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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte PATRICK L. MCGEER, MOONHEE LEE, JIAN-PING GUO, and CLAUDIA SCHWAB

Appeal 2018-005816
Application 13/195,216[1]
Technology Center 1600

Before JEFFREY N. FREDMAN, TAWEN CHANG, and DAVID COTTA, *Administrative Patent Judges*.

COTTA, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a method of selectively inhibiting the membrane attack complex of complement to treat Alzheimer's disease. The Examiner rejected the claims on appeal as obvious under 35 U.S.C. § 103(a).

We reverse.

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[1] We use the word "Appellants" to refer to "Applicants" as defined in 37 C.F.R. § 1.42(a). According to Appellants, the real party in interest is Aurin Biotech Inc. Br. 3.

STATEMENT OF THE CASE

The Specification states that the claimed method "pertains to the use of low molecular weight components of the aurin tricarboxylic acid synthetic complex and their derivatives, to treat human conditions where self damage is caused by the membrane attack complex of complement." Spec. 2. The conditions treated include Alzheimer disease. *Id.*

Claims 1–5 and 10 are on appeal. Claim 1 is illustrative and reads as follows:

> 1. A method of selectively inhibiting the membrane attack complex of complement to treat Alzheimer's disease, the method comprising administering an active ingredient comprising an effective amount of aurin tricarboxylic acid, aurin quadracarboxylic acid, aurin hexacarboxylic acid, and/or esters thereof, wherein the method excludes administration of components of aurin tricarboxylic acid complex greater than or equal to 1 kilodalton in molecular weight, wherein the Alzheimer's disease is associated with host cell self-damage by the membrane attack complex.

Br. 14.

The Examiner rejected claims 1–5 and 10 rejected under 35 U.S.C. § 103(a) as obvious over the combination of Bernstein,[2] Wang,[3] and Rogers.[4]

[2] Bernstein et al., US Patent No. 4,007,270, issued Feb. 8, 1977 ("Bernstein").
[3] Wang et al., *Isolation and Structure Elucidation of Low Molecular Weight Components of Aurintricarboxylic Acid (ATA),* 57 J. Org. Chem. 3861–3866 (1992) ("Wang").
[4] Rogers et al., *Complement Activation by β-amyloid in Alzheimer Disease,* 89 Proc. Natl. Acad. Sci. USA 10016–10020 (1992) ("Rogers").

OBVIOUSNESS

Claim 1 recites a method for inhibiting the membrane attack complex of complement to treat Alzheimer's disease by administering aurin tricarboxylic acid, aurin quadracarboxylic acid, aurin hexacarboxylic acid, and/or esters thereof. The Specification expressly defines aurin tricarboxylic acid to be a compound having a molecular weight of 422 kDa, aurin quadracarboxylic acid to be a compound having a molecular weight of 572 kDa, and aurin hexacarboxylic acid to be a compound having a molecular weight of 858 kDa. Spec. 4.

The express definition of aurin tricarboxylic acid ("ATA") provided by Appellants differs from how the term "aurin tricarboxylic acid" was used in the art. For example, Wang discloses "ATA is actually a heterogeneous mixture of polymers." Wang, 3862. Similarly, Gonzalez[5] discloses that "aurintricarboxylic acid is a mixture of polymers of the phenol-formaldehyde type." Gonzalez, 535. This is consistent with the teaching in the Specification that aurin tricarboxylic acid having a molecular weight of 422 kDa, aurin quadracarboxylic acid having a molecular weight of 572 kDa, and aurin hexacarboxylic acid having a molecular weight of 858 kDa, were obtained by separating the "commercially purchased" "triammonium salt of the aurin tricarboxylic acid complex known as Aluminon" "into high and low molecular weight components." Spec. 4.

[5] Gonzalez et al., *Fractionation and Structural Elucidation of the Active Components of Aurintricarboxylic Acid, a Potent Inhibitor of Protein Nucleic Acid Interactions,* 562 Biochimica et Biophysica Acta 534–545 (1979) ("Gonzalez"). Gonzalez was cited by Appellants as evidence that the method of making aurin tricarboxylic acid utilized in Bernstein "produces a complex mixture of components." Br. n. 1, p. 5–6.

