

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 15

UNITED STATES PATENT AND TRADEMARK OFFICE

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

Ex parte JOHN A. ZOLTEWICZ, WILLIAM R. KEM
and EDWIN M. MEYER

Appeal No. 2001-1294
Application No. 08/473,667

ON BRIEF

Before WINTERS, WILLIAM F. SMITH, and ADAMS, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 9 and 25-32, which are all the claims pending in the application.

Claim 9 is illustrative of the subject matter on appeal and is reproduced below:

9. A pharmaceutical learning and memory improving composition comprising brain cholinergic neurocortical stimulating amounts of anabaseine or DMAB-anabaseine together with a pharmaceutically inert carrier.

The references relied upon by the examiner are:

Leeson

4,965,074

Oct. 23, 1990

(Tu), William R. Kem, Worm Toxin in 3 HANDBOOK OF NATURAL TOXINS 353-60 (Anthony T. Tu ed., Marcel Dekker, New York, 1988)

Meyer et al. (Meyer), "Effects of Nucleus Basalis Lesions on the Muscarinic and Nicotinic Modulation of [³H]Acetylcholine Release in the Rat Cerebral Cortex," J. Neurochemistry, Vol. 49, pp. 1758-62 (1987)

Kem et al. (Kem), "Differential Actions of Anabaseine and its 3 DMAB Adduct Upon Brain and Neuromuscular Nicotinic Receptor," Biosis Abstr., No. 42075229 (1991)

Swanson et al. (Swanson), Nicotinic Acetylcholine Receptor Function Studied with Synthetic(+)-Anatoxin-a and Derivatives in MARINE TOXINS ORIGIN, STRUCTURE, AND MOLECULAR PHARMACOLOGY 107-17 (Sherwood Hall et al. eds., American Chemical Society, Washington, DC, 1990)

(Rawlins), BENTLEY'S TEXTBOOK OF PHARMACEUTICS 16 (E. A. Rawlins ed., 8th ed., Bailliere Tindall, London 1978)

(Remington), REMINGTON'S PHARMACEUTICAL SCIENCE, 1691-92 (A. Oslo ed., 17th ed., Mack, Easton PA 1985)

GROUND OF REJECTION

Claims 9 and 25-32 stand rejected under 35 U.S.C. § 103. As evidence of obviousness the examiner relies on the combination of Tu, Meyer, Kem¹, Remington, Rawlins and/or Swanson and Leeson.²

We reverse.

DISCUSSION

¹ According to the examiner (Answer, page 6), "the Kem (1991) reference ... [was] published after the very first filing date...." Therefore, Kem appears to have been improperly applied in the examiner's rejection. Nevertheless, the examiner finds that Kem was merely cumulative to the teachings of Meyer. (Answer, bridging paragraph, pages 6-7). Accordingly we will not consider Kem in our deliberations.

² We recognize that in the Final Office Action the examiner set forth three separate rejections under 35 U.S.C. § 103. For administrative convenience we have consolidated all three rejections into one ground of rejection.

“In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness. Only if that burden is met, does the burden of going forward with evidence or argument shift to the applicant.” In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). The test of obviousness is “whether the teachings of the prior art, taken as a whole, would have made obvious the claimed invention.” In re Gorman, 933 F.2d 982, 986, 18 USPQ2d 1885, 1888 (Fed. Cir. 1991).

According to the examiner (Answer, page 4), “Tu disclosed naturally occurring nicotine agonists with structural formula as anabaseine and DMBA-anabaseine ... and their function as a nicotine agonist...” The examiner also finds (Answer, page 7), “Tu taught that anabaseine and DMAB-anabaseine are naturally occurring toxin[s] which function as nicotinic agonists and ... [are] 15 times more potent than nicotine....” The examiner relies on Meyer (Answer, page 4) to teach “that anabaseine and DMAB-anabaseine have high affinity in animal brain nicotine receptor,” and on Swanson (Answer, page 5) to teach the use of “naturally occurring nicotine agonists as therapeutical [sic] agents for treating nicotinic receptor pathology i.e. Alzheimer’s disease.” The examiner relies on Remington (Answer, page 4) to teach the preparation of pharmaceutical compositions, and on Remington and Rawlins (Answer, page 5) to teach aqueous or liposome formulations.

