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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte STEPHEN HSU, LEE H. LEE, and TIN-CHUN CHU

Appeal 2018-008685¹
Application 14/333,279
Technology Center 1600

BEFORE FRANCISCO C. PRATS, RACHEL H. TOWNSEND, and
CYNTHIA M. HARDMAN, *Administrative Patent Judges*.

HARDMAN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a method for killing spores using certain esterified catechins. We heard oral argument on October 22, 2019. We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM.

¹ In this Decision we use the word “Appellant” to refer to “Applicant” as defined in 37 C.F.R. § 1.42(a). Appellant identifies the real parties in interest as Augusta University Research Institute, Inc., Seton Hall University, and Montclair State University. Appeal Br. 2.

STATEMENT OF THE CASE

The claims at issue are directed to a method for killing spores. Claim 1, reproduced below, is illustrative of the claimed subject matter:

1. A method for killing spores comprising contacting the spores with an effective amount of an anti-spore composition comprising (-)-epigallocatechin-3-gallate (EGCG) esterified at the 4' position with a fatty acid having a hydrocarbon chain length of between 14 and 22 to kill the spores.

Appeal Br. 11 (Claims Appendix).

Claims 1, 4, 6–8, 19, and 26–29 are on appeal. Non-Final Act. 2. The claims stand rejected as follows:

Claims 1, 4, 19, and 29 are rejected under 35 U.S.C. § 103 as unpatentable over Fukami,² Kudo,³ and Hsu.⁴ Non-Final Act. 4.

Claim 28 is rejected under 35 U.S.C. § 103 as unpatentable over Fukami, Kudo, Hsu, Baugh,⁵ and Keynan.⁶ Non-Final Act. 7.

Claims 6–8 and 26 are rejected under 35 U.S.C. § 103 as unpatentable over Fukami, Kudo, Hsu, and Walker.⁷ Non-Final Act. 8.

Claim 27 is rejected under 35 U.S.C. § 103 as unpatentable over Fukami, Kudo, Hsu, and Hara.⁸ Non-Final Act. 10–11.

² Fukami et al., EP 1849779 A1, published Oct. 31, 2007 (“Fukami”).

³ Hara-Kudo et al., *Antibacterial Action on Pathogenic Bacterial Spore by Green Tea Catechins*, 85(14) J. Sci. Food Agric. 2354–61 (2005) (“Kudo”).

⁴ Hsu, US 2012/0172423 A1, published July 5, 2012 (“Hsu”).

⁵ Baugh et al., US 6,656,919 B1, Dec. 2, 2003 (“Baugh”).

⁶ Keynan et al., *Activation of Bacterial Endospores*, 88(2) J. Bacteriol. 313–18 (1964) (“Keynan”).

⁷ Walker, US 7,192,601 B2, issued Mar. 20, 2007 (“Walker”).

⁸ Hara, JP 02276562 A, published Nov. 13, 1990 (“Hara”).

DISCUSSION

“[T]he examiner bears the initial burden . . . of presenting a *prima facie* case of unpatentability. If that burden is met, the burden of coming forward with evidence or argument shifts to the applicant.” *In re Oetiker*, 977 F.2d 1443, 1445 (Fed. Cir. 1992). We have considered those arguments made by Appellant in the Appeal Brief and properly presented in the Reply Brief; arguments not so presented in Appellant’s briefs are waived. *See* 37 C.F.R. § 41.37(c)(1)(iv) (2015); *see also Ex Parte Borden IV*, 93 USPQ2d 1473, 1474 (BPAI 2010) (informative) (“Any bases for asserting error, whether factual or legal, that are not raised in the principal brief are waived.”).

Rejection of Claims 1, 4, 19, and 29 as Obvious Over Fukami, Kudo, and Hsu

The Examiner found that Fukami teaches catechins modified with medium chain fatty acids having between 8–12 carbon atoms at positions including the 4' hydroxyl group. Non-Final Act. 4 (citing Fukami ¶ 20, claims 8, 23). According to the Examiner, Fukami discloses that these catechins can suppress spore formation. Non-Final Act. 4 (citing Fukami Abstract, Examples 6–10, claim 10, ¶ 32). The Examiner further found that Fukami contacted spores with the modified catechins overnight, and that it would have been obvious to adjust the contact time “in order to provide sufficient and complete antibacterial killing.” Non-Final Act. 5.

The Examiner additionally found that Kudo teaches that catechins such as epigallocatechin gallate (“EGCG”) damage bacterial spore membranes, thus killing spores. Non-Final Act. 4–5 (citing Kudo at Abstract, 2360–61 (last paragraph)). According to the Examiner, because

Kudo “discloses that catechins damage and thus kill spore membranes,” the modified catechins in Fukami must also “necessarily act[] to kill spores.” Non-Final Act. 4–5.

The Examiner further found that Hsu teaches EGCG esterified at the 4' position with stearic acid (i.e., “EGCG stearate”). Non-Final Act. 6 (citing Hsu at claim 2). The Examiner acknowledged, however, that Hsu teaches use of this compound as an antiviral agent, not as a sporicide. *Id.*

The Examiner found that a person of ordinary skill in the art would have been motivated to substitute the medium chain fatty acid ester of Fukami with stearic acid because “homologs (compounds differing regularly by the successive addition of the same chemical group, e.g., by -CH₂- groups) are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties.” Non-Final Act. 6. The Examiner found that there would have been a reasonable expectation of success because “Fukami already teaches esterified epigallocatechin gallates with fatty acids.” Non-Final Act. 7.

We agree with the Examiner’s factual findings and conclusion that the subject matter of claims 1, 4, 19, and 29 would have been obvious to one of ordinary skill in the art in view of Fukami, Kudo, and Hsu. We address Appellant’s arguments below.

Appellant argues that the asserted combination of prior art does not teach or suggest the claimed method because Fukami discloses a method of ***inhibiting the growth*** of spore-forming bacteria rather than ***killing spores***; Kudo “does not teach or suggest a method of contacting spores with an esterified catechin;” and Hsu does not teach a method of contacting spores. Appeal Br. 6; *see also* Reply Br. 2–3 (arguing that Fukami does not teach

killing spores). We are not persuaded by this argument, which attacks the references individually for each failing to teach all of the claimed limitations. The test for obviousness is not whether the claimed invention is expressly identified in any one or all of the references, but whether the claimed subject matter would have been obvious to one of ordinary skill in the art in light of the combined teachings of the prior art. *See In re Keller*, 642 F.2d 413, 425 (CCPA 1981). As discussed above, we agree with the Examiner that the references collectively teach the claimed subject matter, because Fukami teaches that esterified catechins inhibit spore growth (*see, e.g.*, Fukami abstract), Kudo teaches that catechins kill spores (*see, e.g.*, Kudo abstract), and Hsu teaches EGCG stearate, an esterified catechin compound that falls within the scope of claims 1, 4, 19, and 29 (*see, e.g.*, Hsu claim 2).

Appellant further argues that a person of ordinary skill in the art would not have been motivated to carry out the claimed method because Fukami and Kudo suggest that it would not have been successful. Appeal Br. 7. Specifically, Appellant asserts that Fukami's modified catechins provide the strongest growth inhibition on spore-forming *Bacillus* species, yet Kudo suggests that catechins "are not effective at reducing the number of *Bacillus cereus* spores over a course of 12 weeks," and could not inhibit enterotoxin production by *Bacillus cereus*. Appeal Br. 7. Appellant further argues that Fukami's teaching that "esterifying catechins at the 4' position with medium chain fatty acids confers weak antibacterial activity on vegetative bacteria," in view of Kudo's teaching that "catechins require long incubation periods to affect spores," would have undermined any motivation

or reasonable expectation of success in carrying out the claimed method.

Reply Br. 3–4.

We are not persuaded by these arguments. First, Appellant focuses on Kudo’s results relating to minimal efficacy on *B. cereus* spores, while ignoring its results relating to decreasing *C. botulinum* and *C. butyricum* spores to undetectable levels. As indicated in Kudo, catechins at 1000 µg/ml and 500 µg/ml each decreased *C. botulinum* spores to undetectable levels after 12 weeks (Figure 1(a)); catechins at 1000 µg/ml decreased *C. butyricum* spores to undetectable levels after 2 weeks (Figure 1(b)); and catechins at 500 and 250 µg/ml each decreased *C. butyricum* spores to undetectable levels after 4 weeks (Figure 1(b)). Kudo 2355 (Figure 1), 2356 (Results and Discussion). Kudo further indicates that catechins damage not only the bacterial vegetative membrane, but the spore membrane as well. Kudo 2361.

Accordingly, at a minimum, Kudo demonstrates that catechins kill spores of at least *C. botulinum* and *C. butyricum*. See also Non-Final Act. 5 (“Kudo [] discloses that catechins damage and thus kill spore membranes.”); Ans. 7 (“Kudo et al. [] teaches that catechins damage bacterial spore membranes of spore-forming bacterial pathogens, [and] thus function in killing spores, see last paragraph.”). Indeed, Appellant conceded that Kudo teaches killing spores, stating: “The only cited prior art reference that explicitly discusses a method of killing spores is Kudo et al.” Appeal Br. 8.

