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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte LUDGER KOLBE, JULIA ECKERT, GITTA NEUFANG,
STEFANIE KNAUPMEIER, and NILS PETERS

Appeal 2018-009052
Application 12/933,231
Technology Center 1600

Before JEFFREY N. FREDMAN, DEBORAH KATZ, and
JOHN E. SCHNEIDER, *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 of reducing itching or paraesthesias using various compounds. The Examiner rejected the claims as obvious. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

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 BEIERSDORF AG of Hamburg Germany (*see* App. Br. 3).

² We have considered and refer to the Specification of Sept. 17, 2010 (“Spec.”); Final Action of Nov. 24, 2017 (“Final Act.”); Appeal Brief of June 18, 2018 (“Appeal Br.”); Examiner’s Answer of July 27, 2018 (“Ans.”); and Reply Brief of Sept. 26, 2018 (“Reply Br.”). We also note our previous Decision on Nov. 16, 2016 (“Dec.”).

Statement of the Case

Background

“Itching is an independent sensation of the skin and occurs independently of pain sensation. . . . The different sensations of itching such as pure itch, stabbing or burning itch, painful tingling, etc. are explained by the different neurotransmitters” (Spec. 1:13–17). “One object of the present invention was to remedy the drawbacks of the prior art and to reduce the itching and other problems that can occur with aged skin or due to sunburn by means of preparations that are easy to produce, are tolerated well and are odorless” (Spec. 2:15–18).

The Claims

Claims 30–49 are on appeal. Claim 30 is representative and reads as follows:

30. A method of at least one of reducing itching, reducing paraesthesias with dry skin or aged skin, and reducing dermatological paraesthesias caused by sunburn, wherein the method comprises applying to skin of a subject in need thereof a cosmetic or dermatological preparation that comprises (1R,2S,5R)-2-isopropyl-5-methyl-N-(2-(pyridin-2-yl)ethyl)cyclohexane-carboxamide in an amount that is effective for at least one of reducing itching, reducing paraesthesias with dry skin and aged skin, and reducing dermatological paraesthesias caused by sunburn.

The issues

A. The Examiner rejected claims 30–35 under 35 U.S.C. § 103(a) as obvious over Wei³ and Bell⁴ (Final Act. 2–8).

³ Wei, US 2005/0187211 A1, published Aug. 25, 2005.

⁴ Bell et al., WO 2007/019719 A1, published Feb. 22, 2007.

- B. The Examiner rejected claims 30–39 under 35 U.S.C. § 103(a) as obvious over Wei, Bell, and De Rijk⁵ (Final Act. 11–12).
- C. The Examiner rejected claims 40–43 and 45 under 35 U.S.C. § 103(a) as obvious over Wei and Rovner⁶ (Final Act. 13–16).
- D. The Examiner rejected claims 40–45 under 35 U.S.C. § 103(a) as obvious over Wei, Rovner, and Galopin⁷ (Final Act. 17–18).
- E. The Examiner rejected claims 40–49 under 35 U.S.C. § 103(a) as obvious over Wei, Rovner, and De Rijk (Final Act. 19–21).

A. *35 U.S.C. § 103(a) over Wei and Bell*

The Examiner finds

Wei teaches a method of reducing itching (para. [0003] and [0047]) and reducing paraesthesia with dry skin or aged skin (pruritus caused by xerosis in the elderly (para. [0038] and [0047]), and reducing dermatological paraesthesia caused by sunburn (sunburn (para. [0047]), comprising applying composition comprising an N-(Substituted-heterocyclyl-alkyl)-cycloalkyl carboxamide compositions to the skin (para. [0045]-[0046] and claim 7), wherein the heterocyclyl can be a pyridinyl group (para. [0017]) and the alkyl can be a C1-C3 alkyl (claim [0015]), and the cycloalkyl carboxamide moiety can be 1R,2S,5R)-2-isopropyl-5-methylcyclohexyl (para. [0014]).

(Final Act. 3). The Examiner acknowledges that in Wei, “the main moiety does not have the same position as in the claimed compound (3 v. 2). Hence,

⁵ De Rijk, WO 2007/099398 A2, published Sept. 7, 2007.

⁶ Rovner, *Better than mint*, 85 CHEMICAL ENGINEERING NEWS 95 (2007). We number the pages of this reference sequentially from the first page.

⁷ Galopin et al., US 2006/0276667 A1, published Dec. 7, 2006.

Wei fails to suggest (1R,2S,5R)- 2-isopropyl-5-methyl-N-(2-(pyridin-2-yl)ethyl)cyclohexane carboxamide))” (Final Act. 4).

The Examiner finds that Bell teaches “methods for providing a cooling effect to a skin composition such as a skin cream or ointment” that may use “1R,2S,5R)- 2-isopropyl-5-methyl-N-(2-(pyridin-2-yl)ethyl) cyclohexanecarboxamide (FEMA 4549) as a particular example of a compound that is effective for providing a surprisingly strong and long-lasting cooling effect” (Final Act. 4).

The Examiner finds it obvious to use Bell’s compound either in combination with, or in place of, the compound of Wei because Bell’s compound resulted in a “significantly longer perception of cooling than other known cooling agents” and “because the perception of cooling suppresses the perception of itch and pain, as taught by Wei” (Final Act. 6). The Examiner finds that the combination of the compounds of Wei and Bell would have been obvious because Bell teaches “using the newly identified cooling compounds with cooling compounds known in the prior art” (Final Act. 6).

The issue with respect to this rejection is: Does the evidence of record support the Examiner’s finding that Wei and Bell render the claims obvious?

Findings of Fact

1. Wei teaches “compositions that are useful in sensory refreshment and alleviation of skin irritation, itch and pain” and that these compounds activate “TRP-M8 and TRP-A1 receptors that are present in sensory nerves” (Wei ¶ 3). Wei specifically teaches “[t]herapeutic indications for which a topical formulation may be beneficial include

irritation, itch and pain from various forms of dermatitis (atopic, contact and irritant); pain from burned, traumatized or irritated skin . . . itch and discomfort from skin infections . . . sunburn” (Wei ¶ 47).

2. Wei teaches compounds of Formula 1 that comprise (1R,2S,5R)-2-Isopropyl-5-methyl-cyclohexyl linked by a CO-NH group to a C₁–C₃ n-alkyl that is linked to a pyridinyl group (*see* Wei ¶¶ 12–17).

3. Wei teaches that the disclosed compounds “act on specific receptors to stimulate ion channels of peripheral sensory neurons” to “relay signals to the spinal cord and brain. These signals generate sensations of coolness and refreshment. If pathological conditions are present, these signals also suppress perception of signals for tissue irritation” (Wei ¶ 24).

4. Wei explains that “[f]or topical uses, either as a cosmetic or as a therapeutic, it is desirable to have more coolness than cold, more cold than intense cold, and to have a duration of action that permits a practical application” (Wei ¶ 38).

5. Bell teaches “[c]ooling compounds, that is, chemical compounds that impart a cooling sensation to the skin or the mucous membranes of the body, are well known to the art and are widely used in a variety of products” including “skin creams and ointments, both cosmetic and medicinal” (Bell 1:2–4, 4:3–4).

6. Bell teaches, in Example 2, the preparation of “[(1R,2S,SR)-2-isopropyl-5-methyl-N-(2-(pyridin-2-yl)ethyl)cyclohexanecarboxamide” (Bell 5:3–15).

7. Table 2 of Bell teaches that at a concentration of 0.02 ppm, the compound of Example 2 has a longevity of 60 minutes, and Bell further teaches that compounds in Table 2 are “up to 100 times stronger and last

longer than menthol, the reference cooling compound” and are “also much stronger than WS-3, the best cooling compound of the prior art” (Bell 6:1–20).

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 (Final Act. 2–8; FF 1–7) and agree that the claims are rendered obvious by Wei and Bell. We address Appellant’s arguments below.

