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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/825,985	04/22/2013	Natarajan Ranganathan	KBI0027US.NP	3945

26259 7590 11/22/2019

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ART UNIT	PAPER NUMBER
1655	

NOTIFICATION DATE	DELIVERY MODE
11/22/2019	ELECTRONIC

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte NATARAJAN RANGANATHAN

Appeal 2018-008062
Application 13/825,985
Technology Center 1600

Before JEFFREY N. FREDMAN, JOHN G. NEW, and JAMIE T. WISZ, *Administrative Patent Judges*.

FREDMAN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal[1,2] under 35 U.S.C. § 134 involving claims to a method for removing nitrogenous waste products from the blood. The Examiner rejected the claims as obvious. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

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[1] We use the word "Appellant" to refer to "applicant" as defined in 37 C.F.R. § 1.42. Appellant identifies the Real Party in Interest as Kibow Biotech, Inc. (*see* App. Br. 1).

[2] We have considered and refer to the Specification of Mar. 26, 2013 ("Spec."); Final Action of July 20, 2017 ("Final Act."); Appeal Brief of Jan. 15, 2018 ("App. Br."); Examiner's Answer of June 15, 2018 ("Ans."); and Reply Brief of Aug. 8, 2018 ("Reply Br.").

Statement of the Case

Background

"One of the main functions of the kidney . . . is the disposal of waste products" (Spec. ¶ 2). "Any impairment of excretory function can lead to the accumulation of a variety of nitrogenous waste products" (*id.*). "Nitrogenous waste products accumulating in the blood stream have detrimental affects on health. Removal of nitrogenous wastes by diverting them into the colon is a viable approach to decrease the negative impact that waste product accumulation has on an individual's physiology" (*id.* ¶ 12). "The present invention combines the properties of a probiotic and edible protein into a product to both provide a source of protein and effectively reduce the blood concentration of nitrogenous waste products" (*id*. ¶ 12).

The Claims

Claims 4–7 are on appeal. Claim 4 is representative and reads as follows:

> 4. A method for removing nitrogenous waste products from the blood comprising administering to a subject with diabetic nephropathy, hypertensive nephrosclerosis, glomerulonephritis, interstitial nephritis or polycystic kidney disease and stage 5 renal failure an effective amount of a nutritional product comprising at least one probiotic component and 10 grams to 100 grams per serving of at least one isolated edible protein thereby removing nitrogenous waste products from the blood of the subject.

The Issue

The Examiner rejected claims 4–7 under 35 U.S.C. § 103(a) as obvious over Ranganathan,[3] Krenitsky, [4] and WebMD[5] (Ans. 3–5).

[3] Ranganathan, WO 2005/032591 A1, published Apr. 14, 2005.

The Examiner finds "Ranganathan teaches a method for removing nitrogenous waste products from the blood by administering a probiotic bacteria in combination with an edible protein" (Ans. 3). The Examiner finds Ranganathan teaches "Streptococcus as the bacteria and whey protein as the edible protein" and further teaches "the composition can be administered to patients who are in need of dialysis" and therefore stage 5 renal failure (Ans. 3).

The Examiner acknowledges that Ranganathan "does not specifically teach that the subject treated is suffering from both stage 5 renal failure and diabetic nephropathy" but finds Ranganathan teaches "accumulation of nitrogenous waste products that damages the kidneys can be caused by diabetes" (Ans. 3–4; citing WebMD).

The Examiner also finds Ranganathan does not teach "formulating the composition so that it contains 10 grams to 100 grams of protein per serving" (Ans. 4). The Examiner finds Krenitsky teaches "patients with stage 5 renal failure need 1.2 grams/kg/day of protein" and that "this amount of protein is about 54 grams per day for a 100 lb. patient" (Ans. 4).

Based on these teachings, the Examiner finds it obvious "to administer the composition taught by the reference to subjects with diabetic nephropathy and stage 5 renal failure" and "that a single dose with 100 grams would be suitable to meet the total protein requirements of a patient" (Ans. 4–5).

