Date	November 21, 2017	Court	Intellectual Property High Court, Fourth Division
Case number	2017 (Gyo-Ke) 10003		
– A case in which the court held that the JPO's determination in its decision concerning the effect of inventions titled "topical ophthalmic formulation containing doxepin derivatives to treat allergic eye diseases" (the "Inventions") was erroneous, by finding that the Inventions are not found to have an outstanding effect that is hard to predict based on the structure of the Inventions, which a person ordinarily skilled in the art could have easily conceived of based on the cited inventions.			

Reference: Article 29, paragraph (2) of the Patent Act

Number of related rights, etc.: Patent No. 3068858, Invalidation Trial No. 2011-800018, 2013 (Gyo-Ke) 10058 (the "former judgment")

Summary of the Judgment

1. In this case, the plaintiff sought the rescission of the JPO decision in question (the "JPO Decision") that dismissed the request for an invalidation trial for the Inventions titled "topical ophthalmic formulation containing doxepin derivatives to treat allergic eye diseases." In relation to the Inventions, a court decision that rescinded the JPO decision that dismissed the request for an invalidation trial (the former judgment) has become final and binding.

Based on the binding effect of the former judgment, the JPO found as follows in the JPO Decision: A person ordinarily skilled in the art who has read Cited Invention 1 and Cited Invention 2 could have easily conceived of the difference between Invention 1 and Cited Invention 1. However, the facts that [i] "11-(3-dimethylaminopropylidene)-6, 11-dihydrodibenz[b, e] oxepin-2-acetic acid" (hereinafter referred to as "Compound A") exerts a high histamine release inhibition ratio for human conjunctival mast cells, and [ii] the range of concentration of the cis isomer of Compound A wherein the maximum histamine release inhibition ratio is obtained is very wide were particularly outstanding effects that a person ordinarily skilled in the art could not have predicted based on the cited invention and the common technical knowledge as of the priority date of the patent in question (the "Patent"). These should be included in consideration as advantageous effects compared to the cited invention when finding an inventive step of the Inventions. Based on these findings, the JPO concluded that it cannot be said that a person ordinarily skilled in the art could have easily conceived of the Inventions. The plaintiff alleged errors in the JPO's determination of outstanding effects of the Inventions as a ground for invalidation.

2. In this case, the court held as follows and rescinded the JPO Decision.

Whether a person ordinarily skilled in the art could have easily conceived of an invention should be determined based on whether said invention has an outstanding effect that is hard to predict, in addition to whether there is a motivation or obstruction for applying the secondary cited invention to the primary cited invention. Moreover, in order to consider the effect of said invention, it is necessary that said effect is stated in the description, or, even if said effect is not stated in the description, said effect must be presumed by a person ordinarily skilled in the art based on the description and drawings. [...] According to the former judgment, which has become final and binding, it is found that a person ordinarily skilled in the art who has read Cited Invention 1 and Cited Invention 2 could have confirmed that KW-4679 (hydrochloride of the cis isomer of Compound A) conducts actions to inhibit histamine release from human conjunctival mast cells ("human conjunctival mast cell stabilization" actions) and easily conceived of the idea to apply KW-4679 to the intended use as "human conjunctival mast cell stabilizer," when attempting to apply an eye drop containing KW-4679 for controlling allergic conjunctivitis stated in Cited Invention 1 as an eye drop for allergic eye diseases in humans. There is no conflict regarding this point between the parties. Then, it cannot be said that the effect of Compound A to conduct actions to inhibit histamine release from human conjunctival mast cells is an outstanding effect that is hard to predict for a person ordinarily skilled in the art.

