

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.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. 23

UNITED STATES PATENT AND TRADEMARK OFFICE

---

BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES

---

Ex parte ERIC C. REYNOLDS

---

Appeal No. 1997-2364  
Application 08/137,086<sup>1</sup>

---

ON BRIEF

---

Before WILLIAM F. SMITH, SPIEGEL and SCHEINER, Administrative Patent Judges.  
SCHEINER, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 1 through 18, all the claims pending in the application. Claims 1, 2, 7, 10, 12 and 17 are representative of the claims on appeal and read as follows:

---

<sup>1</sup> Application for patent filed March 4, 1994.

1. A method for the preparation of selected phosphopeptides comprising the steps of:

completely digesting a soluble monovalent cation salt of casein in solution, introducing a di or trivalent metal ion to cause aggregation of at least the selected phosphopeptides in said digested solution, and

diafiltering the digested solution containing the aggregating ion through a filter having a molecular weight exclusion limit selected to retain at least said aggregated phosphopeptides while passing the bulk of the remaining phosphopeptides in a filtrate, wherein the metal ion concentration during diafiltration is maintained at a level effective to maintain the aggregated phosphopeptides in aggregate form.

2. The method of claim 1, wherein the selected phosphopeptides are anticariogenic phosphopeptides and the molecular weight exclusion limit adopted during the filtering step substantially falls within the range 10,000 to 20,000.

7. A method for the preparation of selected phosphopeptides having anticariogenic and other activities, comprising the steps of:

completely digesting a soluble monovalent cation salt of casein in solution with a proteolytic enzyme,

adding a mineral acid to the solution to adjust the pH to about 4.7,

removing any precipitate produced,

adding  $\text{CaCl}_2$  to the digested solution to a level of about 1.0% w/v to cause aggregation of at least the selected phosphopeptides in said digested solution, and separating the aggregated phosphopeptides from the solution by filtration including

diafiltration with the  $\text{CaCl}_2$  containing solution through a filter having a molecular weight exclusion limit lying substantially within the range 10,000 to 20,000 while passing the bulk of the remaining phosphopeptides and non-phosphorylated peptides and solution in a filtrate, wherein the metal ion concentration during diafiltration is maintained at a level effective to maintain the aggregated phosphopeptides in aggregate form.

10. Phosphopeptides when produced by the method of claim 1.

12. The method of claim 1, wherein the diafiltering step further comprises diafiltering the digested solution with one or more volumes of a solution of the metal ion.

17. An anticariogenic composition consisting essentially of phosphopeptides prepared by the method of claim 1, wherein the composition is substantially free of phosphopeptides having a molecular weight of less than about 10,000.

The reference relied on by the examiner is:

Appeal No. 1997-2364  
Application 08/137,086

Brule et al. (Brule)

4,816,398

Mar. 28, 1989

In the Examiner's Answer (paper no. 19), the examiner withdrew the two rejections (under 35 U.S.C. §§ 102 and 103) set forth in the final rejection (paper no. 11), and entered two new rejections. In response to the new grounds of rejection, appellant proposed amendments to the claims, and submitted arguments largely directed to the proposed claims (Reply Brief, paper no. 21). The examiner refused to enter the amendments, maintaining that the amendments would require additional searching and more than a cursory review of the record, and continued to address the claims as presented at the time of the final rejection (Supplemental Answer, paper no. 22). Appellant made no further response. As matters now stand, the claims are rejected as follows:

I. Claims 1 through 6, 8 through 14, 17 and 18 under 35 U.S.C. § 102(b) as anticipated by, or in the alternative, under 35 U.S.C. § 103 as obvious over Brule.

II. Claims 1 through 18 stand rejected under 35 U.S.C. § 103 as obvious over Brule.

We reverse both rejections.

