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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte CHRISTIAN S. MINTON, STEPHEN D. MINTON, and J. W. RANDOLPH MILLER

Appeal 2018-003717
Application 14,274,419
Technology Center 1600


JENKS, Administrative Patent Judge.

DECISION ON APPEAL

Appellant\(^1\) submits this appeal under 35 U.S.C. § 134(a) involving claims directed to a method of increasing vasodilation. Examiner rejected the claims as anticipated and obvious. We have jurisdiction under 35 U.S.C. § 6(b). We REVERSE.

\(^1\) Appellant is the Applicant, SyK Technologies, LLC, which, according to the Brief, is the real party in interest. Appeal Br. 2. We have considered, and herein refer to, the Specification of May 9, 2014 (“Spec.”); Final Office Action of March 23, 2016 (“Final Act.”); Appeal Brief of Aug. 16, 2016 (“Appeal Br.”); Supplemental Appeal Brief of Oct. 17, 2016 (“Suppl. Appeal Br.”); Examiner’s Answer of Feb. 10, 2017 (“Ans.”); and Reply Brief of March 30, 2017 (“Reply Br.”).
STATEMENT OF THE CASE

Claims 1–14 and 19–23 are on appeal, and can be found in the Claims Appendix of the supplemental Appeal Brief. Claim 1 is representative of the claims on appeal, and reads as follows:

1. A method for increasing vasodilation comprising:
   providing a mammal with an epidermal surface and a bloodstream having an initial systemic vasodilation of the bloodstream;
   providing a first medium comprising a nitrite compound;
   providing a second medium comprising at least two reducing agents;
   creating a mixture of the first medium and the second medium thereby initiating production of nitric oxide;
   applying the mixture onto the epidermal surface of the mammal;
   absorbing at least 500 ppm of nitric oxide transdermally within 10 minutes after the applying; and
   increasing the systemic vasodilation of the bloodstream of the mammal as compared to the initial vasodilation.

Suppl. Appeal Br. 8 (Claims Appendix) (emphasis added). Claims 10 and 19, the only other independent claims, similarly recite a method that increases systemic vasodilation.

Appellant requests review of following rejections made by Examiner:

I. Claims 1–3, 6, 7, and 19–21 under 35 U.S.C. § 102(b) as being anticipated by Tucker.3

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2 Appellant contends that the June 1, 2016 After-Final Amendment should have been entered. See Appeal Br. 4. We are not in a position to grant relief on this matter. Refusal by Examiner to enter an amendment is a petitionable matter under 37 C.F.R. § 1.181 and not within the jurisdiction of the Board. 37 C.F.R. § 1.127; In re Berger, 279 F.3d 975, 984 (Fed. Cir. 2002); see MPEP 1201.

II. Claims 1–3, 5–7, and 19–21 under 35 U.S.C. § 102(b) as being anticipated by Balaban. 4

III. Claims 1–3, 5–9, and 19–23 under 35 U.S.C. § 103(a) as unpatentable over Tucker in view of Balaban.

IV. Claims 4 and 10–14 under 35 U.S.C. § 103(a) as unpatentable over Tucker in view of Balaban and further in view of Kevil. 5

I. Anticipation by Tucker

The issue presented is whether the preponderance of the evidence of record supports Examiner’s finding that Tucker teaches systemic vasodilation after applying a nitric oxide (NO) generating composition to the skin of a patient.

Findings of Fact

FF1. Example 7 of Tucker teaches testing of a microcirculatory response of a NO-generating gel.

The nitric oxide generating gel consisting of 330 mM of both sodium nitrite and ascorbic acid in KY jelly™ was applied directly to the forearm skin and simultaneously to Sympatex™ 10 µm membrane (Akzo Nobel), which was then applied to the forearm skin of the contralateral limb if nine healthy subjects ... . Laser Doppler Fluxmetry (LDF) measured the skin microcirculatory flux.

Tucker ¶ 74. “[T]he vasodilator response to the direct treatment reached a plateau phase in all patients within 10 minutes of gel application. . . . [While it took] 16 minutes when the NO-generation gel was applied to the

membrane and reflects a lag phase which is related to membrane diffusion characteristics.” Id. ¶ 75.

FF2. Example 1 of Tucker teaches application of NO-generating gel on one forearm and “placebo treatment was measured simultaneously on the contra-lateral limb.” Id. ¶ 57.

