

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte THOMAS P. DOOLEY and LIN CHENG

Appeal 2007-3899
Application 10/328,404
Technology Center 1600

Decided: November 14, 2007

Before DONALD E. ADAMS, NANCY J. LINCK, and JEFFREY N. FREDMAN, *Administrative Patent Judges*.

FREDMAN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 in the above referenced case¹. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

¹ The application was filed on December 23, 2002. The real party in interest is MediQuest Therapeutics, Inc.

BACKGROUND

“The perceived color of skin and hair is determined by the ratio of eumelanins to pheomelanins, and in part on blood within the dermis. The balance in skin hue is genetically regulated by many factors, including but not limited to: (a) the levels of expression of tyrosinase.” (Specification 1.) The Specification indicates that modification of skin color can be desirable, noting “a global market demand has developed for skin-lightening agents as “vanity” cosmeceutical products, because lighter skin color is preferred by some dark-skinned individuals in many countries and races, for psychological or sociological reasons.” (Specification 2.)

Appellants state: “The invention thus provides a method for lightening mammalian skin that includes applying or otherwise administering an effective treatment amount of benzohydroxamic acid or a derivative thereof, or a pharmaceutically acceptable salt thereof, optionally in a pharmaceutically acceptable carrier, to a mammalian subject in need thereof.” (Specification 9.)

STATEMENT OF THE CASE

The Claims

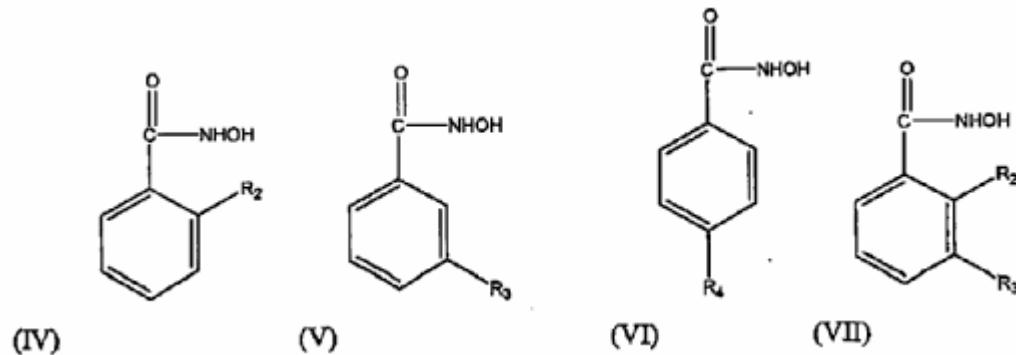
Claims 1, 3-7, 11, 36, 44, 48, 53, 55, 56, 60-63 are on appeal. Claims 1, 3, and 4 are independent claims². Claim 48 is representative of these claims and of the separately argued subset, claims 11, 48 and 60-62. It reads:

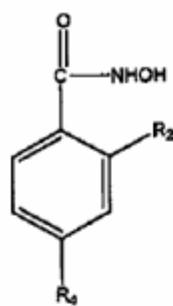
² The Examiner imposed an election/restriction requirement (Office Action 2,7 (mailed June 15, 2005)). In response, Appellants elected 3-methylbenzohydroxamic acid (Response to Restriction Requirement 4 (rec'd July 15, 2006).

48. The method of claim 4 whereto the compound is the following, or a pharmaceutically acceptable salt thereof:
3-methylbenzohydroxamic acid.

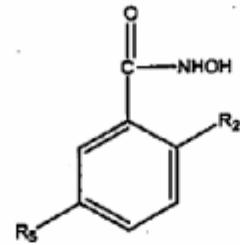
Claim 4, upon which claim 48 depends, reads:

4. A method of inhibiting pigment production in a mammal comprising administering to the mammal an effective amount of a compound defined by one of structures (IV)- (XII) and XIV-(XXII)

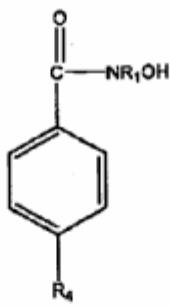




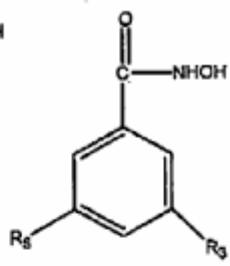
(VIII)



