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BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte BRIAN CORNBLATT, GRACE CORNBLATT, ANTON BZHELYANSKY and ROBERT HENDERSON[1]

Appeal 2019-004702
Application 15/244,374
Technology Center 1600

Before ERIC B. GRIMES, ULRIKE W. JENKS, and MICHAEL A. VALEK, *Administrative Patent Judges.*

GRIMES, *Administrative Patent Judge.*

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134(a) involving claims to composition for oral administration, which have been rejected as anticipated and obvious. We have jurisdiction under 35 U.S.C. § 6(b).

We REVERSE and enter a NEW GROUND OF REJECTION.

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[1] Appellant identifies the real party in interest as Nutramax Laboratories, Inc. Appeal Br. 3. We use the word Appellant to refer to "applicant" as defined in 37 C.F.R. § 1.42(a).

STATEMENT OF THE CASE

"The use of natural products is becoming increasingly popular. . . . There is a need in the art for supplements which are useful as chemoprotective and/or antioxidant agents." Spec. ¶ 2. "An example of a natural product thought to have chemoprotective and antioxidant properties is sulforaphane." *Id*. ¶ 6.

"The sulforaphane precursor, glucoraphanin, can be obtained from vegetables of the *Brassicaceae* family." *Id*. "Glucoraphanin is converted into sulforaphane by a thioglucosidase enzyme called myrosinase, which occurs in a variety of exogenous sources such as *Brassicaceae* vegetables and endogenously in the gut microflora." *Id*. "Ascorbic acid, also known as ascorbate or vitamin C, can potentiate the activity of myrosinase." *Id*. ¶ 48.

"A number of mushrooms have been used or studied for their medicinal effects. . . . Examples of medicinal mushrooms include maitake, shiitake, reishi," etc. *Id*. ¶ 8. Maitake, shiitake, and reishi mushrooms contain glucans. *Id*. ¶¶ 9–11.

Claims 1–27 are on appeal. Claims 1 and 14 are illustrative and read as follows:

> 1. An orally administrable composition comprising a synergistic combination of:
>
> a sulforaphane precursor;
>
> a glucosidase enzyme capable of converting the sulforaphane precursor to sulforaphane;
>
> a glucosidase enzyme cofactor; and
>
> a glucan.

> 14. An orally administrable composition comprising a synergistic combination of:
>
> a sulforaphane or sulforaphane derivative; and
>
> a glucan.

Claims 26 and 27 are also independent and are directed to the same compositions as claims 1 and 14, respectively, but in "[a]n enteric-coated dosage form."

The claims stand rejected as follows:

Claims 1, 2, 4, 6, 7, 9–13, 16, 18, 19, and 21–25 under 35 U.S.C. § 102(b) as anticipated by, or alternatively under 35 U.S.C. § 103(a) as obvious based on, Mini[2] (Ans. 3);

Claims 1, 2, 4–14, and 16–25 under 35 U.S.C. § 103(a) as obvious based on Mini and Jamas[3] (Ans. 5); and

Claims 1–4, 6, 7, 9–16, 18, 19, and 21–27[4] under 35 U.S.C. § 103(a) as obvious based on Mini and West[5] (Ans. 6).

OPINION

Rejections under 35 U.S.C. §§ 102(b) or 103(a)

The Examiner has rejected all of the claims on appeal under 35 U.S.C. § 102(b) or 35 U.S.C. § 103(a) based on Mini, by itself or combined with

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[2] Mini et al., WO 2008/115583 A1, published September 25, 2008.
[3] Jamas et al., US 5,607,677, issued March 4, 1997.
[4] The statement of this rejection in the Final Action (mailed June 6, 2018) includes claims 26 and 27, but the statement of the rejection in the Answer does not. Appellant understood the rejection to apply to claims 26 and 27. *See* Appeal Br. 10, 21. However, in view of the disposition discussed below, the issue of whether claims 26 and 27 stand rejected is moot.
[5] West et al., US 2008/0311192 A1, published December 18, 2008.

Jamas or West. We reverse all of the prior art rejections on procedural grounds because we conclude the claim language is indefinite, for the reasons discussed in the new ground of rejection below. *See In re Steele*, 305 F.2d 859, 862 (CCPA 1962). It should be understood, however, that the reversal is not based on the merits of the §§ 102(b) and 103(a) rejections. If the indefiniteness issues are resolved, the cited references are available as prior art if the Examiner decides later in prosecution that they support a rejection of the claims.

New Ground of Rejection

Under the provisions of 37 C.F.R. § 41.50(b), we enter the following new ground of rejection:

Claims 1–27 are rejected under 35 U.S.C. § 112, second paragraph, as indefinite. Each of claims 1, 14, 26, and 27 (all of the independent claims) recites a "synergistic combination of" either (a) a sulforaphane precursor, a glucosidase enzyme capable of converting the sulforaphane precursor to sulforaphane, a glucosidase enzyme cofactor, and a glucan; or (b) a sulforaphane or sulforaphane derivative, and a glucan.