Moreover, even though *B. cereus* spores did not reach undetectable levels in Kudo’s experiment (Kudo Figure 1(c)), Kudo does note that “the decrease in spores was significant at [a] concentration of greater than 250 µg/ml.” Kudo 2358. Kudo further notes that “[t]he effect of crude catechins

on *C botulinum*, *C butyricum* and *B cereus* depended on the concentration of the former” (Kudo 2358), thus suggesting that catechins kill spores in a concentration-dependent manner. Accordingly, Kudo also demonstrates that catechins killed at least some *B. cereus* spores, and suggests that an increased concentration of catechins would increase the number of spores killed. *See also* Ans. 7 (noting Kudo’s teaching that decrease in *B. cereus* spores was concentration-dependent).

Accordingly, we find that the prior art provides a reasonable expectation of success that catechins modified at the 4' position with a long chain fatty acid would kill spores. Appellant’s reliance on Fukami’s statement about relatively weak antibacterial activity for catechins modified at the 4' position, and Kudo’s teaching that catechins require long incubation periods, is unavailing. Claims 1, 4, 19, and 29 are broadly directed to killing “spores” (or “bacterial spores” in claim 29) using “an effective amount” of the claimed modified catechins, e.g. EGCG stearate. The claims do not recite an upper limit on the amount of modified catechins that can be used, nor are they limited to killing any specific species of spores. The claims also do not recite a time component shorter than the experiments disclosed in Kudo, which lasted up to twelve weeks. *See, e.g.*, Kudo Fig. 1. (Claim 19 does recite a time component, which includes “months” and “years.”) The claims also do not recite any specific degree of “killing,” and thus killing even a minimal number of spores falls within the claim. In view of the scope of the claims and the teachings of the prior art as discussed above, we determine that the combination of Kudo, Fukami, and Hsu would have provided a person of ordinary skill in the art with a reasonable expectation of success that catechins modified at the 4' position with a fatty acid having a

hydrocarbon chain length of between 14 and 22 would kill spores, as recited in claims 1, 4, 19, and 29.

Relying on a declaration submitted by inventor Dr. Hsu,⁹ Appellant argues that the claimed subject matter demonstrates unexpected results. Appeal Br. 8–9. Specifically, Appellant asserts that the claimed compounds “showed a significant inhibition of germination for *B. cereus* when the endospores were treated for 5 minutes with esterified polyphenol,” and a “complete inhibition (100%) [] when treated for 15 minutes.” Appeal Br. 8 (quoting Hsu Declaration ¶ 7). Appellant further argues that in contrast to Kudo which teaches that “it takes up to 12 weeks to achieve maximal growth inhibition of spores,” “[t]he method of [the] pending claims has been shown to kill over 90% of spores within 30 minutes of application of the esterified EGCG.” Appeal Br. 8–9.

We are not persuaded that Appellant’s data demonstrate unexpected results. Appellant must prove a nexus between the alleged unexpected results and the merits of the claimed invention. *See In re GPAC Inc.*, 57 F.3d 1573, 1580 (Fed. Cir. 1995). Here, however, Figure 1 in the Hsu Declaration demonstrates inhibition of endospore germination, which as Appellant itself has argued, is distinct from the claimed method of “killing spores.” *See, e.g.*, Appeal Br. 6; Reply Br. 3 (“It is understood in the art that growth inhibition and cell death (killing) are not one in the same.”).

Further, unexpected results “must be shown to be unexpected compared with the closest prior art.” *In re Baxter Travenol Labs.*, 952 F.2d 388, 392 (Fed. Cir. 1991). Neither Figure 1 nor Figure 3 in the Hsu

⁹ Declaration Under 37 C.F.R. § 1.132, submitted by Stephen Hsu, dated October 6, 2016 (“Hsu Declaration”).

Declaration compare the claimed compounds to the closest prior art, which the Examiner identified as Fukami's EGCG esterified with lauric acid. *See, e.g.,* Ans. 10–13. Figure 1 compares EGCG stearate to LTP, which is catechins randomly modified at multiple sites with 18-carbon lipid chains. *See* Hr'g Tr. 4:24–5:12; *see also* Spec. 52 (discussing LTP). Figure 3 compares EGCG stearate to EGCG, not to EGCG esterified with lauric acid.

Because the record is lacking a comparison of the spore-killing effects of the claimed compounds with the closest prior art, we determine that on this record, Appellant has not demonstrated unexpected results sufficient to outweigh the evidence of obviousness presented in the Examiner's *prima facie* case.

Rejection of Claim 28 as Obvious Over Fukami, Kudo, Hsu, Baugh, and Keynan

Claim 28 depends from claim 1, and further specifies that “the spores are contacted for 5 minutes, 10 minutes, 15 minutes, 30 minutes, or one hour.” Appeal Br. 12 (Claims Appendix). The Examiner found that a person of ordinary skill in the art would have been motivated “to provide the modified Fukami's composition in contact with spores for 15 minutes, 30 minutes or an hour” because Baugh teaches that “generally spores need to be exposed [to sporicides] for a time of about 15 minutes to 60 minutes in order to achieve a useful level of spore reduction.” Non-Final Act. 7–8 (citing Baugh 4:1–22).

