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EXAMINER

KRISHNAN, GANAPATHY

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte PAUL LEONARD GREENHAFF and
DUMITRU CONSTANTIN-TEODOSIU¹

Appeal 2015-006392
Application 10/549,384
Technology Center 1600

Before RYAN H. FLAX, TIMOTHY G. MAJORS, and DAVID COTTA
Administrative Patent Judges.

MAJORS, *Administrative Patent Judge.*

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to methods of promoting carnitine accumulation in a subject's skeletal muscle, which have been rejected as obvious. We have jurisdiction under 35 U.S.C. § 6(b).

We reverse.

STATEMENT OF THE CASE

“[C]arnitine is essential in muscle metabolism and function . . . [and] the muscle store of carnitine is important for energy production in muscle.

¹ Appellants identify the Real Parties in Interest as The University of Nottingham and Lonza Sales, Ltd. (App. Br. 3.)

If the store of carnitine declines, the function of the muscle can be impaired.” (Spec. 1:7–10.) Appellants’ “invention relates to carnitine retention in biological tissue. More particularly, but not exclusively, the invention relates to compositions and methods of increasing carnitine retention in the animal and/or human body.” (*Id.* at 1:3–5.)

Claims 160 and 166–198 are on appeal. Claim 166 is representative and reads as follows:

166. A method for promoting carnitine accumulation in skeletal muscle of a subject in need thereof comprising increasing the serum insulin concentration to greater than 50 mU/L in the subject and orally administering L-carnitine to the subject, wherein the amount of L-carnitine is 0.25g to 3g.

(App. Br. 16 (Claims App’x).)

The claims stand rejected as follows:

- I. Claims 166–168, 183–186, 188, 189, and 196–198 under 35 U.S.C. § 103(a) over Cavazza,² Boyns,³ and Georges⁴ (“Rejection I”).

² Cavazza, US 4,320,145, issued Mar. 16, 1982 (“Cavazza”).

³ Boyns et al., *Oral Glucose Tolerance and Related Factors in a Normal Population Sample*, 1 BRIT. MED. J. 595–98 (1969) (“Boyns”).

⁴ Georges et al., *Carnitine Transport into Muscular Cells. Inhibition of Transport and Cell Growth by Mildronate*, 59 BIOCHEM. PHARMACOL. 1357–63 (2000) (“Georges”).

- II. Claims 160, 169–182, and 187–195 under 35 U.S.C. § 103(a) over Cavazza, Kamarei,⁵ Boyns, Van Loon,⁶ Georges, and Brantman⁷ (“Rejection II”).

DISCUSSION

Because the same issues are dispositive for both Rejection I and Rejection II, we address the rejections together. As indicated above, we select claim 166 as representative. 37 C.F.R. § 41.37(c)(1)(iv).

For both Rejections I and II, the Examiner relies on the teachings of Cavazza, Boyns, and Georges.⁸ (Ans. 3–5, 7–8.) The Examiner finds that “Cavazza teaches the administration of two 5% glucose solutions wherein one of them has L-carnitine admixed in it in an amount of 40mg/Kg to a subject.” (*Id.* at 4.) According to the Examiner, “Cavazza [] does not expressly teach the amount in grams of glucose in his compositions and that the administration of glucose . . . in his example causes increase in [the] insulin level to greater than 50mU/L as in claim 166.” (*Id.*)⁹

⁵ Kamarei, US 5,985,339, issued Nov. 16, 1999 (“Kamarei”).

⁶ Van Loon et al., *Plasma insulin responses after ingestion of different amino acid or protein mixtures with carbohydrate*, 72 AM. J. CLIN. NUTR. 96–105 (2000) (“Van Loon”).

⁷ Brantman, US 4,687,782, issued Aug. 18, 1987 (“Brantman”).

⁸ Rejection II further cites teachings of Kamarei, Van Loon, and Brantman.

⁹ The Examiner notes, however, that “in two instances a higher insulin level has been observed” (Ans. 4 (citing Cavazza Table 3.)) We understand the “two instances” to be the two subjects (among ten) whose insulins levels were “61.7” and “88.6” at the end of infusion of a 5% glucose solution + L-carnitine. (Cavazza col. 8 (Table 3.))

The Examiner finds that Boyns and Georges disclose the elements not taught by Cavazza. The Examiner finds Boyns teaches “insulin levels increase to about 75mU/mL after administration of 50g of glucose” and Georges teaches “carnitine is transported to the skeletal muscles and is found to be about fifty times higher in skeletal muscles.” (*Id.* (emphasis omitted).)

The Examiner concludes that “one of ordinary skill in the art would [] expect carnitine accumulation to be promoted in the human skeletal muscle by increasing the insulin concentration to greater than 50mU/L in a subject . . . since the method of Cavazza performs the same function.” (*Id.* at 4–5.) According to the Examiner, “analogous compositions comprising carnitine, glucose, amino acids and proteins are taught in the art and proteins and amino acids are also known to increase insulin levels and increase in insulin levels parallels the increase in sugar concentration.” (*Id.* at 6.)

