

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.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. 20

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte GEORGE M. HAIK JR.,

Appeal No. 2002-1871
Application No. 09/079,329

ON BRIEF

Before ADAMS, MILLS, and GREEN, Administrative Patent Judges.

GREEN, 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 47-49, 54-57 and 237-244. Claims 47-58 and 237-244 are pending, and claims 50-53 and 58 stand withdrawn from consideration as being drawn to a non-elected species. This appeal applies to the claims to the extent they read on the use of the elected species, D-arginine, in the claimed method.¹

Claims 47 and 237 are representative of the subject matter on appeal, and read as follows:

47. A method of blocking toxic carbonyl containing compounds and/or dicarbonyl containing compounds in a subject suffering from a condition associated with carbonyl containing compounds and/or dicarbonyl containing compounds by treating blood and/or blood products in a dialysis system for return to the subject comprising administering in the dialysis system a therapeutically effective dose to the subject's blood and/or blood products of a blocking agent selected from the group consisting of arginine, substituted arginine, or modified arginine.
237. A method of blocking toxic carbonyl containing compounds and/or dicarbonyl containing compounds in a subject suffering from a condition associated with carbonyl containing compounds and/or dicarbonyl containing compounds by treating blood and/or blood products in a dialysis system for return to the subject comprising administering in the dialysis system a therapeutically effective dose of D-arginine to the subject's blood and/or blood products.

The examiner relies upon the following references:

Lo et al. (Lo) "Binding and Modification of Proteins by Methylglyoxal under Physiological Conditions," The Journal of Biological Chemistry, Vol. 269, No.51, pp. 32299-32305 (1994)

Khaidar et al. (Khaidar) "L-Arginine Reduces Heart Collagen Accumulation in the Diabetic db/db Mouse," Circulation, Vol. 90, pp. 479-483 (1979)

Selwood et al. (Selwood) "Binding of Methylglyoxal to Albumin and Formation of Fluorescent Adducts, Inhibition by Arginine, Na Acetylarginine and Aminoguanidine," Biochemical Society Transactions, Vol. 21, AN 489354 p. 170S pp. 32299-32305 (1994)

Claims 47-49, 54-57 and 237-240 stand rejected under 35 U.S.C. § 112, first paragraph, on the grounds that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims. Claims 47-49, 54-57 and 237-240 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly

¹ In Paper No. 7, appellants elected D-arginine as the species to be examined.

claim the subject matter that applicant regards as the invention. Claims 47-49, 54,56, 237-244 stand rejected under 35 U.S.C. § 103(a) as obvious over Selwood or Lo as combined with the admitted prior art, and claims 47-49, 54-56 and 237-244 stand rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Khaidar and Lo. After careful review of the record and consideration of the issues before us, we reverse all of the rejections of record.

DISCUSSION

1. 35 U.S.C. § 112, First Paragraph, Enablement

Claims 47-49, 54-57 and 237-240 stand rejected under 35 U.S.C. § 112, first paragraph, on the grounds that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims.

The rejection asserts that the specification only illustrates the effects of arginine on methylglyoxal, while the claim reads on any carbonyl compound “as the term ‘toxic’ does not define any specific structure or origin of the carbonyl compounds being blocked.” Examiner’s Answer, page 5. The rejection contends further that there are no examples presented by the specification of blocking other carbonyl containing compounds, and that the disclosure provides no guidance as to what other compounds may be blocked and under what conditions. See id.

The rejection cites Lo and Selwood for their teachings of the blocking of methylglyoxal, and also cites Khaidar for is teaching of the possible interaction of arginine and carbonyl compounds involved in collagen cross-linking. But then

the rejection asserts that since the prior art “does not teach or suggest that arginine is capable [of interacting] with any carbonyl containing compound taken at random,” the state of the art is rendered unpredictable. See id.

The rejection thus concludes that as the prior art is unpredictable, and as there is insufficient guidance and working examples, “one skilled in the art could not make and/or use the invention with the claimed breadth without an undue amount of experimentation.” Id. at 6-7.

Appellant argues that the specification is enabling for carbonyl groups other than methylglyoxal. Appeal Brief, page 3. We agree.

“[A] specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.” In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971) (emphasis in original). “[It] is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement.” Id. at 224, 169 USPQ at 370. Here, the examiner has not provided “acceptable evidence or reasoning which is inconsistent” with the specification, and therefore has not met the initial burden of showing nonenablement.

The specification points to Table 1 as examples of dicarbonyl structures that can act as targets for the arginine blockers. See Specification, page 7, and Table 1. The rejection fails to provide evidence or scientific reasoning one of skill in the art would not expect them to be targets in the claimed method, and in fact, fails to address the Table at all.

The examiner also appears to be concerned with the use of the term “toxic” in the claims, asserting that the term “toxic” does not define any specific structure or origin of the carbonyl compounds being blocked. The specification at page 2, however, defines “toxic” carbonyl compounds as reactive carbonyl compounds that react with native proteins to form adducts and/or cross-linked complexes. There is no evidence of record that the skilled artisan would not recognize reactive carbonyl compounds that are present in the blood and are capable of reacting with D-arginine.

2. 35 U.S.C. § 112, Second Paragraph

Claims 47-49, 54-57 and 237-240 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that applicant regards as the invention.

The rejection objects to the use of the term “blocking.” According to the
Answer:

The term “blocking” in the claims is a relative term which renders the claims indefinite. It is not clear whether “blocking” means blocking from having a certain effect, physically blocking, chemically blocking, e.g., by forming coordinate or covalent bonds, etc. The term is not defined by the claim, or in the art, and one of ordinary skill in the art would not be reasonably apprised of the scope of the rejection.

Examiner's Answer, page 4.