In addition, although Cited Invention 1 or Cited Invention 2 does not contain any clear statement regarding whether Compound A conducts actions to inhibit histamine release from human conjunctival mast cells or regarding the level of the effect in the case where Compound A conducts such actions, [...] it cannot be said that the effect of the human conjunctival mast cell stabilizer containing Compound A regarding Invention 1 to conduct actions to inhibit histamine release from human conjunctival mast cells, which is stated in the description in question, was an outstanding effect that exceeded the scope of what a person ordinarily skilled in the art would expect based on the common technical knowledge as of the priority date of the Patent, when the circumstances as of said date where it was known that a compound that has a strong effect to inhibit histamine release from human conjunctival mast cells other than Compound A exists. [...] Therefore, it cannot be said that the effect of Invention 1 is an outstanding effect that is hard to predict based on the structure of Invention 1, which could have been easily conceived of by a person ordinarily skilled in the art based on Cited Inventions 1 and 2. Thus, the JPO's determination concerning the effect of Invention 1 in the JPO Decision was erroneous.

Invention 2 adds a matter specifying the invention to Invention 1, stating that Compound A "inhibits histamine release from human conjunctival mast cells by 66.7 percent or more." It cannot be said that the effect to "inhibit histamine release from human conjunctival mast cells by 66.7 percent or more" is an outstanding effect that is hard to predict based on the structure of the Invention 2, which could have been easily conceived of by a person ordinarily skilled in the art based on Cited Inventions 1 and 2, due to the same reasons stated above. Therefore, the JPO's determination concerning the effect of Invention 2 in the JPO Decision was also erroneous.

Judgment rendered on November 21, 2017
2017 (Gyo-Ke) 10003
Case of Seeking Rescission of JPO Decision
Date of conclusion of oral argument: October 3, 2017

Judgment

Plaintiff: X
Defendant: Alcon Research, Ltd.
Defendant: Kyowa Hakko Kirin Co., Ltd.

Main Text

1. The Trial Decision made on Invalidation Trial No. 2011-800018 by the Japan Patent Office on December 1, 2016 shall be rescinded.

2. Defendants shall bear court costs.

3. For Defendant, Alcon Research Ltd., the additional period for filing a final appeal and a petition for acceptance of final appeal against this judgment shall be specified as 30 days.

Facts and Reasons

I. Claims

Same gist as the main text.

II Outline of The Case

1 Outline of procedures at the JPO

(1) Present Patent

Defendants filed a patent application for an invention titled "Topical ophthalmic formulations containing doxepin derivatives for treating allergic eye diseases" on May 3, 1996 (priority claimed: June 6, 1995, US); the establishment thereof was registered on May 19, 2000 (Patent No. 3068858. Number of claims: 12. Exhibit Ko 81. Hereinafter, this patent is referred to as "Present Patent.").

(2) Primary Trial Decision

A Plaintiff filed a request for an invalidation trial of Present Patent, which was kept pending with Invalidation Trial No. 2011-800018.

B Defendants filed a request for correction on May 23, 2011, in which the Claims of Present Patent were corrected (hereinafter, referred to as "Primary Correction").

C On December 16, 2011, the JPO allowed Primary Correction and made a trial decision to invalidate the patent on the inventions according to Claims 1 to 12 (hereinafter, referred to as "Primary Trial Decision") (Exhibit Ko 82).

D Defendants instituted an action seeking rescission of Primary Trial Decision (2012 (Gyo-Ke) 10145) on April 24, 2012, and then filed a request for correction trial, which seeks corrections of the claims of Present Patent, on June 29, 2012.

E The Intellectual Property High Court made an order to rescind the Primary Trial Decision on July 11, 2012, in accordance with Article 181, paragraph (2) of the Patent Act prior to the revision by Act No. 63, 2011.

(3) Secondary Trial Decision

A As a result of the order of the above (2) E, the JPO resumed the examination on Invalidation Trial No. 2011-800018. On August 10, 2012, Defendants filed a request for correction, in which Claims 2 to 4 and 6 to 12 in the scope of claims of the Present Patent were canceled (hereinafter, referred to as "Secondary Correction").