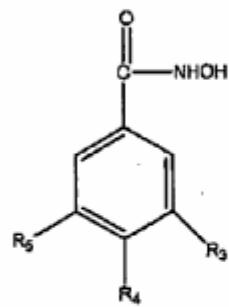
(IX)



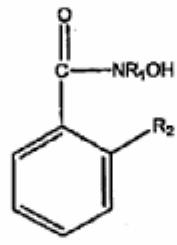
(X)



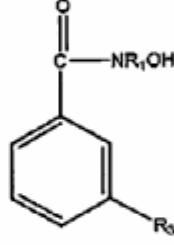
(XI)



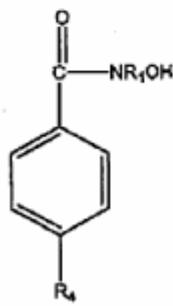
(XII)



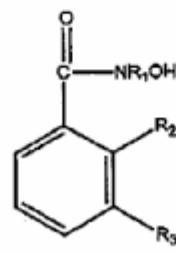
(XIV)



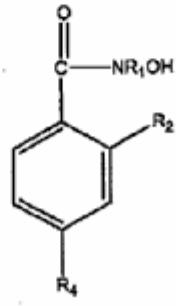
(XV)



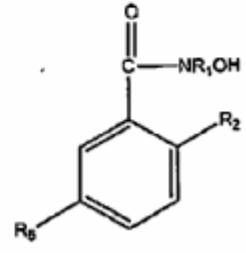
(XVI)



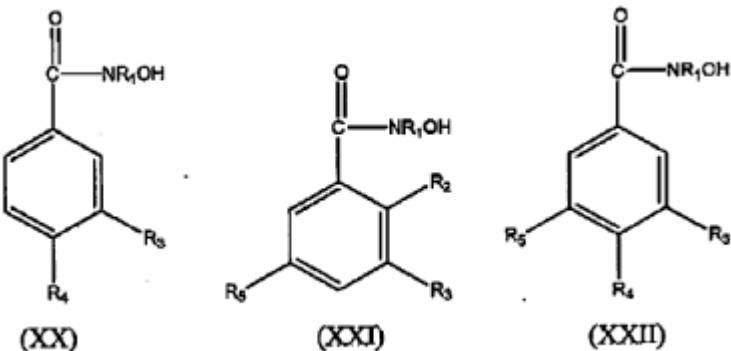
(XVII)



(XVIII)



(XIV)



or a pharmaceutically acceptable salt, wherein:

R_1 is H or C_{1-6} alkyl or cycloalkyl;

R_2 , R_3 , R_4 , R_5 , and R_6 are independently selected from (i) hydrogen,
(ii) halogen, (iii) NO_2 , (iv) $-\text{CN}$, (v) $-\text{OR}_{10}$ or phenoxy, (vi) $-\text{NHSO}_2-$
 C_{1-3} alkyl, (vii) NHCO-C_{1-5} alkyl, (viii) oxime, (ix) hydrazine, (x) $-\text{NR}_9\text{R}_{10}$, (xi) SO_2 , (xii) SO_3 , (xiii) SR_{10} , (xiv) C_{1-5} acyloxy, (xv) PO_3 ,
(xvi) PO_4 (xvii) thiol, (xviii) $-\text{COOR}_9$, (xix) C_{2-5} alkynyl, (xx) $\text{C}(\text{O})\text{C}_{1-3}$ alkyl, and (xxi) $-\text{C}_{1-8}$ alkyl, $-\text{C}_{2-8}$ alkenyl, aryl, heteroaryl, or
heterocycle, optionally substituted with one or more of -OH, -SH,
 $\text{C}(\text{O})\text{H}$, COOR_9 , C_{1-5} acyloxy, halogen, NR_9R_{10} , C_{1-5} thioether or C_{1-5} alkoxy;

alternatively, R_3 and R_4 , or R_4 and R_5 , combine to form a fused ring-structure which is cycloalkyl, aryl, heterocyclyl or heteroaryl selected from phenyl, cyclopentyl, cyclohexyl, pyrrole, furan, thiophene, pyrazole, pyridine, $-\text{X}-(\text{CH}_2)_2\text{X}-$ wherein X is independently NH, S, or O; and provided that at least one are of R_2 , R_3 , R_4 , R_5 , and R_6 is other than H;