Placebo treatment did not have any effect upon microcirculatory blood flow in either the forearm or the finger of the normal subjects. The vasodilator response to the active treatment reached a plateau phase in all patients within the ten minutes of active gel application. Forearm skin and finger pulp blood flow increased markedly following topical application of a NO-generating gel in the healthy volunteers. When the active gel was applied to the forearm skin all subjects showed a large vasodilator response to active gel treatment in both volume and flux. This increase in blood flow was sustained after removal of the active gel. The active gel had no significant effect on finger microcirculatory volume (PPG) . . . .

Id. ¶ 58.

FF3. Tucker teaches multiple acidifying agents including: ascorbic acid (vitamin C), salicylic acid, acetyl salicylic acid, a (C₁ -C₆) alkyl carboxylic acid, for example ethanoic acid (acetic acid), and citric acid to name a few. Id. ¶¶ 26–28.

FF4. The Specification describes using a perfusion index, or blood flow, as a measure vasodilation.

One method for measuring vasodilation is to monitor the perfusion index, or blood flow. Perfusion index is a relative assessment of the blood pulse strength at the monitoring site in pulse oximetry. If the perfusion index trends up, it indicates vasodilation and improved peripheral perfusion, or tissue blood flow. If the perfusion index trends down, it indicates a decrease in peripheral perfusion. The perfusion index (Pl) may be expressed as
a rate of inflow pulsatile arterial light absorbed (AC) divided by the non-pulsatile absorbed light, venous and non-pulsatile blood or tissue (DC). PI = AC/DC. 

Spec. ¶ 33.

Analysis

Examiner found that Tucker teaches applying a mixture that produced nitric oxide to the epidermal surface of a mammal. Final Act. 3–4. Examiner found that the application increased vasodilation. Id. at 4 (citing Tucker Example 7); FF1. Examiner found that “Tucker teaches using citric acid and ascorbic acid which the requirements for the at least two reducing agents called for in claim 1.” Id. (citing Tucker ¶¶ 26–28); FF3. Examiner relies on inherency to establish “absorbance of at least 500 ppm nitric oxide transdermally.” Id.

Appellant contends that “Tucker does not teach each and every claim element.” Appeal Br. 5. Appellant contends “that Tucker, taken as whole, does not support the assertion that Tucker discloses increasing the ‘systemic’ vasodilation of a mammal.” Id. at 7.

On this record, we agree with Appellant that the evidence does not support Examiner’s anticipation rejection. We recognize that Tucker provides a list of reducing agents that include citric acid and ascorbic acid. FF3. Tucker’s example 7, relied on by Examiner in formulating the rejection, uses only one acid in the mixture and not two as currently claimed. FF1–FF2. We further note that Tucker’s list does not suggest using these acids in combination. Thus, the problem is that Tucker does not expressly suggest putting two different acids into the reducing agent mixture. Examiner has not explained how Tucker meets the claim limitation of applying a composition that contains a nitrite compound and a second
medium containing at least two reducing agents. “A rejection for anticipation under section 102 requires that each and every limitation of the claimed invention be disclosed in a single prior art reference.” In re Paulsen, 30 F.3d 1475, 1478–79 (Fed. Cir. 1994). Because Tucker does not disclose the use of two acids in the mixture, the reference thereby does not meet each and every limitation as recited in the claim. Although the combination of acids may be obvious, this is not the rejection before us.

Even if we were to agree with Examiner that Tucker teaches NO producing mixture as claimed, we do not agree, however, that the evidence supports Examiner’s inherency argument. Specifically, the record does not support the conclusion that the method disclosed and Tucker necessarily meets the limitation of “absorbance of at least 500 ppm nitric oxide transdermally within ten minutes called for in claim 1.” See Final Act. 4.

Tucker’s example 1 applies the NO producing composition to the forearm of a patient and measures vasodilation at the application site as well as blood flow through the finger. FF2. Appellant points out that Tucker teaches applying the mixture to the skin and measuring vasodilation in the patient but does not establish that the effect is systemic. 6 Appeal Br. 7.