Appellant contends “it is clear from Tables 2 and 3 thereof that the compound with the by far highest cooling effect is (1R,2S,5R)-2-isopropyl-5-methyl-N-(2-(pyridin-3-yl)ethyl)cyclohexane-carboxamide, not (1R,2S,5R)-2-isopropyl-5-methyl-N-(2-(pyridin-2-yl)ethyl)cyclohexane-carboxamide” (Appeal Br. 7–8). Appellant contends “the question arises why one of ordinary skill in the art would allegedly have selected a compound . . . which is a by far less effective cooling compound (by a factor of 5) than another compound also disclosed in BELL . . . for inclusion in a composition according to WEI” (Reply Br. 3). Appellant contends therefore, that “one of ordinary skill in the art would not be motivated to replace any of the compounds for use in the method of WEI by (1R,2S,5R)-

2-isopropyl-5-methyl-N-(2-(pyridin-2-yl)ethyl)cyclohexane-carboxamide”
(Appeal Br. 9).

We are not persuaded. As the Examiner pointed out (Ans. 3), *Gurley* found that a “known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use.” *In re Gurley*, 27 F.3d 551, 553 (Fed. Cir. 1994). Even if we agree with Appellant that Bell teaches the 3-yl cooling compound is superior to the 2-yl cooling compound disclosed in Bell and claimed here, Appellant does not identify any teaching in Bell that criticizes, discredits, or otherwise discourages the use of the 2-yl cooling compound as useful as a cooling agent in anti-itch or sunburn creams. *See In re Fulton*, 391 F.3d 1195, 1201 (Fed. Cir. 2004) (“The prior art’s mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed.”)

Indeed, Bell teaches that compounds of Formula I are “also much stronger than WS-3, the best cooling compound of the prior art” (FF 7). Thus, Bell provides a specific reason to incorporate any of the disclosed cooling compounds into a cream such as Wei’s where cooling is desired (*see* FF 3). All of Bell’s compounds would have been obvious equivalent cooling compounds and all were superior to the prior art, and thus when “the combination of references results in a product or process that is more desirable . . . there exists in these situations a motivation to combine prior art references even absent any hint of suggestion in the references themselves.” *DyStar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick Co.*, 464 F.3d 1356, 1368 (Fed. Cir. 2006).

Appellant contends that “there is no disclosure in BELL or WEI that would cause one of ordinary skill in the art to assume that even the compounds with the highest cooling activity which are covered by formula I of BELL are better in this respect than any of the compounds disclosed in WEI” (Appeal Br. 9). Appellant contends that Bell’s results “relate to the cooling effect of the tested compounds in the mouth (in the form of aqueous solutions), not on the skin” and therefore “there is no reason for one of ordinary skill in the art to assume that the tested compounds according to BELL are superior to WS-3 in the case of the application thereof to the skin” (Appeal Br. 8–9).

We find these arguments unpersuasive. First, as to the issue of whether the compounds are better, the evidence of Bell expressly teaches that these compounds have superior cooling effect (FF 7). However, even if Bell’s compounds only had roughly equivalent cooling effects, their substitution or use in Wei’s composition, where Wei desires cooling compounds (FF 3), would have been obvious because the claims “recite[] a combination of elements that were all known in the prior art, and all that was required to obtain that combination was to substitute one well-known . . . agent for another.” *Wm. Wrigley Jr. Co. v. Cadbury Adams USA LLC*, 683 F.3d 1356, 1364 (Fed. Cir. 2012). Indeed, *Wrigley* deals with the obviousness of cooling compositions including WS-23 and finds “it is fair to say that there were “a finite number of identified, predictable solutions” to the problem of finding physiological cooling agents.” *Id.* at 1364.

Second, as to the issue of administration orally or topically, both Wei and Bell suggest topical use (FF 4–5). Bell specifically suggests using the compounds in “skin creams and ointments, both cosmetic and medicinal”

(FF 5). Thus, the ordinary artisan would have had reason to incorporate Bell's cooling compositions into Wei's topical anti-itch composition in order to get the cooling activity desired by Wei (FF 3) in a medicinal skin cream (FF 5).

Third, Appellant lacks any evidence in rebuttal. "[A]ttorney argument [is] not the kind of factual evidence that is required to rebut a prima facie case of obviousness." *In re Geisler*, 116 F.3d 1465, 1470 (Fed. Cir. 1997).

Appellant contends "it is only with the benefit of hindsight that one can arrive at the conclusion that because of the disclosure of BELL one of ordinary skill in the art would have replaced the compounds of WEI in the method disclosed in WEI by the compounds according to BELL" (Appeal Br. 11).

We are not persuaded. While we are aware that hindsight bias may plague determinations of obviousness, *Graham v. John Deere Co.*, 383 U.S. 1, 36 (1966), we are also mindful that the Supreme Court has clearly stated that the "combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *KSR*, 550 U.S. at 416. Here, selection of known cooling agents such as the compounds of Bell (FF 5–6), demonstrated to be superior, would have been obvious equivalent cooling compounds for use in the composition of Wei, where Wei expressly teaches a need for cooling compounds (FF 4).

Conclusion of Law

The evidence of record supports the Examiner's finding that Wei and Bell render the claims obvious.

B. 35 U.S.C. § 103(a) over Wei, Bell, and De Rijk

Appellant does not separately argue this obviousness rejection, instead relying upon their arguments to overcome the combination of Wei and Bell (*see* Appeal Br. 11–12). Having affirmed the obviousness of claims 30–35 for the reasons given above, we also find that the further combination with De Rijk renders the rejected claims obvious for the reasons given by the Examiner (*see* Final Act. 11–12).

C. 35 U.S.C. § 103(a) over Wei and Rovner

The Examiner relies on Wei as discussed above and further notes that “Wei teaches that compounds capable of activating TRP-M8 receptors generate sensations of coolness and refreshment” (Final Act. 13). The Examiner acknowledges that “Wei does not teach a compound having the cyanomethyl substitution of the aryl group i.e., (1R,2S,5R)-N-(4-(cyanomethyl)-phenyl)-2-isopropyl-5-methylcyclohexane carboxamide” (Final Act. 13).

The Examiner finds that Rovner teaches a compound that falls within the scope of claim 40, EVERCOOL 180, and that “EVERCOOL 180 was developed using a TRPM8 bioassay evaluating cooling activity *in vitro*” (Final Act. 14). The Examiner finds “Rovner teaches that EVERCOOL 180 has a three hour duration” (Final Act. 14).

The Examiner finds it obvious “to modify the method of Wei by using the cyanomethyl substitution of N-aryls_salkyl-cCarboxamide shown above (i.e. EVERCOOL 180) to improve the duration of alleviation of itching, pain, and inflammation” (Final Act. 14). The Examiner finds the “skilled artisan would have reasonably expected EVERCOOL 180 to inhibit the

perception of itch and paraesthesia in the skin because the compound modulates TRPM8 activity . . . because modulation of ion fluxes via TRPM8 inhibits the perception of itch and discomfort in skin” (Final Act. 14).

The issue with respect to this rejection is: Does the evidence of record support the Examiner’s finding that Wei and Rovner render the claims obvious?

Findings of Fact

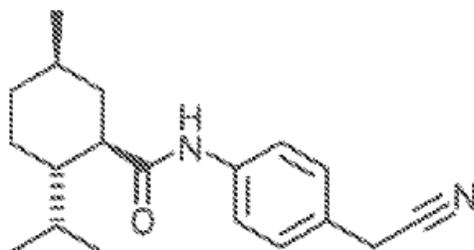
8. Rovner teaches “[m]arket demands continue to evolve, prompting . . . flavor producers to look for compounds that provide even more intense and longer lasting cooling effects than the current ingredients” (Rovner 2).