B On January 22, 2013, the JPO allowed Secondary Correction and made a trial decision to dismiss the request of the present trial on Claims 1 and 5 (hereinafter, referred to as "Secondary Trial Decision") (Exhibit Ko 83).

C Plaintiff instituted an action seeking rescission of Secondary Trial Decision on March 1, 2013 (2013 (Gyo-Ke) 10058).

D The Intellectual Property High Court made a judgment to rescind the Secondary Trial Decision (hereinafter, referred to "Former Judgment") on July 30, 2014, and the judgment became final and binding on January 12, 2016, since the nonacceptance of the final appeal was decided (Exhibit Ko 84).

(4) Present Trial Decision

A As a result of Former Judgment, the JPO resumed the examination on Invalidation Trial No. 2011-800018. On February 1, 2016, Defendants filed a request for correction on the scope of claims of Present Patent (hereinafter, referred to "Present Correction").

B On December 1, 2016, the JPO allowed the Present Correction and made a trial

decision that "the request of Present Trial shall be dismissed" (hereinafter, referred to as "Present Trial Decision"), and the certified copy of the trial decision was dispatched to Plaintiff on December 9, 2016.

C Plaintiff instituted Present Action seeking rescission of the Present Trial Decision on January 6, 2017.

2 Description of the scope of claims

The description of Claims 1 and 5 of Present Patent after Present Correction is as follows. Hereinafter, the invention according to Claim 1 is referred to as "Present Invention 1," the invention according to Claim 5 is referred to as "Present Invention 2" and both of them are collectively referred to as "Present Inventions." Further, the description after Present Correction (Exhibit Ko 205) is referred to as "Present Description."

[Claim 1]

An ophthalmic stabilizing agent for human conjunctival mast cells prepared as a topically administrable eye drop for treating allergic eye diseases in humans, comprising a therapeutically effective amount of 11-(3-dimethylaminopropylidene)-6,11-dihydrodibenz[b,e]oxepin-2-acetic acid, or a pharmaceutically acceptable salt thereof.

[Claim 5]

An ophthalmic stabilizing agent for human conjunctival mast cells prepared as a topically administrable eye drop for treating allergic eye diseases in humans, comprising a therapeutically effective amount of 11-(3-dimethylaminopropylidene)-6,11-dihydrodibenz[b,e]oxepin-2-acetic acid, or a pharmaceutically acceptable salt thereof,

wherein the 11-(3-dimethylaminopropylidene)-6,11-dihydrodibenz[b,e]oxepin-2-acetic acid is (Z)-11-(3-dimentylaminopropylidene)-6,11-dihydrodibenz[b,e]oxepin-2-acetic acid; and the agent is substantially free of (E)-11-(3-dimentylaminopropylidene)-6,11-dihydrodibenz[b,e]oxepin-2-acetic acid and inhibits histamine release from human conjunctival mast cells by 66.7% or more.

3 Gist of the reasons given in Present Trial Decision

(1) The reasons given in Present Trial Decision are described in the attached Trial Decision (copy). In short, Present Inventions: (1) could not have been easily made by

a person ordinarily skilled in the art in view of the invention described in Cited Document 1 indicated below as A (hereinafter, referred to as "Cited Invention 1"), the invention described in Cited Document 2 indicated below as B (Hereinafter, referred to as "Cited Invention 2"), and the common technical knowledge as of the time of the priority date of Present Patent; and (2) could not have been easily made by a person ordinarily skilled in the art in view of the invention described in Cited Document 3 indicated below as C (hereinafter, referred to as "Cited Invention 3") together with Cited Inventions 1 and 2, and the common technical knowledge as of the time of the priority date of Present Patent. Thus, they are not inventions that were patented in spite of violation of Article 29, paragraph (2) of the Patent Act.