#### DISCUSSION

"[F]our of the many phosphopeptides released by tryptic digestion of casein" "contain the active sequence Ser(P)-Ser(P)-Ser(P)-Glu-Glu" and "have anticariogenic (tooth-decay-inhibiting) activity." According to appellant, "[p]hosphopeptides in the presence of 1.0% w/v calcium (II) aggregate" and "[t]he anticariogenic phosphopeptides . . . form hexamers which [can be] separated from the smaller non-anticariogenic

Appeal No. 1997-2364  
Application 08/137,086

phosphopeptide aggregates.” “[I]n order to maintain the integrity of the anticariogenic phosphopeptide aggregates,” and “allow[] separation of the anticariogenic from the non-anticariogenic phosphopeptides,” “[t]he addition of a CaCl<sub>2</sub> solution, or some other suitable di/trivalent metal ion . . . is essential” during diafiltration, and the “molecular weight exclusion limit of the membrane filter should not be less than 10,000 or greater than about 20,000.” Specification, pages 1, 3 and 4.

#### Rejection I

Claims 1 through 6, 8 through 14, 17 and 18 are directed to a process of preparing selected phosphopeptides, and to products of that process. The claims stand rejected as anticipated by, or in the alternative, as obvious over Brule.

It is well settled that the initial burden of establishing unpatentability rests on the examiner, In re Oetiker, 977 F.2d 1443, 1446, 24 USPQ2d 1443, 1445 (Fed. Cir. 1992). That being said, we recognize that there are exceptions where the record justifies shifting the burden to appellant to show a difference between the claimed invention and the prior art. As explained in In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977):

Where . . . the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product . . . Whether the rejection is based on ‘inherency’ under 35 U.S.C. § 102, on ‘prima facie obviousness under 35 U.S.C. § 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO’s

inability to manufacture products or to obtain and compare prior art products  
[footnote omitted].

The examiner believes that shifting the burden of proof to appellant is appropriate in this instance because Brule “generally teaches the limitations that are reproduced in the invention summary,” and “[t]he only difference, if there is one, between the reference and the instant application is that . . . the concentration of the salt solution used for the diafiltration step” is not disclosed in the reference.<sup>2</sup> As Brule’s “final phosphopeptides are recovered as aggregates,” the examiner maintains that “it would have been obvious . . . to use a concentration of a salt solution that would keep the aggregates intact,” thus, “the isolation of the anti-cariogenic phosphopeptides would be inherent in the process.”

We disagree with the examiner’s analysis and conclusion. In our judgment, the facts of this case, as developed on this record, do not justify shifting the burden of proof to appellant.

Claims 1 and 10, which represent the invention in its broadest aspect, are directed to preparing and isolating selected phosphopeptides from casein, and to the isolated phosphopeptides, respectively. The method involves digesting a monovalent cation salt of casein in solution; aggregating at least the selected phosphopeptides in the solution with a

---

<sup>2</sup> We note the emphasis on “the invention summary” and “the instant application” in the statement of the rejection, and remind the examiner that “[a]nalysis begins with a key legal question -- what is the invention claimed?” since “[c]laim interpretation . . . will normally control the remainder of the decisional process,” Panduit Corp. v. Dennison Mfg. Co., 810 F.2d 1561, 1567-68, 1 USPQ2d 1593, 1597 (Fed. Cir.), cert. denied, 481 U.S. 1052 (1987). .

Appeal No. 1997-2364  
Application 08/137,086

di or trivalent metal ion; and diafiltering the digested solution, maintaining the metal ion concentration at a level effective to keep the selected phosphopeptides in aggregate form, and using a molecular weight exclusion limit effective to retain at least the selected phosphopeptides and allow the bulk of the remaining phosphopeptides to pass into a filtrate. Although the “selected phosphopeptides” are not defined in the claim, it is clear that they represent a subset of the total phosphopeptides in the digested solution, and that the molecular weight exclusion limit and the metal ion concentration during diafiltration are coordinated to permit separation of the hydrolysate into two fractions: one containing the selected phosphopeptides, and another containing both the remaining phosphopeptides and non-phosphorylated peptides.

Returning to Brule’s method, we find that a soluble monovalent cation salt of phosphocaseinate

is subjected to enzymatic hydrolysis by means of at least one proteolytic enzyme . . . the thus obtained hydrolyzate is subjected to at least one ultrafiltration step on membranes which allow all the peptides in the hydrolyzate to pass in the permeate; the permeate is added with at least one bivalent cation salt capable of forming aggregates with the phosphorylated fraction of said peptides, this leading to a solution which essentially contains aggregates of phosphopeptides and non phosphorylated peptides; and separation is effected by at least one ultrafiltration step between the non phosphorylated peptides and the phosphopeptides, the latter having a larger particle size, by bringing the solution into contact with at least one membrane capable of retaining said phosphopeptides (column 4, lines 7-25).