The scope of the claims is unclear because the record does not define what amounts of the recited components are required by the claims, or what activities of the claimed composition are relevant in determining whether a given combination of sulforaphane[6] and a glucan are "synergistic," as claimed.

[6] The sulforaphane precursor, glucosidase enzyme, and glucosidase enzyme cofactor recited in, for example, claim 1 collectively generate sulforaphane.

The Specification states that "[s]ynergy refers to the effect wherein a combination of two or more components provides a result which is greater than the sum of the effects produced by the agents when used alone." Spec. ¶ 70. The Specification states that, in preferred embodiments, a combination of components provides "a statistically significant and/or greater than additive effect" than the components alone. *Id*. ¶¶ 71–73.

The Specification does not, however, define what effect(s) of sulforaphane and a glucan are used to determine whether their interaction is synergistic. The Specification states that

> sulforaphane induces nuclear erythroid-2-related factor (Nrf2) which, in turn, upregulates the production of Phase II detoxification enzymes and cytoprotective enzymes such as glutathione S-transferases, NAD(P)H:quinone oxidoreductase (NQO1), and heme-oxygenase-1 (HO-1). . . . The upregulation of Phase II enzymes is thought to play a role in a variety of biological activities, including the protection of the brain from cytotoxicity, the protection of the liver from the toxic effects of fat accumulation, and the detoxification of a variety of other tissues.

Id. ¶ 6. Consistent with this disclosure, the Specification states that, "[i]n some embodiments, the method relates to increasing levels or increasing gene expression of NAD(P)H:quinone oxidoreductase 1 (NQO-1) in a subject." *Id*. ¶ 76.

The Specification provides working examples of the effect of a combination of sulforaphane and a mushroom extract (from either maitake or shiitake mushrooms) on gene expression of NQO-1 in vitro. *Id*. ¶¶ 103,

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Spec. ¶¶ 38, 42, 48. For simplicity, we refer to the combination of these three components, and to sulforaphane itself, as "sulforaphane."

108. In both cases, the Specification states that the results showed that the combination had a synergistic effect compared to each component alone. *Id*. ¶¶ 106, 110.

These disclosures suggest that the claim language, read in light of the Specification, could be interpreted to mean that the claimed compositions provide a greater effect *on inducing expression of NQO-1* than the sum of the effects of the glucan alone and sulforaphane alone.

However, the claims do not limit the recited "synergistic" interaction to an effect on NQO-1 expression. And the Specification recites numerous other activities of the disclosed composition. The Specification states that,

> [i]n some embodiments, the method relates to treating, preventing, reducing the occurrence of, decreasing the symptoms associated with, and/or reducing secondary recurrences of, cancer. . . . The present invention provides methods of treating, preventing, decreasing the symptoms associated with, and/or reducing secondary recurrences of diseases and conditions associated with the reproductive system (including but not limited to the breast and prostate), colon, liver, bladder, kidney, central nervous system, cardiovascular system, pulmonary system, genitourinary system, hematopoietic system, and joints. The present invention also provides for methods of treating, preventing, decreasing the symptoms associated with, and/or reducing secondary recurrences of cysts, such as benign cysts.

Id. ¶ 75. The Specification also states that,

> [i]n some embodiments, the method relates to treating, preventing, reducing the occurrence of, decreasing the symptoms associated with, and/or reducing secondary recurrences of a disease or condition associated with elevated levels of quinone estrogen. Examples of such diseases or conditions include, but are not limited to . . . cancer,

> myelodysplastic syndrome, cardiovascular disease, and tardive dyskinesia.

Id. ¶ 77. In addition, the Specification states that,

> [i]n some embodiments, the methods relate to providing a beneficial effect on biomarkers, and treating, preventing, reducing the occurrence of, decreasing the symptoms associated with abnormal levels of these biomarkers. Examples of such biomarkers include, but are not limited to NADPH-dependent enzymes, thioredoxin (TXN), thioredoxin reductase-1 (Txnrd-1), glutamate-cysteine ligase subunit (GCLC), sulfotransferase 1A1 (SULT1A1), heme oxygenase-1 (HMOX1), glutathione peroxidase-3 (GPx-3), glutathione S-transferse [sic] theta 2 (GSTT2), microsomal glutathione S-transferase 1 (MGST1), aldehyde oxidase (AOX1), aldo-keto reductase 1B8 (Akr1b8), flavin-containing monooxygenase 2 (FMO2), Fc receptor region receptor III (Fcgr3), tryptase beta 1 (TPSB1), mast cell protease-6 (Mcpt6), neurexin-1-alpha (NRXN-1), microphthalmia-associated transcription factor (MITF), type II iodothyronine deiodinase (DIO2), angiopoietin-14 (Angpt14), cluster of differentiation (CD36), and Ntel. Diseases or conditions associated with elevated or abnormal levels of these biomarkers include, but are not limited to cancer, pulmonary and central nervous system tuberculosis, multiple sclerosis, Crohn's disease, atherosclerosis, osteoarthritis, asthma, stroke, emphysema, diabetic nephropathy, chronic histiocytic intervillositis of the placenta, hypertension, abdominal aortic aneurysm, inflammatory bowel disease, chronic rhinosinusitis, coronary artery disease, and kidney disease.