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[4] Krenitsky, *Nutrition in Renal Failure: Myths and Management*, Practical Gastroenterology 40, 42, 44, 46, 47, 51, 52, 54, 55, 58, 59 (2004).
[5] WebMD, http:/www.webmd.com/diabetes/tc/diabetic-nephropathy-topic-overview (2015) (accessed Sept. 28, 2015). We number the pages sequentially.

The issue with respect to this rejection is: Does a preponderance of the evidence of record support the Examiner's conclusion that Ranganathan, Krenitsky, and WebMD render the claims obvious?

Findings of Fact

1. Ranganathan teaches:

> In normal, healthy humans, metabolic waste nitrogen is primarily excreted via the kidneys as urea, uric acid creatinine, etc. in the urine. However, in individuals with kidney disease, as well as a number of other diseases such as inborn errors in urea cycle enzyme deficit, waste nitrogen accumulates in the body thereby manifesting toxic symptoms.

(Ranganathan 1:16–22).

2. Ranganathan teaches that "[i]n kidney failure there is a decrease in the glomerular filtration rate and . . . Nitrogenous wastes accumulate and a condition referred to as uremia develops" (Ranganathan 7:19–27).

3. Ranganathan teaches that "nearly 350,000 Americans suffer from end stage renal disease (ESRD), which is the final stage in chronic renal failure" (Ranganathan 1:13–15).

4. Ranganathan teaches:

> In renal failure the phosphorous levels in a subject may increase and lead to mineralization of various sites in the body. In addition there are several known and unknown substances of low and middle molecular weight which have been identified as uremic toxins which also accumulate. If untreated, acidosis and uremia can cause coma and eventually death.

(Ranganathan 8:17–23).

5. Ranganathan teaches "a composition for augmenting kidney function, particularly in subjects with renal insufficiency, comprising at least one probiotic bacterium" (Ranganathan 9:14–17).

6. Ranganathan teaches "[c]ompositions of the present invention can further contain . . . at least one protein" and "proteins include, for example, but are not limited to, cereal proteins, milk proteins, egg proteins, animal proteins, vegetable proteins, whey protein" (Ranganathan 15:16–18; 18:7–10).

7. Ranganathan teaches an example "of using a probiotic bacterium to reduce nitrogenous waste build up due to renal failure, probiotic compositions were fed to uremic rats" (Ranganathan 13:4–6).

8. Ranganathan teaches "the composition removes sufficient levels of uremic toxins such that a patient suffering from uremia either does not require dialysis, requires dialysis less frequently or for shorter durations, or does not require initiation of dialysis as soon as would be needed without treatment" (Ranganathan 20:28–33).

9. Ranganathan teaches the "precise amount of the compositions of the present invention ingested by a subject may be decided according to the judgment of a practitioner or dietician and each subject's circumstances" (Ranganathan 22:13–16).

10. Ranganathan teaches "waste products tend to accumulate in the gastrointestinal tract in any condition which disrupts the kidneys ability to excrete the build up of nitrogenous waste products . . . Conditions that affect nitrogen metabolism include, but are not limited to . . . Diabetes" (Ranganathan 21:5–15).

11. WebMD evidences that "[d]iabetic nephropathy is damage to your kidneys caused by diabetes. In severe cases it can lead to kidney failure" (WebMD 1).