Brule teaches that “the amount of [bivalent cation salt] . . . is not critical,” and “it rests with those skilled in the art to select the bivalent compounds and amount thereof to be

used, also taking into account the subsequent stage of separation between the phosphopeptide aggregates and non phosphorylated peptides, said separation being effected . . . by an ultrafiltration step.” Moreover, Brule cautions that “due attention should also be paid especially to the cut off threshold of the ultrafiltration membrane, so as to avoid passage of the phosphopeptidic aggregate through this membrane” (column 6, line 67, through column 7, line 14, emphasis added).

Although “each of the above ultrafiltration steps may be followed by a diafiltration step during which there is added, continuously or discontinuously, a liquid such as water or aqueous salt-containing solution, with a view to further purify the ultrafiltration products,” there is no indication that maintaining the concentration of the bivalent cation will affect the end result. Indeed, Brule indicates that “water proved to be suitable for diafiltration.” Column 7, lines 30-36. Regardless, it is clear that the casein hydrolysate is separated into two fractions by Brule’s method: “on the one hand, as a permeate, non phosphorylated peptides, and on the other, as a retentate, phosphopeptides” (column 7, lines 45-47). This is in contrast to the claimed invention wherein one fraction contains selected phosphopeptides, and the other contains a mixture of other phosphopeptides and non-phosphorylated peptides.

Thus, we see no basis for the examiner’s assertion that Brule anticipates the claimed invention, even in its broadest aspect. Nor do we see any basis for concluding that it would have been obvious to adjust the concentration of the bivalent cation and/or the

Appeal No. 1997-2364  
Application 08/137,086

molecular weight exclusion limit to separate a subset of the phosphopeptides from the casein hydrolysate, especially as Brule purposely retains all of them.

As the examiner has not made out a prima facie case for even the broadest claim on appeal, the rejection of claims 1 through 15, 17 and 18 as anticipated by, or in the alternative, as obvious over Brule, is reversed.

### Rejection II

Claims 1 through 18 stand rejected as obvious over Brule, the same reference as in the previous rejection.

According to the examiner (Examiner's Answer, page 5):

The only elements in the references that absent is the specific aqueous salt solution,  $\text{CaCl}_2$  used in the diafiltration steps. The reference teaches generally that in the diafiltration step is added, "continuously or discontinuously, a liquid such as water or aqueous salt-containing solution" . . . wherein the molecular weight cut-off is chosen between 2000 to 50,000. The reference further teaches that the phosphopeptides recovered are as phosphopeptide aggregates (see claims). Therefore, although the reference does not specifically recite the specific salt-containing solution, it is the examiners position that it would have been prima facie obvious to one of ordinary skill in the art to use  $\text{CaCl}_2$  in the diafiltration step for isolating the phosphopeptide as an aggregated phosphopeptide because this was the aqueous salt solution used to form the aggregates.

As for the isolation of the anticariogenic peptides, the process would have inherently isolated those phosphopeptides with anti-cariogenic activity . . .

Again, we see no basis for concluding that it would have been obvious to adjust the concentration of the bivalent cation and/or the molecular weight exclusion limit to separate a subset of the phosphopeptides from the casein hydrolysate, as Brule purposely retains all of them.

Appeal No. 1997-2364  
Application 08/137,086

Accordingly, the rejection of claims 1 through 18 as obvious over Brule is reversed.

REVERSED

|                             |   |                 |
|-----------------------------|---|-----------------|
|                             | ) |                 |
| William F. Smith            | ) |                 |
| Administrative Patent Judge | ) |                 |
|                             | ) |                 |
|                             | ) |                 |
|                             | ) | BOARD OF PATENT |
| Carol A. Spiegel            | ) |                 |
| Administrative Patent Judge | ) | APPEALS AND     |
|                             | ) |                 |
|                             | ) | INTERFERENCES   |
|                             | ) |                 |
| Toni R. Scheiner            | ) |                 |
| Administrative Patent Judge | ) |                 |

Foley & Lardner  
P.O. Box 229

Appeal No. 1997-2364  
Application 08/137,086

Alexandria, VA 22313-0299