given to large scale applications (pilot plant, semi-industrial, industrial) to the problem of sanitizing IME-systems and to the potential uses of lactose-hydrolyzed products [Gekas, p.1, col. 1, para. 5].

Gekas provides a Table listing known lactases from yeast, bacteria and fungi. Gekas discloses that

In general, fungal lactases have pH optima in the acid range (2.5-4.5) and yeast and bacterial lactases in the almost neutral region (6-7 and 6.5-7.5), respectively. This pH optimum property makes each lactase suitable for a specific application. Thus, fungal lactases are used for acid whey hydrolysis while yeast and bacterial lactases are suitable for milk (pH 6.6) and sweet whey (pH 6.1) hydrolysis [Gekas, p. 2, col. 2, para. 1].

Kan discloses the use of two different lactases, produced by different microorganisms, to hydrolyze lactose and to produce a sweet monosaccharide mixture

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of glucose and galactose which can be added to food and drinks. Kan, col. 1, lines 9-16.

The addition of the monosaccharide mixture to food and drinks is said to provide fewer calories than conventional additives. Id.

Sipos discloses methods of making enterically-coated, enzyme-containing compositions for use in mammals. Sipos, col. 1, lines, 17-20. The compositions are said to protect the enzymes contained therein from inactivation by the gastric conditions of the stomach and to enable release only in the duodenum. Id., col. 2, lines 43-58. Although never mentioned by the examiner, we note that Sipos discloses that lactases from microbial sources are suitable enzymes which can be formulated into an enterically-coated composition. Id., col. 5, lines 35-37.

According to the examiner [Answer, p. 5],

Clearly, the prior art motivates one of ordinary skill in the art to use a lactase enzyme in the treatment of lactose intolerance and to facilitate the hydrolysis of lactose in mammals. In view of the teaching of the prior art taken as a whole, the practitioner would reasonably expect that a "superior processing effect" would be obtained in vivo as well as in vitro by administering both enzymes together as the prior art acknowledges that one of ordinary skill in the art is well aware of the teachings of Rosado which show that either enzyme is individually effective when administered alone. Therefore, it would have been obvious per the disclosure of Kan et al. to optimize the degree of lactose hydrolysis by the administration of two different lactase enzymes having different optimum pH ranges for the purpose of maximizing the amount of lactase hydrolysis as the lactase travels from the stomach and the intestine. Each lactase enzyme is well known for both its activity and optimum pH range.

It is well established that the examiner has the initial burden under § 103 to establish a prima facie case of obviousness. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992); In re Piasecki, 745 F.2d 1468, 1471-72,

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223 USPQ 785, 787-88 (Fed. Cir. 1984). It is the examiner's responsibility to show that some objective teaching or suggestion in the applied prior art, or knowledge generally available [in the art] would have led one of ordinary skill in the art to combine the references to arrive at the claimed invention. Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc., 745 F.3d 1568, 1573, 37 USPQ2d 1626, 1629 (Fed. Cir. 1996). This the examiner has not done.

Here, as we understand it, the examiner is arguing that a species claim which is directed to the use of the two lactases taught by Rosado, and we aren't sure which claim(s) because the examiner does not specify regardless of the fact that they each contain different limitations, would have been obvious in view of the teachings of Kan because one ordinary skill in the art would have expected a "superior processing effect" by combining the individual lactases derived from K. lactis and A. niger into a single treatment. Thus, because the examiner believes that the species claim(s) would have obvious to one of ordinary skill in the art, she concludes that the generic claims also would have been obvious to such persons at the time the application was filed.¹

We find the examiner's arguments unpersuasive for the following reasons.

¹ In making the rejection, we point out that the examiner has only relied on the teachings of Rosado and Kan to support her position. The examiner has not argued any of the teachings of the remaining prior art references cited in the statement of the rejection. Thus, we presume that she believes the remaining references to be cumulative and have treated them accordingly.

First, contrary to the examiner's contention, we find no teaching or suggestion in the Kan patent as to a "superior processing effect" being obtained by simultaneously administering a solid, oral composition comprising lactases derived from K. lactis and A. niger, in vivo or in vitro. Nor do we find any teaching or suggestion in the patent that such an effect will be obtained, in vivo or in vitro, using two different lactases, derived from two different microorganisms. As discussed above, Kan discloses methods of treating lactose, in vitro, to produce monosaccharides to use as food and drink additives. To that end, Kan states that "a superior processing effect" can be obtained when successive lactase treatments are performed. That is, Kan discloses a method wherein one lactase derived from one microorganism is first added to a lactose solution, the hydrolysis reaction performed, and the first enzyme inactivated; then a second lactase is added, a second hydrolysis reaction performed, and the second enzyme inactivated. Kan, col. 3, lines 25-34. Kan discloses that when successive treatments are performed, the reaction can be more easily controlled and, thus, "a superior processing effect can be obtained." Id. Accordingly, we find Kan's teachings with respect to a "superior processing effect" are diametrically opposed to the examiner's interpretation and application of said teachings.

Second, as discussed above, we find no teaching or suggestion in Kan as to a method which involves the simultaneous administration of lactases derived from both K. lactis and A. niger to a lactose-intolerant individual. Nor do we find, and the examiner has

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not pointed out, any teachings or suggestions in Kan as to a method of administering two different lactases, having different optimum pH ranges, to maximize the hydrolysis of lactose as it travels through the stomach to the intestine. On this record, we only find these suggestions in the appellants' disclosure. Thus, we agree with the appellants that the examiner has engaged in impermissible hindsight in making her determination of obviousness. In re Gorman, 933 F.2d 982, 987, 18 USPQ2d 1885, 1888 (Fed. Cir. 1991)("It is impermissible, however, simply to engage in a hindsight reconstruction of the claimed invention, using the applicant's structure as a template and selecting elements from references to fill the gaps"); Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 1138, 227 USPQ 543, 547 (Fed. Cir. 1985); W.L. Gore & Assocs. v. Garlock, Inc., 721 F.2d 1540, 1553, 220 USPQ 303, 312-313 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984)("To imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher").

Third, it appears that the examiner has not fully appreciated the actual subject matter encompassed by the claims. We point out that the most generic claim before us is directed to a method which employs a solid, orally administrable composition having two different lactases; one lactase functions optimally at the pH range found in the stomach and the second at the pH range found in the intestines. See claim 9, above. The more specific

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claims are directed to methods which comprise the use of solid, orally-administrable compositions comprising specific lactases, specific dosages, specific pH ranges, enteric coatings, etc. The examiner fails to address (i) any particular claim, or (ii) the actual limitations in any of the claims. Rather, we find that the rejection consists only of broad, sweeping generalizations as to why the claimed subject matter would have been obvious over the applied prior art. To that end, we remind the examiner that a conclusion of obviousness must be based on fact and not unsupported generalities. In re Freed, 425 F.2d 785, 787, 165 USPQ 570, 571 (CCPA 1970); In re Warner, 379 F.2d 1011, 1017, 154 USPQ 173, 178 (CCPA 1967), cert. denied, 389 U.S. 1957 (1968).

Therefore, on this record, we reverse the rejection.

The decision of the examiner is reversed.

REVERSED

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WILLIAM F. SMITH
Administrative Patent Judge

JOAN ELLIS
Administrative Patent Judge

DEMETRA J. MILLS
Administrative Patent Judge

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