R_9 is hydrogen or C_{1-3} alkyl;

R_{10} is hydrogen, C_{1-8} alkyl, $-\text{C}_{2-8}$ alkenyl, $-(\text{CH}_2)_n\text{O}_m(\text{CH}_2)_{n'}$,- heterocycle, optionally substituted with one or more of -OH, -SH, $\text{C}(\text{O})\text{H}$, COOR_9 , C_{1-8} acyloxy, halogen, NR_9R_{10} , C_{1-5} alkoxy,
 m is 0 or 1; and n and n' are independently 0, 1, 2, or 3.

The Examiner has rejected claims 1, 3-7, 11, 36, 44, 48, 53, 55, 56 and 60-63 under 35 U.S.C. § 103(a) based on:

Aust et al. U.S. Patent 6,365,137 B1, April 2, 2002 (hereafter “Aust”).

The Issues

The Examiner’s position is that Aust discloses a method of inhibiting pigment production using an effective amount of benzohydroxamic acid. According to the Examiner it would have been obvious to substitute the homologue, 3-methyl benzohydroxamic acid, in the absence of unexpected results (Answer 4-5).

Appellants respond (1) “Aust failed to suggest the use of the *substituted carbocycle compounds*” and (2) “[i]n general the 3-mono substituted agents showed superiority over the other isomers tested” (App. Br. 10).

In view of these conflicting positions, we frame the issues before us as follows:

- (1) Would it have been *prima facie* obvious to one of ordinary skill in the art to substitute 3-methyl benzohydroxamic acid for Aust’s benzohydroxamic acid?
- (2) If so, is Appellants’ rebuttal argument and evidence sufficient to overcome the Examiner’s *prima facie* case?

Findings of Fact

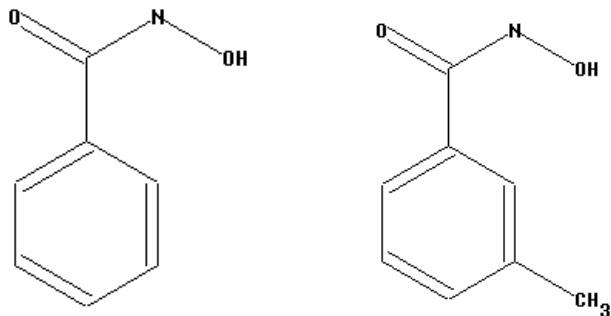
The following findings of fact are believed to be supported by a preponderance of the evidence. To the extent that a finding of fact is a conclusion of law, it may be treated as such. Additional findings as necessary may appear in the Discussion portion of the opinion.

1. Aust teaches a method of inhibiting pigment production, noting “The invention may comprise one or more of any of the tyrosinase inhibitors or pigmentation reversing agents known in the art, and in particular may include one or more of the tyrosinase inhibitors pigmentation reversing agents further described herein.” (Aust, col. 2, ll. 24-28.)

2. Aust teaches the use of benzohydroxamic acid as a “pigmentation reversing agent” in the skin whitening composition. (*Id.*, col. 3, ll. 34-35.)

3. Aust also claims the use of benzohydroxamic acid, along with a limited number of other compounds, in the skin whitening composition. (*Id.*, Aust, col. 10, l. 17; claim 10.)

4. Aust’s disclosed benzohydroxamine and 3-methylbenzohydroxamic differ by a single methyl group, as shown in the structural diagrams below.



Benzohydroxamic acid 3-methylbenzohydroxamic acid

5. The disclosed activity of benzohydroxamic acid and 3-methylbenzohydroxamic acid is the same, i.e., to lighten the skin (Aust, col. 2, ll. 13-15; Specification 7).

6. The Specification shows a value of 60 uM for inhibition of pigment production for the elected compound 3-methylbenzohydroxamic acid (Specification at 39, table 2, ID# 481).

7. The Specification shows a value of 64 uM for inhibition of pigment production for benzohydroxamic acid (Specification 40, table 5, ID# 357).

8. The difference between 60 uM and 64 uM does not provide evidence of unexpected results (FF 5-7).

9. One skilled in the art would have been motivated to use homologues of benzohydroxamic acid to lighten skin and would have had a reasonable expectation of success in doing so (FF 1-5).

Discussion

The analysis for obviousness of chemical variations is based on a long line of Federal Circuit and CCPA decisions. In *In re Dillon*, 919 F.2d 688, 696 (Fed. Cir. 1990), the Federal Circuit noted:

In brief, the cases establish that if an examiner considers that he has found prior art close enough to the claimed invention to give one skilled in the relevant chemical art the motivation to make close relatives (homologs, analogs, isomers, etc.) of the prior art compound(s), then there arises what has been called a presumption of obviousness or a *prima facie* case of obviousness. *In re Henze*, 181 F.2d 196, 37 CCPA 1009, 85 USPQ 261, (CCPA 1950); *In re Hass*, 141 F.2d 122, 127, 130, 31 CCPA 895, 60 USPQ 544, 548, 552 (CCPA 1944). The burden then shifts to the applicant, who then can present arguments and/or data to show that what appears to be obvious, is not in fact that, when the invention is looked at as a whole. *In re Papesch*, 315 F.2d 381, 50 CCPA 1084137 USPQ 43 (CCPA 1963). The cases of Hass and Henze established the rule that, unless an applicant showed that the prior art compound lacked the property or advantage asserted for the claimed compound, the presumption of unpatentability was not overcome.

In re Dillon, 919 F.2d 688, 696 (Fed. Cir. 1990).

The current facts fall squarely within the ambit of *Dillon*, *Henze* and *Hass*. The method of claim 48 utilizes a compound which differs by a single methyl group and is clearly an analog of benzohydroxamic acid (FF 4). The Examiner found prior art that teaches benzohydroxamic acid (*see* FF 1-4; Answer 3-4). Use of benzohydroxamic acid in a method of inhibiting pigment production by Aust (*see* FF 1-3) supports the Examiner's *prima facie* case of obviousness. This is particularly true given Aust's express

recitation of benzohydroxamic acid in claim 10, among a relatively small group of compounds (*see FF 2-3*).

Further, both benzohydroxamic acid and 3-methylbenzohydroxamic acid share the same activity, i.e., inhibiting pigment production (*see FF 5*). Activity of the claimed and prior art compound plays a role in the obviousness inquiry. *See Dillon* 919 F.2d at 696 (“Some of the cited cases also contained language suggesting that the fact that the claimed and the prior art compounds possessed the same activity were added factors in the establishment of the *prima facie* case.”). Because benzohydroxamic acid shares the same activity as 3-methylbenzohydroxamic acid, this common function serves to further support the obviousness determination (*see FF 1-5*).

Appellants contend “no motivation exists for selecting benzohydroxamic acid from the myriad of possibilities in Aust and then modifying it as recited in the present claims” (App. Br. 11). We reject this argument. Aust expressly discloses and claims a limited number of compounds, not a “myriad of possibilities”. *See Pfizer, Inc. v. Apotex, Inc.* 480 F.3d 1348, 1362 (Fed. Cir. 2007) (rejecting a similar argument).

In any case, Aust’s express disclosure of benzohydroxamine as a pigment inhibitor is sufficient to support the Examiner’s *prima facie* case. As the Supreme Court in *KSR* concluded:

When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product [is] not of innovation but of ordinary

skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103.

KSR Int'l v. Teleflex Inc., 127 S. Ct. 1727, 1742 (2007).

Through the application of ordinary skill and common sense, it would have been obvious to try the limited number of compounds disclosed and claimed by Aust and to have modified those of interest, including benzohydroxamine, in such a way as to arrive at Appellants' claimed invention. Based on the above, we conclude the Examiner has made a prima facie case of obviousness under 35 U.S.C. § 103(a) (FF 1-5, 9).