12. Table 2 of Krenitsky is reproduced below:

Table 2
Selected nutritional parameters for varying levels of kidney failure[a]

Nutritional parameter	*Normal kidney function*	*Stages 1–4 Chronic kidney disease*	*Stage 5 Hemodialysis*	*Stage 5 Peritoneal dialysis*	*Transplant*
Calories (kcal/kg/d)	30–37	35 < 60 yrs 30–35 ≥ 60 yrs	35 < 60 yrs 30–35 ≥ 60 yrs	35 < 60 yrs 30–35 ≥ 60 yrs include calories from dialysate	30-35 initial 25–30 for maintenance
Protein (gm/kg/d)	0.8	0.6–0.75 50% HBV[b]	1.2 50% HBV	1.2–1.3 50% HBV	1.3–1.5 initial 1.0 for maintenance
Fat (% total kcal)	30%–35%	Patients considered at highest risk for cardiovascular disease; emphasis on PUFA[c], MUFA[d], 250–300 mg cholesterol/day			<10% saturated fat
Sodium (mg/d)	Unrestricted	2,000	2,000	2,000	Unrestricted; monitor medication effect
Potassium (mg/d)	Unrestricted	Correlated to laboratory values	2,000–3,000 (8–17 mg/kg/d)	3,000–4,000 (8–17 mg/kg/d)	Unrestricted; monitor medication effect
Calcium (mg/d)	Unrestricted	1,200	≤ 2,000 from diet and medications	≤ 2,000 from diet and medications	1,200
Phosphorus (mg/d)	Unrestricted	Correlated to lab values	800–1,000	800–1,000	Unrestricted unless indicted
Fluid (ml/d)	Unrestricted	Unrestricted with normal urine output	1,000 + urine output	Monitored; 1,500–2,000	Unrestricted unless indicated

a Meant as guidelines only for initial assessment; individualization to patient's own metabolic status and co-existing metabolic conditions is essential for optimal care.
b HBV=high biological value.
c PUFA=polyunsaturated fatty acids.
d MUFA=monounsaturated fatty acids.

"Reprinted from *Journal of the American Dietetic Association*, V104: 404-409, Beto JA et al.: "Medical nutrition therapy in chronic kidney failure: integrating clinical practice guidelines" © 2004, with permission from the American Dietetic Association.

Table 2 of Krenitsky discloses nutritional parameters for varying levels of kidney failure, specifically disclosing that stage 5 kidney failure patients may be fed 1.2–1.3 grams/kilogram/day of protein (Krenitsky 45, Table 2).

13. The Examiner calculates that a diet with 1.2 grams/kilograms/day of protein equals 54 grams per day for a 100 pound patient and 100 grams per day for a 180 pound patient (*see* Ans. 4).

Principles of Law

A prima facie case for obviousness "requires a suggestion of all limitations in a claim," *CFMT, Inc. v. Yieldup Int'l Corp*., 349 F.3d 1333, 1342 (Fed. Cir. 2003) and "a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the

claimed new invention does." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007).

Analysis

We adopt the Examiner's findings of fact and reasoning regarding the scope and content of the prior art (Ans. 3–5; FF 1–13) and agree that the claims are rendered obvious by Ranganathan, WebMD, and Krenitsky. We address Appellant's arguments below.

> Appellant contends
>
> > the Examiner has mischaracterized the teachings at page 21 of Ranganathan. In particular, the cited disclosure indicates that "[t]oxins and waste products tend to accumulate in the gastrointestinal tract in any condition which disrupts the kidneys ability to excrete the build up of nitrogenous waste products in the blood." However, this does not constitute a teaching or suggestion of "kidney damage" as the Examiner contends

(App. Br. 8–9).

We find this argument unpersuasive because Ranganathan explains that "in individuals with kidney disease . . . waste nitrogen accumulates in the body thereby manifesting toxic symptoms" (FF 1). Ranganathan connects the teaching that waste products "disrupt[] the kidneys ability to excrete the build up of nitrogenous waste products" (FF 10) with the teaching that in "kidney failure . . . Nitrogenous wastes accumulate and a condition referred to as uremia develops" (FF 2). Thus, Ranganathan directly recognizes that the toxic buildup of nitrogenous wastes is associated with kidney failure (FF 1, 2, 10). Indeed, Ranganathan exemplifies "using a probiotic bacterium to reduce nitrogenous waste build up due to renal failure" when "probiotic compositions were fed to uremic rats" (FF 7).