9. Rovner teaches the

TRPM8 receptor, which is expressed in tissues including the oral mucosa, tongue, and skin, is activated by temperatures around 25 °C or below. The receptor can also be activated by menthol and certain other chemical agents. In either case, activation triggers a biochemical cascade of events that is translated by the brain into a perception of cooling.

(Rovner 2).

10. Rovner teaches that menthol “shortcomings have led to the development of substitutes, including WS-3 and Givaudan’s new Evercool 180” (Rovner 2). The structure of Evercool 180 is reproduced below:



Evercool 180

The image shows the chemical structure of Evercool 180, a menthane carboxamide compound (*see* Rovner 4).

11. Rovner teaches “long-lasting and potent new compounds. ‘If you use a toothpaste with some of our cooling agents, you'll feel a cool sensation for three hours’” (Rovner 4).

Analysis

We adopt the Examiner’s findings of fact and reasoning regarding the scope and content of the prior art (Final Act. 13–16; FF 1–4, 8–11) and agree that the claims are rendered obvious by Wei and Rovner. We address Appellant’s arguments below.

Appellant contends

according to ROVNER only some (but not all) of the new agents provide a cool sensation for three hours. It is not clear from ROVNER whether Evercool 180 is one of the agents which when incorporated into a toothpaste would provide a cool sensation (in the mouth) for three hours. . . . Accordingly, even if one were to assume, merely for the sake of argument, that ROVNER discloses that EVERCOOL 180 has a three hour duration of cooling effect, it is not seen what could have motivated one of ordinary skill in the art to replace the compounds of WEI by a compound whose duration of cooling effect is not longer, and likely shorter, than that of the compounds disclosed in WEI.

(Appeal Br. 13).

We find this argument unpersuasive for similar reasons to those already discussed. First, Rovner provides a specific teaching that the ordinary artisan was interested in new cooling compounds (FF 8) and a teaching that Evercool 180 is a known and improved cooling compound substitute (FF 10). Wrigley finds substitution of one cooling agent for another obvious when the evidence shows “a combination of elements that

were all known in the prior art, and all that was required to obtain that combination was to substitute one well-known . . . agent for another.” *Wrigley*, 683 F.3d at 1364. The same situation applies here, where Evercool 180 is known and superior equivalent cooling agent. Appellant provides no evidence of any secondary consideration.

Appellant contends “ROVNER is not even concerned with topical compositions for alleviating itch, pain, and discomfort of the skin, but relates to flavoring compounds having a cooling effect in the mouth” (Appeal Br. 14).

We find this argument unpersuasive because Rovner expressly teaches that cooling is based on activation of the TRPM8 receptor and that this effect operates on skin (FF 9). Moreover, Wei teaches that the same TRPM8 receptor is a target for skin itch and pain (FF 1). Thus, the ordinary artisan would reasonably have expected that the cooling effect disclosed by Rovner would be applicable to both oral and skin indications. Appellant provides no evidence to the contrary.

Conclusion of Law

The evidence of record supports the Examiner’s finding that Wei and Rovner render the claims obvious.

D. & E. 35 U.S.C. § 103(a) over Wei, Rovner and either Galopin or De Rijk

Appellant does not separately argue these obviousness rejections, instead relying upon their arguments to overcome the combination of Wei and Rovner (*see* Appeal Br. 15–16). Having affirmed the obviousness of claims 40–43 and 45 for the reasons given above over Wei and Rovner, we also find that the further combinations with Galopin or De Rijk renders the

rejected claims obvious for the reasons given by the Examiner (*see* Final Act. 17–21).

DECISION

In summary:

Claims Rejected	35 U.S.C. §	Basis/Reference(s)	Affirmed	Reversed
30–35	103(a)	Wei, Bell	30–35	
30–39	103(a)	Wei, Bell, De Rijk	30–39	
40–43, 45	103(a)	Wei, Rovner	40–43, 45	
40–45	103(a)	Wei, Rovner, Galopin	40–45	
40–49	103(a)	Wei, Rovner, De Rijk	40–49	
Overall Outcome			30–49	

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