In finding the claimed method obvious, the Examiner found that Rogers disclosed that "β-AP activation of complement may contribute significantly to the neurotoxicity of β-AP as well as to the pathophysiology of neuronal dysfunction characteristic of AD [Alzheimer's disease]." Ans. 9. The Examiner found that Bernstein disclosed "inhibiting complement with a heterogeneous mixture of polymers that include aurin tricarboxylic acid, aurin quadracarboxylic acid and other components of the aurin tricarboxylic acid complex of less than 1 kDa in molecular weight." *Id.* at 6. The Examiner concluded:

> [I]t would have been obvious to a person of ordinary skill in the art to combine the teachings of Bernstein et al. which teaches a method of inhibiting complement comprising the administration of aurin tricarboxylic acid with the teachings of Rogers et al. which teaches that β-AP activates complement which may contribute significantly to the neurotoxicity of β-AP as well as to the pathophysiology of neuronal dysfunction characteristic of Alzheimer's Disease. Thus an ordinary skilled artisan would have been motivated to inhibit activation of complement associated with Alzheimer's disease according to the methods of Bernstein et al. with a reasonable expectation that inhibition of complement would significantly reduce the neurotoxicity of β-AP as well as reduce the pathophysiology of neuronal dysfunction characteristic of Alzheimer's disease associated with β-AP activation of complement.

Id. at 9.

With respect to the requirement of claim 1 that the method "exclude[] administration of components of aurin tricarboxylic acid complex of greater than or equal to 1 kilodalton in molecular weight," the Examiner concluded that since commercially available aurin tricarboxylic acid was known to be impure – i.e. was known to be a heterogeneous mixture of polymers – it would have been obvious to "use procedures well-known in the art as taught

by Wang et al. to purify or fractionate the composition such that only ATA which is the triphenylmethane dye is present resulting in the use of the ATA component of less than 1 kDa for inhibiting complement." Ans. 13. We are not persuaded.

We acknowledge that it is often obvious to purify a composition known to be impure. We further acknowledge that the prior art discloses an impure composition known as "aurin tricarboxylic acid" that included the low-molecular weight compounds recited in the claim – i.e., aurin tricarboxylic acid, aurin quadracarboxylic acid, and aurin hexacarboxylic acid. However, the Examiner does not identify in the cited art any teaching that the claimed low-molecular-weight compounds are the compounds in the heterogeneous mixture that have, or would have been expected to have, complement inhibiting activity. Moreover, Gonzalez suggests that compounds in the heterogeneous mixture having a high molecular weight have greater potency than compounds having a lower molecular weight. Gonzalez, 535 ("Evidence will be presented that aurintricarboxylic acid is a mixture of polymers of the phenol-formaldehyde type whose inhibitory potency increases with the average molecular weight of the fraction."); *see also*, Wang, 3865 ("All of these low molecular weight components were considerably less potent in preventing the cytopathic effect of HIV-1 than unfractionated ATA. This is not surprising because prior investigations of the anti-HIV activities of ATA fractions have shown that the antiviral potency increases with the molecular weight of the ATA fraction.") (internal citations omitted). The current record thus does not support the Examiner's finding that it would have been obvious to purify the heterogeneous mixture of polymers known in the art as ATA by excluding compounds having a

molecular weight greater than or equal to 1 kilodalton, because the evidence of record shows that such purification would have been expected to remove active compound, not concentrate it. Accordingly, we reverse the Examiner's rejection of claims 1–5 and 10.

SUMMARY

In summary:

Claim(s) Rejected	**35 U.S.C. §**	**Basis**	**Affirmed**	**Reversed**
1–5, 10	§103(a)	Bernstein, Wang, Fung		1–5, 10
Overall Outcome				1–5, 10

REVERSED