We must now consider any evidence argued to rebut the case of obviousness. *See Dillon*, 919 F.2d at 692-93. (“Such rebuttal or argument can consist of a comparison of test data showing that the claimed compositions possess unexpectedly improved properties or properties that the prior art does not have.”)

Appellants argue the relative effectiveness of different substitutions on the benzohydroxamic acid:

In general the optimal characteristics for a benzohydroxamate inhibitor of mammalian tyrosinase enzyme and of pigmentation in intact mammalian melanocyte cells is: 3-mono substituted > 4-mono substituted > 2-mono substituted or di substituted. Furthermore short chain or low molecular weight R-group substituents are preferred over larger R-groups. There was no *a priori* rationale to expect this resulting pattern based on Aust. The tables [Specification 38-40] indicate a broad array of potencies with regard to enzyme inhibition and cellular pigmentation. In general the 3-mono substituted agents showed superiority over the other isomers tested.

(App. Br. 10).

We do not find Appellants' argument sufficient to establish unexpected results. At best, Appellants are arguing that the 3-mono agents "showed superiority" (App. Br. 10, 13) without pointing to any specific level of improvement. Attorney argument is not the kind of evidence required to rebut a *prima facie* case of obviousness. *In re Geisler*, 116 F.3d 1465, 1470 (Fed. Cir. 1997). Further, Appellants' own specific data in the cited tables fail to show a significant difference in efficacy in inhibition of pigment production between benzohydroxamic acid and 3-methylbenzohydroxamic acid (*see* FF 5-8). The specific data show that the two compounds functioned virtually identically, differing less than 10% in activity in the pigment inhibition assay. (*See* FF 5-8.) Appellants do not argue this difference was unexpected or provide sufficient evidence to support such a position. *See In re Soni*, 54 F.3d 746, 750 (Fed. Cir. 1995) ("[i]t is well settled that unexpected results must be established by factual evidence. Mere argument or conclusory statements in the specification does not suffice")

Based on the above, we conclude Appellants have not evidenced secondary considerations sufficient to overcome the Examiner's *prima facie* case of obviousness under 35 U.S.C. § 103(a).

Appellants also argue that Aust's use of benzohydroxamic acid is "merely an unsupported assertion in the context of a broad multi-component formulation patent" and that Aust is therefore not enabled. (App. Br. 11.) Appellants further argue that while Aust mentions benzohydroxamic acid, there is "no information provided therein showing that this compound is an effective inhibitor of mammalian

tyrosinase (in vitro) or of melanocyte pigmentation (in vitro) or of mammalian skin pigmentation (in vivo).” (App. Br. 10.)

There is a presumption that an issued patent is valid and therefore enabled. Thus, in order to demonstrate that a patent is not enabled, “the patentee . . . must present persuasive evidence of non-enablement to overcome this presumption.” *Amgen Inc. v. Hoechst Marion Roussel Inc.*, 457 F.3d 1293, 1307 (Fed. Cir. 2006).

Appellants present no evidence that benzohydroxamic acid would not have been expected to function as taught by Aust. Appellants also argue that some of Aust’s other claimed compounds might not function, in support of the idea that benzohydroxamic acid would not have been expected to function. We reject this argument because it lacks evidentiary support. Appellants have failed to provide any evidence, much less persuasive evidence, which overcomes the presumption of enablement of the Aust patent, in which benzohydroxamic acid is taught for the purpose of inhibiting pigment production (*see* FF 3, 5).

SUMMARY

We affirm the Examiner’s § 103(a) rejection of claim 48 based on the analysis above. Pursuant to § 41.37(c)(1)(vii)(2006), we also affirm the § 103 rejection of claims 1, 3-7, 11, 36, 44, 53, 55, 56 and 60-63, as these claims were not argued separately.

Appeal 2007-3899
Application 10/328,404

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

Ssc:

BURTON A. AMERNICK
CONNOLLY BOVE LODGE & HUTZ LLP
1990 M. STREET N.W., SUITE 800
WASHINGTON, DC 20036-3425