WebMD evidences that kidney damage "can lead to kidney failure" (FF 7), further demonstrating the association between kidney failure and kidney damage. Thus, the ordinary artisan would reasonably have interpreted Ranganathan's teaching that the probiotic treats uremic syndrome as also treating kidney damage.

Appellant contends "the Examiner has not established that the cited prior art provides evidence that the concentration of protein was recognized to be a result-effective variable for the claimed purpose, *i.e.*, removing nitrogenous waste products from the blood and for ameliorating stage 5 renal failure" (App. Br. 9).

We find this argument unpersuasive because Ranganathan expressly teaches optimization of the amounts of the composition, teaching the "precise amount of the compositions of the present invention ingested by a subject may be decided according to the judgment of a practitioner or dietician and each subject's circumstances" (FF 9). In applying this teaching of choosing amounts of components such as protein for a kidney failure patient, the ordinary artisan would have been guided by teachings in the prior art such as Krenitsky, who suggests diets containing 1.2–1.3 gm/kg/d of protein for patients with kidney failure (FF 12), amounts that the Examiner has calculated overlap with the amounts recited in claim 4 (FF 13). Appellant does not dispute this overlap. To the extent that Ranganathan has a slightly different reason for optimizing the protein concentration to suit a particular patient, that Ranganathan has a different reason for optimization of the parameter of protein amounts is not persuasive. *See In re Kemps*, 97 F.3d 1427, 1430 (Fed. Cir. 1996) ("[T]he

motivation in the prior art to combine the references does not have to be identical to that of the applicant to establish obviousness.").

Appellant contends that Krenitsky does not teach or suggest that the totality of the protein must come from a single dietary source or food product" (App. Br. 10).

We find this argument unpersuasive because none of the claims require that all of the protein eaten by a patient must come from a "single dietary source or food product." Instead, claim 4 recites administering a probiotic with from "10 grams to 100 grams per serving of at least one isolated edible protein." Thus, as the Examiner points out:

> Since Ranganathan suggests one or more daily dosages of the product, the artisan would recognize that a single dose with 100 grams would be suitable to meet the total protein requirements of a patient while a product with a lower dose such as 10 grams would be suitable as a divided dosage or as a supplementary protein source.

(Ans. 8). That is, the ordinary artisan would have appreciated that multiple servings of probiotic and protein could be served to a patient in order to achieve the optimized amounts of these components as suggested by Ranganathan (FF 9) and Krenitzky (FF 12).

Appellant reiterates the argument that "[m]issing from the Examiner's analysis is an explanation as to why it would have been routine optimization to arrive at the claimed invention" (App. Br. 11). Appellant also contends "the Examiner has not articulated why it would have been routine optimization to arrive at 10 grams to 100 grams of protein per serving as claimed" (App. Br. 11).

We find this argument unpersuasive as the Examiner provides detailed reasoning supporting the routine optimization rationale (*see*, *e.g.*, Ans. 7–8).

As discussed above, the ordinary artisan would have had reason to select and optimize amounts of protein for Ranganathan's kidney failure patients (FF 1–4) in patient optimized amounts (FF 9) using known guidance in the prior art such as Krenitsky's teachings of protein amounts for such kidney failure patients (FF 12). In administering the protein to patients, the artisan would reasonably have incorporated either single or multiple doses that resulted in the amount of protein necessary for the patient, calculated by the Examiner for a 180 pound patient as 100 grams of protein per day. Whether this patient was administered 10 doses of 10 grams or a single dose of 100 grams would be based on the "judgment of a practitioner or dietician and each subject's circumstances" (FF 9), but these would have been obvious alternatives given the disclosures of the prior art.

Conclusion of Law

A preponderance of the evidence of record supports the Examiner's conclusion that Ranganathan, Krenitsky, and WebMD render the claims obvious.

DECISION SUMMARY

In summary:

Claim(s) Rejected	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
4–7	103(a)	Ranganathan, WebMD, Krenitsky	4–7	

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED