IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	Attorney Docket No. 2004_1016A
Masayo HIGASHIYAMA	:	**Confirmation No. 2612**
Serial No. 10/500,354	:	Group Art Unit 1611
Filed June 30, 2004	:	Examiner Barbara S. Frazier
AQUEOUS LIQUID PREPARATIONS AND LIGHT-STABILIZED AQUEOUS LIQUID PREPARATIONS	:	**Mail Stop: AMENDMENT**

DECLARATION UNDER 37 CFR 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Masayo HIGASHIYAMA, the undersigned, a citizen of Japan, residing at Suita-shi, Osaka, Japan, do hereby declare:

1. I am the sole inventor of the above-identified application.

2. I graduated from Nagoya City University, Japan, Graduate School of Pharmaceutical Sciences, in March 1995, and received a Doctor's degree in Engineering from Kyushu Institute of Technology, Japan, in September 2007.

3. Since April 1995 up to this time, I have been an employee of Senju Pharmaceutical Co., Ltd., and engaged in the pharmaceutical research of ophthalmic formulation.

4. I have reviewed the Office Action dated November 30, 2011, the Advisory Action dated May 2, 2012 and the Interview Summary dated July 2, 2012, and the references cited therein, in the above-identified U.S. Application Serial No. 10/500,354.

5. I declare the following distinctions between the invention claimed in the above-identified application and the following references: Kita et al. (U.S. Patent No. 6,307,052), Lehmussaari et al. (U.S. Patent No. 5,795,913) and Araki et al. (U.S. Patent Application Publication No. 2003/0139436).

The Distinctions Between the Claimed Invention and the Cited References

I. Carbopol Would Materially Affect the Basic and Novel Characteristics of the Claimed Invention

The Examiner has combined Kita et al., disclosing (+)-(S)-4-[4-[(4-chlorophenyl)(2-pyridyl)methoxy]piperidino] butyric acid (hereinafter, "bepotastine"), with Lehmussaari et al., disclosing a metal chloride, to arrive at the claimed invention.

Claims 1, 10[1] and 13 of the present application recite the transitional phrase "consisting essentially of", which limits the scope of a claim to the specified materials or steps and those that do not materially affect the basic and novel characteristic(s) of the claimed invention (see MPEP 2111.03).

The composition of Lehmussaari et al. requires the inclusion of an ion sensitive, hydrophilic polymer having viscosity, such as Carbopol, to control the formation of the polymer film on the cornea of the eye, and each of the reference's examples contain Carbopol (please see col. 2, line 57 to col. 3, line 6, and the Examples).

Carbopol is degraded by light. This is clear from the Chemical Abstract reference dated January 3, 1972 enclosed with the Amendment filed April 24, 2012. The reference is submitted again herewith in an Information Disclosure Statement. The reference states "CARBOXYVINYL POLYMERS of the type Carbopol 940…and 941 were degraded by light, type 941 presenting the highest DEGRADATION" (emphasis in original). This clearly teaches that it was known that Carbopol is degraded by light well-prior to the U.S. filing date of the present application (2003).

Using an ion sensitive, hydrophilic polymer, such as Carbopol, in the aqueous liquid preparation of claim 1 and the eye drops of claims 10 and 13 would materially affect the basic and novel characteristics of the claimed compositions, because it would introduce a component that degrades in light into a composition that is designed to be "light-stabilized" by a water-soluble metal chloride.

As a result, an ion sensitive, hydrophilic polymer is excluded from the aqueous liquid preparation of claim 1 and the eye drops of claims 10 and 13. Therefore, a person of ordinary

[1] Claim 10 will be amended to recite "consisting essentially of" when this Declaration is filed in the USPTO.

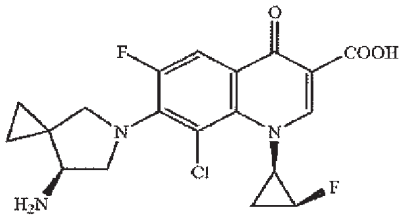
skill in the art could not have arrived at the presently claimed invention from the combination of Kita et al., disclosing bepotastine, and Lehmussaari et al., disclosing a metal chloride in a composition with Carbopol, with any reasonable expectation of success.

II. Araki et al.

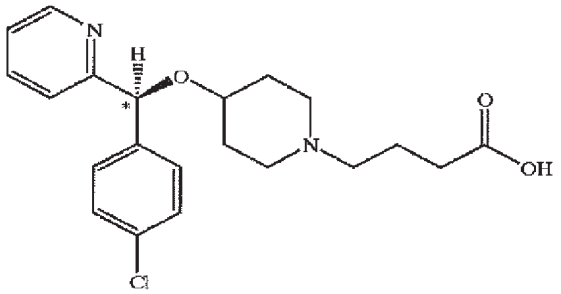
A. The Differences Between Bepotastine and Sitafloxacin

Araki et al. disclose a composition comprising sitafloxacin (see abstract). Sitafloxacin has a completely different chemical structure and has completely different chemical properties as compared to bepotastine, which is contained in the claimed compositions.

Sitafloxacin has the following chemical structure:



Bepotastine has the following chemical structure:



The compounds clearly have different chemical structures, and virtually no similar chemical moieties. For example, sitafloxacin has an oxoquinoline core bonded to a cyclopropyl group and a azaspiro[2,4]heptan group. On the other hand, bepotastine does not have any bicyclic or spiro rings, and has separate pyridine and piperidine rings. There are no common chemical groups in the two compounds that would suggest they share any similar activity or have any similar properties.

Araki et al. disclose light stabilization of sitafloxacin by sodium chloride. Sodium chloride is generally used for isotonization.

Since sitafloxacin has a completely different chemical structure and completely different

chemical properties as compared to bepotastine, as discussed above, there is no predictability or correlation of light stabilization of bepotastine by sodium chloride.

Therefore, one skilled in the art would not expect a metal chloride to have a light-stabilizing effect on bepostatine in view of the light stabilizing effect of sodium chloride on sitafloxacin.

B. <u>There is No Reasonable Expectation that Sodium Chloride Would Suppress Coloration and Precipitation of Bepotastine in view of Araki et al.</u>

Araki et al. state the following:

> [0100] As is understood from Table 1, the aqueous sitafloxacin solutions without sodium chloride or containing D-sorbitol in place of sodium chloride undergo reductions in pH, transmission and sitafloxacin content and an increase of related substances when irradiated.
>
> [0101] However, it is apparent that addition of sodium chloride suppresses these unfavorable changes due to irradiation, showing improvement on sitafloxacin stability against light.

The reference is silent on the suppression of coloration and precipitation. While Araki et al. teach that the addition of sodium chloride results in the suppression of changes in transmission, the reference does not teach or suggest that sodium chloride causes coloration, and, likewise, does not mention the suppression of coloration by sodium chloride.

On the other hand, the present application demonstrates that when an aqueous bepotastine solution free of sodium chloride was subjected to light irradiation, the solution turned black green, and a precipitate was produced (see specification, page 8, lines 8-9, Formulation 1). A person of ordinary skill in the art with the goal of reducing or eliminating this phenomenon would not refer to the teachings Araki et al. and would not have been motivated by the teachings to Araki et al. to include a metal chloride in a bepotastine composition, because the reference provides no description regarding coloration and precipitation.

Accordingly, there would have been no reasonable expectation of success of arriving at the claimed invention from the disclosure of Araki et al.

Therefore, the aqueous liquid preparation of claim 1 and the eye drops of claims 10 and 13 would not have been obvious over Araki et al. in view of Kita et al. and/or Lehmussaari et al., or in view of any other reference.

I further declare that all statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

Signed at Osaka , Japan on this 11th day of September, 2012

Masayo Higashiyama

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