A Cited Document 1: Chiaki Kamei, et al., "Influence of anti-allergic agent on experimental allergic conjunctivitis in guinea pigs," Atarashii Ganka (Journal of the eye) Vol. 11, No. 4 (1994), pages 603 to 605 (Exhibit Ko 1)
B Cited Document 2: Japanese Unexamined Patent Application Publication No. 1988-10784 (Exhibit Ko 4)
C Cited Document 3: Japanese Unexamined Patent Application Publication No. 1987-45557 (Exhibit Ko 3)

(2) It is understood that Present Trial Decision has found Differences between Present Inventions and Cited Invention 1 as described below. It is added that Present Trial Decision does not specifically describe any common feature between Cited Invention 1 and Present Inventions.

A Differences between Present Invention 1 and Cited Invention 1
(a) Difference 1
Regarding allergic eye diseases, Present Invention 1 specifies them as "in humans" while Cited Invention 1 does not so specify.

(b) Difference 2
Regarding ophthalmic compounds (agents), Present Invention 1 specifies it as "an ophthalmic stabilizing agent for human conjunctival mast cells," while Cited Invention 1 does not so specify.

(c) Difference 3
Present Invention 1 specifies "prepared as an eye drop," while Cited Invention 1

does not so specify.

B Differences between Present Invention 2 and Cited Invention 1

(a) The same as Differences 1 to 3.

(b) Difference 4

Present Invention 2 inhibits histamine release from human conjunctival mast cells by 66.7% or more, while Cited Invention 1 does not so specify.

(3) It is understood that Present Trial Decision has found Differences between Present Inventions and Cited Invention 3 as described below. It is added that Present Trial Decision does not specifically describe any common feature between Cited Invention 1 and Present Inventions.

A Differences between Present Invention 1 and Cited Invention 3

(a) Difference 5

Present Invention 1 limits the oxepin derivative to "11-(3-dimethylaminopropylidene)-6,11-dihydrodibenz[b,e]oxepin-2-acetic acid" (hereinafter, sometimes referred to as "Compound A"), while Cited Invention 3 expresses it by a generic concept including Compound A and it exemplifies "11-(3-dimethylaminopropylidene)-6,11-dihydrodibenz[b,e]oxepin-2-carboxylic acid" in Examples.

(b) Difference 6

Present Invention 1 specifies "ophthalmic stabilizing agent for human conjunctival mast cells," while Cited Invention 3 does not so specify.

(c) Difference 7

Present Invention 1 specifies "prepared as an eye drop," while Cited Invention 3 specifies merely "ophthalmic solution."

B Differences between Present Invention 2 and Cited Invention 3

(a) Same as Differences 6 and 7

(b) Difference 8

Present Invention 2 limits the oxepin derivative to a Z-form (cis-isomer) of

Compound A, while Cited Invention 3 expresses it by a generic concept including Compound A and it exemplifies "11-(3-dimethylaminopropylidene)-6,11-dihydrodibenz[b,e]oxepin-2-carboxylic acid" in Examples.

(c) Difference 9

Present Invention 2 inhibits histamine release from human conjunctival mast cells by 66.7% or more, while Cited Invention 3 does not so specify.

4 Regarding Former Judgment that has become final and binding

(1) The description of the scope of the claims examined in Secondary Trial Decision and Former Judgment is as follows (Exhibit Ko 84). Hereinafter, these inventions are collectively referred to as "Inventions after Secondary Correction."

[Claim 1]

An ophthalmic stabilizing agent for human conjunctival mast cells prepared as a topically administrable eye drop for treating allergic eye diseases in humans, comprising a therapeutically effective amount of 11-(3-dimethylaminopropylidene)-6,11-dihydrodibenz[b,e]oxepin-2-acetic acid, or a pharmaceutically acceptable salt thereof. (Same as Claim 1 after Present Correction)

[Claim 2]