The examiner’s statement of the rejection does not address Leeson. The examiner, however, points out (Answer, page 8) that Leeson “described specific

guidelines of how nicotine can be incorporated into pharmaceutical composition[s] for treatment of memory impairment.”

Based on this evidence the examiner concludes (id.):

Because Tu taught that anabaseine is 15 times as potent then [sic] nicotine, Meyes taught that anabaseine and nicotine are functionally equivalent in brain, Swanson suggested that neuromuscular toxin can be useful in treating CNS nicotinic receptor pathology, Leeson provided guidelines in dosage of nicotine to be administered, ... [the] artisan in the field is in possession of a pharmaceutical composition comprising anabaseine or DMAB-anabaseine which Appellants used to improve memory.

While the examiner has accumulated references that touch on each limitation of appellants' claimed invention, for the reasons that follow it is our opinion that the examiner has failed to identify any suggestion that would have led a person of ordinary skill in the art at the time the invention was made to combine the references. Prima facie obviousness based on a combination of references requires that the prior art provide “a reason, suggestion, or motivation to lead an inventor to combine those references.” Pro-Mold and Tool Co. v. Great Lakes Plastics Inc., 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1629 (Fed. Cir. 1996).

[E]vidence of a suggestion, teaching, or motivation to combine may flow from the prior art references themselves, the knowledge of one of ordinary skill in the art, or, in some cases, from the nature of the problem to be solved. . . . The range of sources available, however, does not diminish the requirement for actual evidence. That is, the showing must be clear and particular.

In re Dembiczak, 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999) (citations omitted). The suggestion to combine prior art references must come from the cited references, not from the application's disclosure. See In re Dow

Chemical Co., 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988).

According to appellants (Brief, page 10), Tu “recognizes anabaseine and DMAB-anabaseine as a toxin. ... Based on in vitro studies on frog skeletal muscle, the reference concludes that the functional role of anabaseine is one of paralysis on the muscle.” In addition, appellants point out (id.), Meyer “failed to observe nicotine induced acetylcholine release with anabaseine. This contrasts with appellants’ observation that pharmaceutical compositions of anabaseine of DMAB-anabaseine stimulate brain cholinergic neurocortical receptors.” In this regard we note, Meyer teach (page 1761, bridging paragraph, columns 1 and 2),

It was necessary to use minces which presumably contain intact cholinergic interneurons to observe nicotine-induced [³H]ACh release, and this effect was still not observed with THP or anabaseine. These two compounds have been shown recently to display high-affinity binding to rat brain nicotinic receptors.... Further, very high concentrations of nicotine were necessary to release ACh. ... The lack of effect of anabaseine and THP on ACh release, even at high concentrations that activate peripheral nicotinic receptors, suggests that more than one population of nicotinic receptors exists in the rat brain.

Therefore, we cannot agree with the examiner’s position “that anabaseine and nicotine are functionally equivalent in brain....” Answer, page 8.

We remind the examiner that as required by the claimed invention the pharmaceutical composition must comprise a brain cholinergic neurocortical stimulating amount of anabaseine or DMAB-anabaseine. We recognize the examiner’s argument (Answer, page 9), that the discovery of a new property of an old product is not sufficient, by itself, to support the patentability of the old

composition³. The examiner, however, failed to identify any teaching in the combination of prior art of a composition comprising a brain cholinergic neurocortical stimulating amount of anabaseine or DMAB-anabaseine. Stated differently, the examiner has not demonstrated that the claimed composition is “old.”

While the examiner asserts (id.), “the quantitative values of the prior art and the instant claims are identical,” the examiner provides no factual evidence to support this position. The “quantitative values” for the instant claims are defined at page 13 of appellants’ specification, wherein appellants define the term “therapeutically effective” as “the amount of nicotinic receptor agent used is of sufficient quantity to increase brain cholinergic transmission.” According to appellants’ specification (id.), depending on the “age, condition, sex, and extent of the disease in the patient” this amount ranges from 1 µg/kg to about 1000 µg/kg. In contrast, Meyer used an anabaseine composition varying in concentration between 1 to 100 µM on rat brain minces, of undisclosed weight, and failed to observe an effect on presumably intact cholinergic interneurons. See e.g., Meyer, page 1761, first column and Table 3. Therefore, it is unclear to this Merits Panel how the examiner arrived at her unsupported conclusion that the “quantitative values of the prior art and the instant claims are identical.”