Appellant argues that one of ordinary skill in the art would understand the meaning of "blocking." Appeal Brief, page 3. We agree.

The test for definiteness is whether one skilled in the art would understand the bounds of the claim when read in light of the specification." Miles Laboratories, Inc. v. Shandon, Inc., 997 F.2d 870, 875, 27 USPQ2d 1123, 1126 (Fed. Cir. 1993). Claims are in compliance with 35 U.S.C. § 112, second paragraph, if "the claims, read in light of the specification, reasonably apprise those skilled in the art and are as precise as the subject matter permits." Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1385, 231 USPQ 81, 94-95 (Fed. Cir. 1987).

The specification makes clear that the D-arginine of the method blocks the carbonyl containing compounds by means of a covalent bond. For example, the paragraph bridging pages 5 and 6 of the specification states:

It is an object therefore of the present invention to provide a method of removing toxic carbonyls and/or dicarbonyls, for example from a living body by administering a therapeutically effective dose of L- and/or D-arginine or an arginine-containing compound to a living body, the arginine thereby chemically reacting with the carbonyl group and preventing its reaction with native tissues.

(emphasis added).

Because one skilled in the art would understand "blocking" to mean blocking by covalent reaction, the rejection is reversed.

3. 35 U.S.C. § 103(a)

Claims 47-49, 54-56 and 237-244 stand rejected under 35 U.S.C.

§ 103(a) as being obvious over Selwood or Lo as combined with the admitted prior art.

Selwood and Lo are cited by the rejection for teaching that methylglyoxal covalently binds to blood proteins such as albumin, irreversibly modifying them, and that arginine and N- α -acetyl arginine inhibit that binding by competing for binding to methylglyoxal. The rejection then cites the specification for teaching that “[i]t is known . . . that accumulation of toxic reactive carbonyl compounds is related to some various disorders, e.g, diabetes mellitus, cataract, and kidney disorders,” and that “[t]he carbonyl compounds may be sugar-derived, such as glyoxal, methylglyoxal or their derivatives,”

The Answer concludes:

It would have been obvious to one skilled in the art at the time the invention was made to be motivated to use arginine or its derivatives to prevent undesired modification of albumin and other blood proteins by methylglyoxal because it is known in the art that accumulation of methylglyoxal is related to development of various disorder conditions and because Selwood and Lo teach that arginine and its derivatives inhibit interaction of albumin with methylglyoxal. One would be motivated to remove methylglyoxal from blood circulation as the primary site of its accumulation, and, to achieve that, one would be motivated to deliver arginine into blood either by administration of arginine, or by treatment of blood during blood dialysis, which is a routine procedure for removal of unnecessary contaminations from blood (see, e.g, references listed on p.19, lines 18-26, of the instant specification). One would be motivated to use arginine as methylglyoxal scavenger to preserve albumin and other blood protein from interaction with methylglyoxal because methylglyoxal may cause albumin modification and may cause albumin gelatinization, and preserving the blood proteins from such modifications is a desired effect

In respect to the use of D-arginine instead of L-arginine described in the reference, an optically active isomer is unpatentable over a prior art racemate or optical isomer of opposite rotation in the absence of unexpected or unobvious beneficial properties. In re Adamson et al., 125 USPQ 233 (CCPA 1960).

Id. at 7.

Appellant argues that neither Selwood nor Lo disclose the use of arginine to treat a subject in need thereof, nor do the references teach the use of D-arginine, and nor do the references teach or suggest the use of a blood dialysis system. Appeal Brief, page 4. We agree.

“In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness. Only if that burden is met, does the burden of coming forward with evidence or argument shift to the applicant.” In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). The test of obviousness is “whether the teachings of the prior art, taken as a whole, would have made obvious the claimed invention.” In re Gorman, 933 F.2d 982, 986, 18 USPQ2d 1885, 1888 (Fed. Cir. 1991).

Selwood and Lo, as noted by the rejection, teach that methylglyoxal covalently binds to blood proteins such as albumin, irreversibly modifying them, and that arginine and N- α -acetyl arginine inhibit that binding by competing for binding to methylglyoxal. There is no teaching or suggestion that arginine or N- α -acetyl arginine may be administered in a dialysis system to block the effects of methylglyoxal, nor do the references teach or suggest the use of D-arginine. The rejection asserts that dialysis is a routine procedure for removal of unnecessary contaminations from blood, and also asserts that the use of the

L-isomer renders the use of the D-isomer obvious. But “conclusory statements” as to teaching, suggestion or motivation to arrive at the claimed invention “do not adequately address the issue [of obviousness].” In re Lee, 277 F.3d 1338, 1343-44, 61 USPQ2d 1430, 1433-34 (Fed. Cir. 2002).

Because the examiner has failed to set forth a prima facie case of obviousness, the rejection is reversed.

Claims 47-49, 54-56 and 237-244 stand rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Khaidar and Lo.

According to the rejection, Khaidar teaches that reactive species such as methylglyoxal, which are found in the blood, mediate the cross-linking of physiological proteins, and that arginine can reduce that cross-linking, “it would have been obvious to treat blood to remove this by-products and to use arginine for their removal. As dialysis is a routine procedure for removal of unnecessary contaminations from blood, it would be obvious to remove methylglyoxal or other carbonyls using dialysis system.” Examiner’s Answer, page 8,

Appellant argues that the combination of Khaidar and Lo does not render obvious the claimed invention. Appeal Brief, page 5. We agree.

This rejection suffers the same deficiencies as the prior obviousness rejection, and for the reasons set forth with respect to that rejection, the rejection of claims 47-49, 54-56 and 237-244 over the combination of Khaidar and Lo is also reversed.

REVERSED

Donald E. Adams)	
Administrative Patent Judge)	
)	
)	
)	BOARD OF PATENT
Demetra J. Mills)	
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)	
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