

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.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. 11

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte WOODROW C. MONTE

Appeal No. 1997-3537
Application No. 08/395,867¹

ON BRIEF

Before WINTERS, SPIEGEL, and SCHEINER, Administrative Patent Judges.
SPIEGEL, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1 through 14, which are all of the claims pending in this application.²

Claims 1 and 2 are illustrative and read as follows:

¹ Application for patent filed February 28, 1995. According to appellant, this application is a continuation of application 08/123,794 filed September 20, 1993, now abandoned.

² As acknowledged by appellant, "Claim 6 is objected to because in line 8 "bone" should be -- bovine--". Applicant endeavors to correct this informality at the conclusion of this Appeal" (brief, p. 2). However, this error in claim 6 has not been corrected by amendment as of the mailing date of this decision.

1. An article of manufacture for use in altering the appearance to the immune system of an infant of protein sections of bovine serum albumin, said article of manufacture comprising
 - (a) a sealed container;
 - (b) a nutritionally balanced milk formulation in said sealed container, said milk formulation including bovine serum albumin and including an active protease enzyme in a concentration of 0.025 to 100 milligrams of said enzyme per liter of said milk formulation, said protease enzyme in said container cleaving protein-to-protein bonds to alter the structure of said bovine serum albumin.

2. A dietary enzymatic process for enabling the immune system of an infant to distinguish between the ABBOS amino acid section of bovine serum albumin and the p69 amino acid section of insulin-producing beta cells, comprising the steps of
 - (a) preparing an infant milk formula, said infant milk formula being prepared by
 - (i) sterilizing a milk formulation including bovine serum albumin;
 - (ii) adding a sterilized protease enzyme to said milk formulation in a concentration of 0.025 to 100 milligrams of said enzyme per liter of said milk formulation;
 - (b) packaging said infant milk formula prepared in step (a) in a sealed container such that while said milk formula is in said container, said protease enzyme cleaves peptide bonds of said bovine serum albumin to alter the ABBOS amino acid section of the bovine serum albumin such that anti-ABBOS antibodies produced by an infant ingesting said infant milk formula will not attack the p69 amino acid section of insulin-producing beta cells in the infant; and,
 - (c) feeding the infant by opening said container and administering said infant milk formula to the digestive tract of the infant such that the infant's immune system is exposed to the altered ABBOS amino acid section of the bovine serum albumin.

Appeal No. 1997-3537
Application No. 08/395,867

The references relied on by the examiner are:

Thibault	4,981,704	Jan. 1, 1991
Martinez et al. (Martinez)	5,405,637	Apr. 11, 1995 (filed Jun. 30, 1993)

Karjalainen et al. (Karjalainen), "A Bovine Albumin Peptide as a Possible Trigger of Insulin-Dependent Diabetes Mellitus," The New England Journal of Medicine, Vol. 327, No. 5, pp. 302-307 (July 30, 1992)

A reference relied on by the appellant (brief, p. 8) is:

J. Rennie, "Formula for Diabetes: Cow's milk for infants may contribute to the disease," Scientific American, Vol. 267, No. 4, pp. 24-25 (October 1992).^{3,4}

ISSUE⁵

Claims 1-14 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Thibault or Martinez either in view of Karjalainen. We REVERSE.

In reaching our decision in this appeal, we have given careful consideration to the appellant's specification and claims and to the respective positions articulated by the appellant and the examiner. We make reference to the examiner's answer (Paper No. 9, mailed March 6, 1997) for the examiner's reasoning in support of the rejections and to the

³ Made of record by the examiner on the PTO-849 attached to the Office action mailed July 11, 1995 (Paper No. 2).

⁴ Appellant has apparently inverted the journal title to "American Scientific" on p. 8 of the brief.

⁵ The examiner has withdrawn the final rejection of claims 1-14 under 35 U.S.C. § 112, second paragraph, regarding the term "partially" (answer, p. 3).

Appeal No. 1997-3537
Application No. 08/395,867

appellant's brief (Paper No. 8, filed December 16, 1996) for the appellant's arguments thereagainst.

BACKGROUND

As explained by Karjalainen (p. 302):

Abstract Background. Cow's milk has been implicated as a possible trigger of the autoimmune response that destroys pancreatic beta cells in genetically susceptible hosts, thus causing diabetes mellitus. Studies in animals have suggested that bovine serum albumin (BSA) is the milk protein responsible, and an albumin peptide containing 17 amino acids (ABBOS) may be the reactive epitope. Antibodies to this peptide react with p69, a beta-cell surface protein that may represent the target antigen for milk-induced beta-cell--specific immunity.

Indeed, all of the diabetic patients studied by Karjalainen had elevated levels of anti-BSA antibodies (but not of antibodies to other milk proteins), the bulk of which were specific for ABBOS (abstract, p. 302; p. 303, c. 2, para. 4).

THE INVENTION

The claimed invention is directed to processes for enzymatically hydrolyzing BSA (claims 6 and 11), in particular its 17 amino acid ABBOS portion (claims 2-5, 10 and 12-14), in infant milk formula such that antibodies produced by an infant ingesting the hydrolyzed milk formula will be reactive with an altered, i.e., hydrolyzed, ABBOS epitope and, consequently, will not attack the p69 protein of the infant's pancreatic beta cells (claims 2-5, 10 and 14); and, to sealed containers of infant milk formula containing

hydrolyzing enzyme, i.e., a protease (claims 1 and 7-9). All claims require 0.025 to 100 milligrams of protease per liter of infant milk formula.