The Examiner also concludes that “it is obvious to combine prior art elements and improve the method of the prior art to yield predictable results by making and administering compositions comprising the components in the claimed methods by increasing the concentration of insulin to greater than 50 mU/L.” (*Id.*) According to the Examiner, “[m]ethod improvement is the motivation” and “additional motivation is provided by Cavazza [] in that such a composition also has the effect of increased tissue utilization of the sugar (replenishment of [the] body’s energy reserves) and decreased levels of glucose in the peripheral blood.” (*Id.*)

Appellants argue that Cavazza does not teach all the elements of method claim 166, and that the secondary prior art references do not remedy Cavazza’s deficiencies. (App. Br. 11.) Appellants argue, *inter alia*, that

“Cavassa does not disclose or suggest oral administration of L-carnitine and an agent that increases blood plasma or serum insulin concentration.” (*Id.*) According to Appellants, “Cavazza goes to great lengths to emphasize that the described formulations are intended for parenteral administration only . . . [and] [n]o evidence has been provided by the Examiner to support the argument that Cavazza can be read to teach oral administration of the described formulations.” (*Id.* at 11–12; *see also* Reply Br. 1–2.)

On the present record, Appellants have the better position. As Appellants persuasively argue, Cavazza relates exclusively to parenteral administration (particularly intravenous (IV) infusion) of glucose solutions. (*See Cavazza passim.*) For example, claim 1 of Cavazza recites “[a] parenterally administrable pharmaceutical composition useful for nourishing patients *who cannot be fed via the enteral [i.e., oral] route . . .*” (*Id.* at col. 7, ll. 54–56 (emphasis added).)

Indeed, the formulations disclosed in Cavazza are designed to address unique problems arising with IV administration of glucose — adequately nourishing the patient *who cannot be fed orally* while preventing high blood-sugar levels and excessive secretion of insulin that would otherwise occur when administering IV solutions with high glucose concentrations. (*See id.* at Abstract and col. 1, ll. 5–67.) By combining L-carnitine with glucose in an IV solution, Cavazza teaches “[i]ncreased tissue utilization of glucose and, therefore, reduced glycaemia and decreased glucose level in the peripheral blood . . . [and] [d]isappearance of excessive insulin secretion which would occur in the absence of L-carnitine when administering an equal amount of glucose.” (*Id.* at col. 3, ll. 44–52.)

The Examiner does not identify any specific disclosure in Cavazza teaching or suggesting oral administration of Cavazza's formulations. Instead, the Examiner states that Cavazza's disclosure that the composition "is also for patients who need to receive nutrition via parenteral route for a few days only, as in case of patients who have been subjected to minor abdominal operations such as appendectomy or cholecystectomy" "indicates that . . . for subjects who have had such operations his composition need not be administered via the parenteral route." (Final Act. 12.) The Examiner thus states that Cavazza's composition "can be administered to such patients via other routes including the oral route after a few days." (*Id.* at 12–13; *see also* Ans. 13.)

The Examiner's reasoning and reading of Cavazza is not persuasive. The disclosure of Cavazza cited by the Examiner, in its full context, reveals a picture different from that painted by the Examiner:

[T]he invention relates to a glucose solution for nutrition by drip phleboclysis of any type of patient who may require, over a more or less long period, to be fed via the parenteral route. Such a solution is, therefore, *suitable for the nutrition of patients who need to receive nutrition via the parenteral route for a few days only*, as in the case of patients who have been subjected to minor abdominal operations such as appendectomy or cholecystectomy, *and for patients who cannot receive food via the enteral route for several weeks*, as in the case of patients who have been subjected to extended resections of the *intestinum tenue*, esophageal perforations, etc.

During the postoperative period, there arises, among other problems, the problem of providing the patient with a supply of energy in a utilizable form. The patient, for more or less long periods, according to severity and extension of the surgical operation, is unable to absorb via the enteral route the saccharide,

protein and lipid substrates which provide sources of utilizable energy.

The patient must, therefore, be fed via the parenteral route, generally by intravenous administration.

(Cavazza, col. 1, ll. 8–29 (emphasis added); *see also* App. Br. 12–13.)

Nothing in this disclosure teaches or suggests oral administration, either before or after parenteral administration. Quite the opposite, this disclosure — and the remainder of Cavazza’s teachings — confirms that Cavazza relates to parenteral administration alone.

Absent hindsight gleaned from Appellants’ disclosure, we are not persuaded the skilled artisan would have understood Cavazza as teaching or suggesting oral administration of a solution of glucose and L-carnitine. The Examiner has not identified other persuasive evidence or reasoning to make up for this deficiency in Cavazza. We thus conclude the Examiner has not met the burden to show that claim 166 or Appellants’ other method claims would have been *prima facie* obvious.

Having found that the Examiner did not establish a *prima facie* case of obviousness, we decline to address Appellants’ evidence of alleged unexpected results.

SUMMARY

We reverse the rejection of claims 166–168, 183–186, 188, 189, and 196–198 under 35 U.S.C. § 103(a) over Cavazza, Boyns, and Georges.

We reverse the rejection of claims 160, 169–182, and 187–195 under 35 U.S.C. § 103(a) over Cavazza, Kamarei, Boyns, Van Loon, Georges, and Brantmann.

REVERSED