

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. 28

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. 1999-1229
Application No. 08/543,975

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 1, 3-7, 16 and 18-30, all the claims remaining in the application. Claims 2, 8-15, 17 and 31-46 have been canceled.

As a preliminary matter, we note that this appeal is related to Appeal No. 1999-1216 of Application No. 08/421,825. Thus, concurrent with the present decision, this merits panel is also rendering a decision in Appeal No. 1999-1216. However, we are not

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consolidating the appeals. The issues raised in each appeal have been considered only on the basis of the evidence provided therein and its relevancy to the claims in the involved application.

Claims 1 and 30 are illustrative of the claims in the present appeal and read as follows:

1. A solid, orally administrable composition for the enzymatic hydrolysis of lactose comprising:

a therapeutic effective amount of a first, active lactase having a first optimum pH range; and

a therapeutic effective amount of a second, active lactase having a second optimum pH range, wherein said first and second optimum pH ranges being different; and

a solid pharmaceutically acceptable carrier.

30. A solid, oral dosage form for treating or controlling the symptoms of lactose intolerance in humans, comprising:

an amount of lactase derived from the 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 Kluyveromyces 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 1, 3-7, 16 and 18-30 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 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 composition for hydrolyzing lactose which comprises two different lactases which function optimally within different pH ranges. In addition, the invention is directed to various compositions which comprise a lactase derived from either Aspergillus oryzae or Aspergillus niger and Kluyveromyces lactis. The lactase derived from K. lactis can be enterically coated to prevent deactivation by the gastric enzymes of the stomach environment.

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 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 quantify lactose absorption using a modified hydrogen breath analysis procedure. 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%.

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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 to produce a sweet monosaccharide mixture 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 protect the enzymes contained therein from inactivation by the gastric conditions of the stomach

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and 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, pp. 5-6]:

Clearly, the prior art motivates one of ordinary skill in the art to formulate a lactase enzyme in the treatment of lactose intolerance and to facilitate the hydrolysis of lactose in mammals. The claims differ from the teachings of Barillas, Medow and Rosado in that none of the references teach the combination of the two lactases together in a solid, orally administrable formulation. However, in view of the teaching of the prior art taken as a whole, the practitioner would reasonably expect that a “superior processing effect” (per the teaching of Kan) 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, 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

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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 a solid, orally-administrable composition comprising the two lactases taught by Rosado and Barillas, 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.

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, orally-administrable 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

¹ In making the rejection, we point out that the examiner has apparently only relied on the teachings of Rosado, Barillas and Kan to support her position. The examiner mentions Medow only in the context of how its teachings differ from the claimed invention, but has not applied the teachings of the reference in an affirmative manner. Thus, we find that although cited in the statement of the rejection, the examiner has not relied the teachings of Medow, Gekas or Sipos, to support her arguments. Therefore, we presume that she believes these references to be cumulative and have treated them accordingly.

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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 first one lactase derived from one microorganism is 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 to combine a lactase derived from K. lactis and a lactase derived from A. oryzae into a single solid, oral administrable formulation. Nor do we find, and the examiner has not pointed out, any teachings or suggestions in the Kan patent to administer two different lactases having two different optimum pH ranges to maximize lactose hydrolysis (i) in vitro or in vivo, or (ii) as the lactose travels through the stomach to the intestine. Rather, on this record, we only find such suggestions in the appellants’ disclosure. Thus, we agree with the appellants that the

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examiner has engaged in impermissible hindsight in making her determination of obviousness. In re Gorman, 933 F.2d 982, 987, 18 USPQ2d 1855, 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 solid, orally administrable composition having a therapeutically effective amount of two different lactases, having two different optimum pH ranges, and a solid pharmaceutically acceptable carrier. See claim 1, above. The more specific claims are directed to 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

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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).

Accordingly, we reverse the rejection.

Thus, on this record, the decision of the examiner is reversed.

REVERSED

WILLIAM F. SMITH)	
Administrative Patent Judge)	
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)	BOARD OF PATENT
JOAN ELLIS)	APPEALS
Administrative Patent Judge)	AND
)	INTERFERENCES
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