We adopt the Examiner's findings of fact with respect to this rejection, and agree that claim 28 would have been obvious over Fukami, Kudo, Hsu, Baugh, and Keynan.

In response to this rejection, Appellant relies on the arguments it presented in response to the previously-addressed rejection. Appeal Br. 9. Our prior analysis applies with equal force here.

Appellant additionally argues that “[e]ven though Baugh teaches a method of killing spores in an hour or less, one of skill in the art would not have been motivated to use the method of the pending claims for less than an hour because the combination of Fukami, Kudo, and Hsu suggests that it takes weeks to kill bacterial spores.” Appeal Br. 9. We are not persuaded by this argument. As noted above, Kudo teaches that higher concentrations of catechins reduced the number of *C. botulinum* and *C. butyricum* spores to undetectable levels more quickly than lower concentrations. *See, e.g.*, Kudo Fig. 1(a) and (b). In view of this teaching and Baugh’s statement that spores need to be exposed to sporicides for 15–60 minutes in order to achieve a useful level of spore reduction, we agree with the Examiner that it would have been *prima facie* obvious to contact spores for the periods of time recited in claim 28. We note that like the claims discussed above, claim 28 also does not recite any upper limit on the amount of modified catechins that can be used in the claimed method. Nor does claim 28 require any specific degree of “killing,” and thus even killing a minimal number of spores within the recited time periods falls within the claims.

Finally, Appellant again alleges unexpected results. Appeal Br. 9. For the reasons discussed above, we determine that on this record, Appellant has not demonstrated unexpected results.

Accordingly, we affirm the rejection of claim 28 as obvious over Fukami, Kudo, Hsu, Baugh, and Keynan.

Rejection of Claims 6–8 and 26 as Obvious Over Fukami, Kudo, Hsu, and Walker; Rejection of Claim 27 as Obvious Over Fukami, Kudo, Hsu, and Hara

The Examiner rejected claims 6–8 and 26 as obvious over Fukami, Kudo, Hsu, and Walker. According to the Examiner, Walker teaches “germicidal compositions that kill spores wherein the composition comprises antibacterial agents inclusive of phenolic compounds in combination with other antibacterial agents.” Non-Final Act. 9 (citing Walker 2:5–35).

The Examiner rejected claim 27 as obvious over Fukami, Kudo, Hsu, and Hara. According to the Examiner, Hara teaches “that green tea polyphenols can be added as an antibacterial agent to prevent food from being contaminated with bacteria including *Staphylococcus*.” Non-Final Act. 9 (citing Hara, first paragraph).

We adopt the Examiner’s findings of fact with respect to these rejections, and agree that claims 6–8 and 26 would have been obvious over Fukami, Kudo, Hsu, and Walker, and that claim 27 would have been obvious over Fukami, Kudo, Hsu, and Hara.

In response to these rejections, Appellant argues that one of ordinary skill in the art would not have been motivated to combine the cited references because the combination would not have been successful in killing spores. Appeal Br. 7–8. For the same reasons discussed above with respect to the first-addressed rejection, we are not persuaded by Appellant’s argument. Accordingly, we affirm the rejection of claims 6–8 and 26 over Fukami, Kudo, Hsu, and Walker, and the rejection of claim 27 over Fukami, Kudo, Hsu, and Hara.

CONCLUSION

We affirm the rejection of claims 1, 4, 19 and 29 under 35 U.S.C. § 103 as being unpatentable over Fukami, Kudo, and Hsu.

We affirm the rejection of claim 28 under 35 U.S.C. § 103 as being unpatentable over Fukami, Kudo, Hsu, Baugh, and Keynan.

We affirm the rejection of claims 6–8 and 26 under 35 U.S.C. § 103 as being unpatentable over Fukami, Kudo, Hsu, and Walker.

We affirm the rejection of claim 27 under 35 U.S.C. § 103 as being unpatentable over Fukami, Kudo, Hsu, and Hara.

DECISION SUMMARY

In summary:

Claims Rejected	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
1, 4, 19 and 29	103	Fukami, Kudo, and Hsu	1, 4, 19 and 29	
28	103	Fukami, Kudo, Hsu, Baugh, and Keynan	28	
6–8, 26	103	Fukami, Kudo, Hsu, and Walker	6–8, 26	
27	103	Fukami, Kudo, Hsu, and Hara	27	
Overall Outcome			1, 4, 6–8, 19, and 26–29	

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a). *See* 37 C.F.R. § 1.136(a)(1)(iv).

AFFIRMED