We agree with Appellant that the results shown in Tucker do not support Examiner’s position that the application of Tucker’s NO producing

mixture to the skin results in systemic vasodilation as claimed. The results show that vasodilation response to the active treatment reached a plateau within 10 minutes and forearm skin and finger pulp flow increased markedly following this topical application. FF2. In Tucker the effect of the placebo treatment was measured simultaneously on the contra-lateral limb, in other words, one forearm was used for the application of the active agent while the other forearm received the placebo. When measuring the microcirculatory blood flow in either the forearm or finger of the placebo treated arm no increase in vasodilation was observed. FF2. Thus, as Appellant points out, the treatment supplied in Tucker does not have a systemic effect, because if it did the measurements in the placebo treatment area would have increased as well. We agree with Appellant that Examiner’s inherency argument fails because in this case Tucker shows that the application of NO producing material onto the skin does not produce systemic increase in the microcirculatory response.

Examiner found that Appellant has “made no showing and have provided no evidence regarding the relationship if any between the microcirculatory system tested and systemic vasodilation.” Ans. 9. The burden, however, is not on Appellant to establish a relationship between the microcirculatory system tested in Tucker and systemic vasodilation. See Appeal Br. 12; see Reply Br. 5.

[T]he examiner bears the initial burden, on review of the prior art or on any other ground, 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.

After evidence or argument is submitted by the applicant in response, patentability is determined on the totality of the record, by a preponderance of evidence with due consideration
to persuasiveness of argument.

In re Oetiker, 977 F.2d 1443, 1445 (Fed. Cir. 1992).

Tucker applies a NO generating compositions to the skin of patients and measures microcirculatory flow in the contralateral limbs of the subject. See FF1–FF3. Examiner in making the prima facie rejection relied on inherency to establish two elements: (1) systemic vasodilation and (2) the limitation of “absorbing at least 500 ppm of nitric oxide transdermally within 10 minutes after the applying.” See Ans. 9 (“Increased systemic circulation is an inherent property that will necessarily be possessed by following the method and composition taught in Tucker because the exact same composition is used and the exact same method steps are followed.”). “In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art.” Ex parte Levy, 17 USPQ2d 1461, 1464 (BPAI 1990) (emphasis omitted). Examiner is relying on Tucker’s disclosure of applying a NO generating composition onto the skin of a patient for at least the recited time as set out in the claims to establish that the NO composition results in the absorption of the 500 ppm nitric oxide and thereby results systemic vasodilation.

Here, we find that Appellant adequately traversed Examiner’s inherency rejection by pointing to evidence in Tucker that Tucker’s treatment method does not establish an increase in the microcirculatory flow in the placebo treated area of the patient. Appeal Br. 6; FF2. The meaning of systemic is “pertaining to or affecting the body as a whole.” See above fn. 6. Given this definition, the results disclosed in Tucker would lead one
of ordinary skill in the art to conclude that the treatment described is not sufficient to produce a systemic effect. In other words, there is no evidence that Tucker’s method inherently meets the limitation of “absorbing at least 500 ppm of nitric oxide transdermally within 10 minutes after the applying” step, because Tucker does not show its method as having an increased effect on the whole body – the microcirculatory measurements on the contra lateral limb resulted in no measured increase as compared to a treated limb. This reasonably shifted the burden back to Examiner to establish that an increase in systemic circulation would not necessarily result in an increase in microcirculatory measurements as disclosed in Tucker.

We find that the preponderance of evidence of record does not support Examiner’s conclusion that Tucker anticipates the claimed method. Accordingly, we reverse the anticipation rejection based on Tucker.

II. Anticipation by Balaban

The issue presented is whether the preponderance of the evidence of record supports Examiner’s finding that Balaban teaches systemic vasodilation after applying a nitric oxide (NO) generating composition onto the skin of a patient.

Findings of Fact

FF5. Balaban teaches mixing two gels to produce a mixture that generates NO and applying the mixture to the skin a patient and measuring blood flux. Nitric Oxide donor gel “N” contains the following ingredients listed in the table below:
The nitric oxide activator gel “A” ingredients are listed in the table below:

<table>
<thead>
<tr>
<th>Each ml contains:</th>
<th>Weight Percentage</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium nitrite*</td>
<td>5.0 mg</td>
<td>0.50%</td>
</tr>
<tr>
<td>Euxyl PE9010</td>
<td>3.0 mg</td>
<td>0.30%</td>
</tr>
<tr>
<td>Hydroxyethylcellulose (HEC) 750000</td>
<td>28.8 mg</td>
<td>2.88%</td>
</tr>
<tr>
<td>Water to make 1 ml.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*In the case of the placebo formulation, the sodium nitrite above was replaced with 6.1 mg sodium bicarbonate, which is provided as a concentration in the composition of 73 mM and a weight percentage of 9.61%. The placebo concentration will not release any NO when it is mixed with Gel “A”, the composition for which is shown below.