Id. ¶ 78.

Thus, in addition to the effect on NQO-1, the Specification also describes effects of the disclosed composition in treating or preventing a variety of diseases and disorders, and in affecting a variety of biomarkers and symptoms associated with abnormal levels of them. In view of the Specification's description as a whole, it is unclear which of the disclosed

activities are encompassed as a basis for concluding that the interaction of sulforaphane and a glucan is synergistic, as recited in the claims.

With regard to amounts of each of the component recited in the claims that is required in order to provide synergy, the Specification provides very little guidance. The Specification states that, "[i]n some embodiments, the composition comprises sulforaphane or a derivative thereof, preferably sulforaphane, in an amount of about 1 μg to about 10 g." *Id*. ¶ 35. The amount of sulforaphane precursor is also disclosed to be about 1 μg to about 10 g. *Id*. ¶ 40. The amount of enzyme is disclosed to be about 1 pg to about 1 μg. *Id*. ¶ 43. The amount of enzyme potentiator or cofactor is disclosed to be about 1 mg to about 500 mg. *Id*. ¶ 49.

The Specification states that a mushroom extract or powder can be used, and can be "standardized to contain about 1% to about 75% . . . of one or more glucans." *Id*. ¶¶ 57–59. If a yeast preparation is used as a source of glucans, it "comprises about 0.1% to about 50% . . . of one or more glucans." *Id*. ¶ 61. The ratio of glucan to sulforaphane (or derivative or precursor) can be "about 50:1 to about 1:50." *Id*. ¶ 63.

The Specification's working examples provide evidence that combinations of 0.5 μM sulforaphane and 100–750 μg/mL mushroom extract have a synergistic effect in vitro on NQO-1 gene expression. *Id*. ¶¶ 102–110. As discussed above, however, the claims are not limited to an effect on NQO-1 expression, and the Specification does not provide data for any effect of the combination of sulforaphane and glucans in vivo.

In summary, the Specification fails to inform those skilled in the art, with reasonable certainty, of the physical or functional characteristics of the

"synergistic" combinations that are encompassed by the claims. The scope of the claims is unclear and therefore the claims are indefinite. *See Nautilus, Inc. v. Biosig Instruments, Inc.*, 572 U.S. 898, 901 (2014) ("[A] patent is invalid for indefiniteness if its claims, read in light of the specification delineating the patent, and the prosecution history, fail to inform, with reasonable certainty, those skilled in the art about the scope of the invention.").

We have considered Appellant's summary of the claimed subject matter and arguments presented in the Appeal Brief and Reply Brief, but do not find that they clarify the indefiniteness issue discussed above.

DECISION SUMMARY

In summary:

Claims Rejected	35 U.S.C. §	Reference(s)/ Basis	Affirmed	Reversed	New Ground
1, 2, 4, 6, 7, 9–13, 16, 18, 19, 21–25	102(b)/103(a)	Mini		1, 2, 4, 6, 7, 9–13, 16, 18, 19, 21–25	
1, 2, 4–14, 16–25	103(a)	Mini, Jamas		1, 2, 4–14, 16–25	
1–4, 6, 7, 9–16, 18, 19, 21–27	103(a)	Mini, West		1–4, 6, 7, 9–16, 18, 19, 21–27	
1–27	112	Indefiniteness			1–27
Overall Outcome				1–27	1–27

TIME PERIOD FOR RESPONSE

This decision contains a new ground of rejection pursuant to 37 C.F.R. § 41.50(b). Section 41.50(b) provides "[a] new ground of rejection

pursuant to this paragraph shall not be considered final for judicial review."

Section 41.50(b) also provides:

> When the Board enters such a non-final decision, the appellant, within two months from the date of the decision, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of the appeal as to the rejected claims:
>
> (1) *Reopen prosecution*. Submit an appropriate amendment of the claims so rejected or new Evidence relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the prosecution will be remanded to the examiner. The new ground of rejection is binding upon the examiner unless an amendment or new Evidence not previously of Record is made which, in the opinion of the examiner, overcomes the new ground of rejection designated in the decision. Should the examiner reject the claims, appellant may again appeal to the Board pursuant to this subpart.
>
> (2) *Request rehearing*. Request that the proceeding be reheard under § 41.52 by the Board upon the same Record. The request for rehearing must address any new ground of rejection and state with particularity the points believed to have been misapprehended or overlooked in entering the new ground of rejection and also state all other grounds upon which rehearing is sought.

Further guidance on responding to a new ground of rejection can be found in the Manual of Patent Examining Procedure § 1214.01.

REVERSED, 37 C.F.R. § 41.50(b)