Appellants further argue (Brief, bridging paragraph, pages 10-11), Swanson “is a review of the molecular pharmacology of anatoxin-a compounds

³ In re Spada, 911 F.2d 705, 708, 15 USPQ2d 1655, 1657 (Fed. Cir. 1990) (“The discovery of a new property or use of a previously known composition, even when that property and use are unobvious from the prior art, can not impart patentability to claims to the known composition.” (Citations omitted)).

... they are significantly different in structure from anabaseine and DMAB-anabaseine....” In addition, appellants point out (Brief, page 11), “neither the Tu nor the Swanson references suggest a beneficial therapeutic effect for either class of compound.” Regarding Leeson, appellants argue (Brief, page 11), “[t]he Leeson reference relates to nicotine analogs and nicotinic compositions which have been prepared as pharmaceutical compositions and administered to patients. The active agents of the present invention are anabaseines, not nicotine compounds.”

As set forth in In re Kotzab, 217 F.3d 1365, 1369-70, 55 USPQ2d 1313, 1316 (Fed. Cir. 2000) citations omitted:

A critical step in analyzing the patentability of claims pursuant to section 103(a) is casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field. ... Close adherence to this methodology is especially important in cases where the very ease with which the invention can be understood may prompt one “to fall victim to the insidious effect of a hindsight syndrome wherein that which only the invention taught is used against its teacher.”

...
Most if not all inventions arise from a combination of old elements. ... Thus, every element of a claimed invention may often be found in the prior art. ... However, identification in the prior art of each individual part claimed is insufficient to defeat patentability of the whole claimed invention. ... Rather, to establish obviousness based on a combination of the elements disclosed in the prior art, there must be some motivation, suggestion or teaching of the desirability of making the specific combination that was made by the applicant.

In other words, “there still must be evidence that ‘a skilled artisan, ... with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed.’” Ecolochem Inc. v.

Southern California Edison, 227 F.3d 1361, 1375, 56 USPQ2d 1065, 1075-76
(Fed. Cir. 2000).

On this record, the examiner has not provided the evidence necessary to meet her burden of establishing a prima facie case of obviousness. Instead, the examiner appears to have misapprehended the facts in evidence. Contrary to the examiner finding, Meyer does not teach that anabaseine and nicotine are functionally equivalent in brain. See supra. Furthermore, to the extent that Swanson is relied on to teach that a neuromuscular toxin can be useful in treating CNS nicotinic receptor pathology, the examiner has not demonstrated that anabaseine or DMAB-anabaseine would be reasonably expected to function in a similar manner to Swanson's structurally different toxins. We remind the examiner that in order to establish a prima facie case of obviousness, there must be both some suggestion or motivation to modify the references or combine reference teachings and a reasonable expectation of success. In re Vaeck, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991). On this record, the examiner has identified neither a suggestion to modify the references, nor a reasonable expectation of success in arriving at appellants' claimed invention.

In our opinion, the teaching in Leeson that nicotine can be used for treating memory dysfunction (Answer, page 8) and the teachings in Rawlins and Remington of pharmaceutically acceptable formulations do not make up for the deficiencies in the combination of Tu, Swanson and Meyer.

For the foregoing reasons it is our opinion that the examiner failed to meet her burden of establishing a prima facie case of obviousness. Accordingly, we reverse the rejection of claims 9 and 25-32 under 35 U.S.C. § 103.

REVERSED

Sherman D. Winters)	
Administrative Patent Judge)	
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)	
)	BOARD OF PATENT
William F. Smith)	
Administrative Patent Judge)	APPEALS AND
)	
)	INTERFERENCES
)	
Donald E. Adams)	
Administrative Patent Judge)	

DA/dym

Barbara S. Kitchell
Williams, Morgan & Amerson, P.C.
7676 Hillmont Ste. 250
Houston, TX 77040