Balaban ¶ 82.

The nitric oxide activator gel “A” ingredients are listed in the table below:

<table>
<thead>
<tr>
<th>Each ml contains:</th>
<th>Weight Percentage</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citric acid</td>
<td>14.0 mg</td>
<td>1.40%</td>
</tr>
<tr>
<td>Sodium citrate</td>
<td>4.7 mg</td>
<td>0.47%</td>
</tr>
<tr>
<td>3-O-ethyl ascorbic acid</td>
<td>15.0 mg</td>
<td>1.5%</td>
</tr>
<tr>
<td>Euxyl PE9010</td>
<td>3.0 mg</td>
<td>0.30%</td>
</tr>
<tr>
<td>Hydroxyethylcellulose (HEC) 750000</td>
<td>28.8 mg</td>
<td>2.88%</td>
</tr>
<tr>
<td>Water to make 1 ml.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Id. ¶ 83.*

Each set of two gels were individually mixed in a one-to-one ratio (about 0.5 ml gel “N”+0.5 ml gel “A” for the active composition; and 0.5 ml placebo gel+0.5 ml gel “A” for the placebo composition) and applied to the marked area of each forearm. The placebo mixture was applied to the right arm, while the active ingredient mixture was applied to the left arm. After 1-2 min for air drying, the residual gel was removed and the probes [to measure
blood flux] were reattached to exactly the same position to continue the measurements.

*Id.* ¶ 84.

FF6. Balaban teaches that blood flux was measured using a dual channel Laser Doppler Perfusion Monitor (Moor DRT4) with probes applied to each forearm. *Id.* ¶ 84. “The blood perfusion increased immediately after applying the active ingredient gel. The perfusion initially decreased with a time constant of about 10 minutes, but remained elevated throughout the test. The placebo mixture appeared to have no effect on blood perfusion.” *Id.* ¶ 85. Balaban concluded the application of NO producing gel “increased local blood flow.” *Id.* ¶ 86.

**Analysis**

Examiner found that Balaban teaches a method of increasing vasodilation. Final Act. 5. Examiner found that Balaban teaches a medium containing sodium nitrite and the second medium containing citric acid. *Id.* Examiner relies on inherency to establish “absorbance of at least 500 ppm nitric oxide transdermally.” *Id.* at 6.

Appellant contends that Balaban does not disclose each and every element of the claim. Appeal Br. 8. Specifically, “Appellant asserts that Balaban does not support the assertion that Balaban discloses increasing the systemic vasodilation of a mammal.” *Id.*

We agree with Appellant that Balaban does not teach a method of applying a NO generating composition in sufficient amount to show increased systemic vasodilation. The meaning of systemic is “pertaining to or affecting the body as a whole.” *See above* fn. 6. Here, Balaban shows
that the application of the composition onto one forearm has no effect on the blood flow or perfusion on the contra-lateral arm. See FF5–FF6. The Specification relies on perfusion measurements to establish vasodilation. FF4. Here, Balaban teaches the application of a NO generating composition that contains at least two reducing agents but still does not show any increase in systemic vasodilation as determined by blood perfusion measurements. FF6. Therefore, we agree with Appellant that the evidence does not support Examiner’s inherency argument. Accordingly, we reverse the anticipation rejection based on Balaban.

III. Obviousness over Tucker and Balaban.

This obviousness rejection relies upon the underlying anticipation rejection based on Tucker, where Tucker is relied upon to address the claimed systemic vasodilation. See Final Act. 6–8. For the obviousness rejection, Examiner acknowledges that “Tucker does not expressly teach sodium bicarbonate” and looks to Balaban for this teaching. Id. at 7. Thus, Examiner does not rely on the teaching of Balaban to teach systemic vasodilation, a limitation missing in Tucker. We therefore reverse the obviousness rejection because even in the combination of Tucker and Balaban this limitation is still missing.

IV. Obviousness over Tucker, Balaban, and Kevil

This rejection relies upon the underlying obviousness rejection over Tucker and Balaban. Having reversed the rejection based on the combination of Tucker and Balaban, we necessarily reverse the obviousness
rejection that further includes Kevil, since Kevil is not relied upon to teach the “systemic vasodilation” limitation as claimed.

SUMMARY

We reverse the rejection of all claims.

REVERSED