OPINION

Thibault and Martinez both describe hypoallergenic milk products containing partially hydrolyzed whey proteins prepared by enzymatic hydrolysis using a mixture of chymotrypsin/trypsin. Thibault uses an enzyme mixture having a chymotrypsin/trypsin activity ratio between 1.5 and 3.0 under defined conditions until the alpha-lactalbumin is totally eliminated, followed by separation of the enzymes and residual unhydrolyzed proteins (c. 2, ll. 36-50; c. 3, ll. 46-53), principally serum albumin and immunoglobulins (c. 7, ll. 23-26). Martinez uses an enzyme mixture having a trypsin/chymotrypsin activity ratio of 1.3 to 18 (i.e., a chymotrypsin/trypsin activity of about 0.8 to about 5.6) to result in a 4 to 10% degree of hydrolysis (c. 2, ll. 11-18; c. 3, ll. 16-21) and discloses packaging infant formula hydrolysate in any type of conventional container, e.g., glass, plastic, coated metal cans, etc. (c. 6, ll. 24-26). Optionally, Martinez preheats the protein solution prior to hydrolysis to insure denaturation of whey protein fractions, e.g., BSA and immunoglobulin (c. 3, ll. 25-28).

Karjalainen has been discussed above. The examiner found that "Karjalainen teaches that ABBOS is the BSA peptide responsible for triggering diabetes because anti-

BSA antibodies form against ABBOS and subsequently bind to p69, pancreatic beta-cell surface proteins, causing the development of diabetes" (answer, p. 6).

According to the examiner,

[i]t would have been obvious ... to prepare an infant milk formula ... as claimed since Thibault and Martinez clearly suggest using proteases to reduce large peptides in infant milk (BSA)-containing foods, and Karjalainen teaches that BSA is not desirable in infant milk formulae due to the presence of ABBOS (a large peptide). ... [R]emoval [of ABBOS prior to infant digestion] alters the appearance of BSA to an infant's immune system which prevents the creation of antibodies against ABBOS so that the p69 amino acid section is not affected. [Answer, para. bridging pp. 6-7.]

However, the examiner has not pointed out, and we do not find, where Karjalainen discloses or suggests using enzymatically hydrolyzed BSA in milk formulas to prevent onset of milk-induced diabetes. Rather, Karjalainen appears to suggest preventing exposure to cow's milk early in life to prevent onset of milk-induced diabetes by analogy to a diabetes-prone rodent model.⁶

Furthermore, to the extent the examiner relies on inherency to establish that "the hypoallergenic milk formulation is basically the same as the milk formulation claimed" (answer, p. 9), that reliance appears misplaced for several reasons. First, both Thibault and Martinez use enzyme mixtures comprising trypsin and chymotrypsin. Karjalainen

⁶ Karjalainen "suggests that an active, antigen-driven immune response against the BSA-derived ABBOS peptide is a feature of the autoimmune response in patients with insulin-dependent diabetes. This likens the disease in humans to that in diabetes-prone rodents, in which the prevention of exposure to cow's milk early in life prevents the development of the disease." (p. 307, c. 1, ll. 1-7, footnote omitted, emphasis added).

explicitly states that trypsin "leaves much of the ABBOS sequence intact" (p. 306, c. 2). Second, Thibault explicitly states that albumin is "hydrolysable with the most difficulty by the enzyme system adopted," and explicitly states that serum albumin and immunoglobulins are the principal "residual proteins" left by the described trypsin/chymotrypsin enzyme system (c. 7, ll. 23-26). Similarly, Martinez describes an "optional preliminary step prior to hydrolysis ... [of] preheating of the protein solution to insure denaturation of whey protein fractions, e.g., serum albumin (BSA) and immunoglobulins (particularly IgG)" (c. 3, ll. 25-28). Thus, Martinez also suggests that the disclosed trypsin/chymotrypsin enzyme system may not be effective to hydrolyze BSA. Third, while Martinez states that its hydrolysate "is preferably devoid of detectable intact milk protein" (c. 4, ll. 18-20), the examiner has not established on this record that the loss of "detectable intact milk protein" necessarily means that the milk proteins have been hydrolyzed, i.e., cleaved, as opposed to denatured such that their quaternary structure is simply unfolded somewhat. Thus, it is unclear on this record that the enzymatic hydrolysis steps of Thibault or Martinez will inherently result in the claimed invention. In other words, the examiner has not established a factual basis upon which to conclude that the trypsin/chymotrypsin hydrolysis method and resulting hydrolysate of Thibault or Martinez would reasonably be expected to hydrolyze BSA, in particular its ABBOS sequence so as to result necessarily in the claimed invention.

Appeal No. 1997-3537
Application No. 08/395,867

Based on this record, we find that the examiner has relied on impermissible hindsight in making her determination of obviousness. In re Fritch, 972 F.2d 1260, 1266, 23 USPQ2d 1780, 1784 (Fed. Cir. 1992) (“It is impermissible to engage in hindsight reconstruction of the claimed invention, using the applicant’s structure as a template and selecting elements from references to fill the gaps”).

Accordingly, the rejection is reversed.

CONCLUSION

To summarize, the decision of the examiner to reject claims 1-14 under 35 U.S.C. § 103(a) as unpatentable over Thibault or Martinez either in view of Karjalainen is reversed.

REVERSED

SHERMAN D. WINTERS)	
Administrative Patent Judge)	
)	
)	
)	BOARD OF PATENT
CAROL A. SPIEGEL)	APPEALS
Administrative Patent Judge)	AND
)	INTERFERENCES
)	
)	
TONI R. SCHEINER)	
Administrative Patent Judge)	

Appeal No. 1997-3537
Application No. 08/395,867

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APPEAL NO. 1997-3537 - JUDGE SPIEGEL
APPLICATION NO. 08/395,867

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DECISION: **REVERSED**

Prepared By: **Cheryl**

DRAFT TYPED: 24 Sep 01

FINAL TYPED: 13 Oct 00