A topically administrable ophthalmic composition for treating allergic eye diseases comprising a therapeutically effective amount of 11-(3-dimethylaminopropylidene)-6,11-dihydrodibenz[b,e]oxepin-2-acetic acid, or a pharmaceutically acceptable salt thereof, wherein the 11-(3-dimethylaminopropylidene)-6,11-dihydrodibenz[b,e]oxepin-2-acetic acid is (Z)-11-(3-dimentylaminopropylidene)-6,11-dihydrodibenz[b,e]oxepin-2-acetic acid; the agent is substantially free of (E)-11-(3-dimentylaminopropylidene)-6,11-dihydrodibenz[b,e]oxepin-2-acetic acid and produces a human conjunctival mast cell stabilizing effect. (Through Secondary Correction, Claim 5 was renumbered as Claim 2. The above differs from Claim 5 after Present Correction in that: the above refers to "ophthalmic composition" instead of "an ophthalmic composition for stabilizing agent for human conjunctival mast cells prepared as an eye drop"; the above does not describe "inhibit histamine release from human conjunctival mast cells by 66.7% or more"; and the above refers to "composition that produces a human conjunctival mast cell stabilizing effect.")

(2) Secondary Trail Decision and Former Judgment do not specifically find differences between Cited Invention 1 and the inventions after Secondary Correction, but it is understood that they are premised on the same gist as in the above 3(2) except Differences 4 and 9.

(3) Gist of the reasons given in Secondary Trial Decision

Secondary Trial Decision stated that: Secondary Correction was allowed; the invention-specifying matter "human conjunctival mast cell stabilizing effect" in the inventions after Secondary Correction was not conceived through a motivation based on Cited Documents 1 and 2; thus, the reasons for invalidation alleged by Plaintiff regarding the lack of inventive step based on Cited Document 1 as the primary cited document were groundless; and the request for the patent invalidation trial should be dismissed.

(4) Gist of the reasons given in Former Judgment

Former Judgment rescinded Secondary Trial Decision and the reason therefor in brief is as follows.

It is found that

in making an attempt to apply an eye drop containing KW-4679 (a hydrochloride of a cis-isomer of Compound A) for controlling allergic conjunctivitis described in Cited Document 1 as an eye drop for allergic eye diseases in humans,

a person ordinarily skilled in the art who has learned of Cited Documents 1 and 2 could have confirmed that KW-4679 has an inhibiting action on histamine released from human conjunctival mast cells (human conjunctival mast cell stabilizing action) and could have easily conceived of using the same as a human conjunctival mast cell stabilizing agent. Therefore, the above decision of Secondary Trial Decision is erroneous.

5 Grounds for Rescission

(1) Error in the decision on the inventive step based on Cited Invention 1 (Ground for Rescission 1)

Error in the decision on the prominent effects of Present Inventions

(2) Error in the decision on the inventive step based on Cited Invention 3 (Ground for Rescission 2)

A Error in the decision on whether Difference 5 could have been easily conceived of

B Error in the decision on whether Difference 6 could have been easily conceived of

(omitted)

IV Judgment of this court

1 Regarding Present Inventions

(1) The description of Claims 1 and 5 in the scope of the claims on Present Inventions is deemed to be such as stated in the above II. 2, and Present Description generally has the following description (Regarding Table 1 cited in the following description, see the attachment for the list of figures and tables of the present description.).

A Field of the Invention

The present invention relates to topical ophthalmic formulations used for treating allergic eye diseases, such as allergic conjunctivitis, vernal conjunctivitis, vernal keratoconjunctivitis, and giant papillary conjunctivitis. More particularly, the present invention relates to therapeutic and prophylactic topical use of 11-(3-dimethylaminopropylidene)-6,11-dihydrodibenz[b,e]oxepin-2-acetic acid for treating and/or preventing allergic eye diseases. (page 3, lines 3 to 9)

