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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte SHUHUA GU,
CHANGLIN MEI, DINGFENG SU,
JUAN DU, and RONG FAN

Appeal 2011-010613
Application 12/128,568
Technology Center 1600

Before TONI R. SCHEINER, DEMETRA J. MILLS, and
FRANCISCO C. PRATS, *Administrative Patent Judges*.

PRATS, *Administrative Patent Judge*.

DECISION ON APPEAL

This appeal under 35 U.S.C. § 134 involves claims to compositions and methods for treating myocardial ischemia. The Examiner entered a rejection for obviousness.

We have jurisdiction under 35 U.S.C. § 6(b). We reverse.

STATEMENT OF THE CASE

Claims 1-20 stand rejected and appealed (App. Br. 2). Claim 1 illustrates the appealed subject matter and reads as follows:

1. A pharmaceutical composition, comprising a) levocarnitine or its derivatives, and b) trimetazidine or its pharmaceutical acceptable salts; wherein the dosage of a) and b) of the composition is effective in treating myocardial ischemia and reducing the area of myocardial infarction, and wherein the weight ratio of a) and b) is 1:0.000016-1:0.4.

The sole rejection before us for review is the Examiner's rejection of claims 1-20 under 35 U.S.C. § 103(a) as obvious over Tracey¹ and Cavazza² (Ans. 4-8).

DISCUSSION

The Examiner cited Tracey as describing the use of trimetazidine combined with an NHE-1 inhibitor for reducing tissue damage resulting from ischemia (Ans. 5). The Examiner conceded that Tracey did not describe including levocarnitine, undisputedly also known as L-carnitine, in its therapeutic combination (*id.* at 6).

To address that deficiency, the Examiner cited Cavazza as evidence that L-carnitine was known in the art to be useful in the treatment of acute and chronic myocardial ischemia (*id.*).

Based on the references' combined teachings the Examiner reasoned that it would have been obvious to combine trimetazidine and L-carnitine to produce a composition useful for treating ischemia (*id.* at 8 (citing *In re Kerkhoven*, 626, F.2d 846, 850 (CCPA 1980)) (idea of combining ingredients "flows logically" from their having been individually taught in the prior art as being useful for the same purpose)).

As stated in *In re Oetiker*, 977 F.2d 1443, 1445 (Fed. Cir. 1992):

¹ U.S. Patent No. 6,423,705 B1 (issued July 23, 2002).

² U.S. Patent No. 4,743,621 (issued May 10, 1988).

[T]he examiner bears the initial burden . . . of presenting a *prima facie* case of unpatentability. . . .

After evidence or argument is submitted by the applicant in response, patentability is determined on the totality of the record, by a preponderance of evidence with due consideration to persuasiveness of argument.

We agree with Appellants that a preponderance of the evidence does not support the Examiner's *prima facie* case of obviousness.

As our reviewing court has explained, “section 103 requires a fact-intensive comparison of the claimed process with the prior art rather than the mechanical application of one or another *per se* rule.” *In re Ochiai*, 71 F.3d 1565, 1571 (Fed. Cir. 1995); *see also id.* at 1572 (“[R]eliance on *per se* rules of obviousness is legally incorrect and must cease.”).

Ultimately, therefore, “[i]n determining whether obviousness is established by combining the teachings of the prior art, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art.” *In re GPAC Inc.*, 57 F.3d 1573, 1581 (Fed. Cir. 1995) (internal quotations omitted).

Here, each of the independent claims recites either a composition that contains levocarnitine and trimetazidine (claim 1), or recites methods that require administering both agents for treating myocardial ischemia (claim 11), or recites methods that require combining the two agents to prepare a medicament (claims 17-20) (*see* App. Br. 14-18).

As the Examiner pointed out, Tracey discloses treating ischemia, including cardiac ischemia (Tracey, col. 3, ll. 14-20), with an inhibitor of the sodium/hydrogen exchange type-1 transport system (NHE-1 inhibitor) combined with a second compound which may be a “metabolic modulator”

(*id.* at col. 2, l. 30). As the Examiner also pointed out, a preferred metabolic modulator is “a partial fatty acid oxidation (pFOX) inhibitor, preferably ranolazine *or trimetazidine*” (*id.* at col. 8, ll. 27-29 (emphasis added)).

As Tracey explains, the purpose combining the metabolic modulator with the NHE-1 inhibitor was to increase glucose oxidation, and decrease fatty oxidation, thereby achieving a cardioprotective effect:

With respect to the methods and pharmaceutical compositions of the present invention, metabolic modulators such as pyruvate dehydrogenase kinase inhibitors, for example, dichloroacetate (DCA), activate the myocardial dehydrogenase (PDC) complex, thus increasing glucose oxidation *and decreasing fatty acid oxidation in the ischemic myocardium*. Accordingly, reduction of ischemic tissue damage by treatment with a combination of an **NHE-1** inhibitor and a metabolic modulator should elicit additional cardioprotective benefit.

(*Id.* at col. 8, ll. 8-18.)

While Tracey does not include levocarnitine in its formulations, as the Examiner pointed out, Cavazza discloses that “L-carnitine is used in the field of cardiovascular diseases for the treatment of acute and chronic myocardial ischemia” (Tracey, col. 1, ll. 32-34).

As Appellants point out, however, Müller describes a study showing that “oral L-carnitine supplementation results in an increase in long-chain fatty acid oxidation in vivo in subjects without L-carnitine deficiency or without prolonged fatty acid metabolism” (Müller 1389 (abstract); *see also, id.* at 1391 “[O]ur data show for the first time that supplementary L-carnitine significantly increases fatty acid oxidation as determined by the cumulative ¹³CO₂ exhalation method.”)).

Thus, while it may be true that levocarnitine was known in the art to be useful for treating cardiac ischemia, it was also undisputedly known in the art that administering levocarnitine significantly increased fatty acid oxidation. In contrast, as noted above, the purpose of including trimetazidine in Tracey's compositions was to *inhibit* fatty acid oxidation, and Tracey in fact discloses that trimetazidine was considered a fatty acid oxidation *inhibitor*.

We are therefore not persuaded that a preponderance of the evidence supports the Examiner's finding that an ordinary artisan would have been prompted to include levocarnitine, a known fatty acid oxidation stimulator, in Tracey's trimetazidine-containing, fatty acid oxidation-inhibiting compositions, nor are we persuaded that an ordinary artisan would have combined levocarnitine and trimetazidine in compositions or methods for treating cardiac ischemia, as the Examiner posits. We therefore reverse the Examiner's obviousness rejection.

REVERSED

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