B Description of the Related Art

As taught in U.S. Patent Nos. 4,871,865 and 4,923,892, ... ("the Burroughs Wellcome Patents"), certain carboxylic acid derivatives of doxepin, including 11-(3-dimethylaminopropylidene)-6,11-dihydrodibenz[b,e]oxepine-2-carboxylic acid and 11-(3-dimethylaminopropylidene)-6,11-dihydrodibenz[b,e]oxepine-2(E)-acrylic acid, have antihistamine and antiasthmatic activity. These two patents classify the carboxylic acid derivatives of doxepin as mast cell stabilizers with antihistaminic action ... Although both of the Burroughs Wellcome Patents claim that the variety of pharmaceutical formulations disclosed are effective both for veterinary and for human medical use, neither patent contains an example demonstrating that the carboxylic acid derivatives of doxepin have activity in humans. ... It is now well established, however, that the species of mast cells which exist in rodents are different from those in humans. ... Moreover, there exist mast cell populations within the same species that differ in phenotype, biochemical properties, functional and pharmacological responses and ontogeny. These recognized differences in mast cells

both between and within species are referred to as mast cell heterogeneity. ... Because different mast cells exhibit different responses to pharmacological agents, it is not obvious that compounds claimed to be anti-allergic ("mast cell stabilizers") will have clinical utility in specific mast cell populations. The assumption that mast cells are a homogeneous population and that therefore the effects of anti-allergic drugs observed in experiments in rat mast cells would be predictive of those in human cells is known to be incorrect. ... (page 3, line 10 to page 4, line 20)

C Topical ophthalmic formulations which contain drugs having conjunctival mast cell activity may only need to be applied once every 12-24 hours instead of once every 2-4 hours. One disadvantage to the ophthalmic use of reported anti-allergic drugs which in fact have no human conjunctival mast cell stabilizing activity is an increased dosage frequency. Because the effectiveness of ophthalmic formulations containing drugs which do not have conjunctival mast cell activity stems primary from a placebo effect, more frequent doses are typically required than for drugs which do exhibit conjunctival mast cell activity. ... What is needed are topically administrable drug compounds which have demonstrated stabilizing activity on mast cells obtained from human conjunctiva, the target cells for treating allergic eye diseases. ... (page 5, line 10 to page 6, line 6)

D Summary of the Invention

The present invention provides a method for treating an allergic eye disease characterized by administering to the eye a topical ophthalmic formulation which contains a therapeutically effective amount of 11-(3-dimethylaminopropylidene)-6,11-dihydrodibenz[b,e]oxepin-2-acetic acid (referred to as "Compound A" hereinafter) or a pharmaceutically acceptable salt thereof. The formulation may contain the cis isomer of Compound A (Z-11-(3-dimethylaminopropylidene)-6,11-dihydrodibenz[b,e]oxepin-2-acetic acid), the trans isomer of Compound A (E-11-(3-dimethylaminopropylidene)-6, 11-dihydrodibenz[b,e]oxepin-2-acetic acid), or a combination of both the cis and the trans isomers of Compound A, and unless specified otherwise, "11-(3-dimethylaminopropylidene)-6,11-dihydrodibenz[b,e]oxepin-2-acetic acid" or "Compound A" means the cis isomer, the trans isomer, or a mixture of the two. ... Compound A has human conjunctival mast cell stabilizing activity, and may be applied as infrequently as once or twice a day in some cases. In addition to its mast cell stabilizing activity, Compound A also possesses significant antihistaminic activity. Thus, in addition to a prophylactic effect, Compound A will also have a therapeutic

effect. (page 6, lines 7 to 29)

E Detailed Description of the Invention

Compound A is a known compound and both the cis and the trans isomers of Compound A can be obtained by the methods disclosed in U.S. Patent No. 5,116,863, ... The inhibitory effects of reported anti-allergic, mast cell stabilizing drugs on mast cells obtained from human conjunctiva (the target cells for topical ophthalmic drug preparations claimed useful in treating allergic conjunctivitis) were tested according to the following experimental method. Human conjunctival tissues obtained from organ/tissue donors were weighed ... Cell suspensions containing 5000 mast cells were added to TGCM containing tubes and challenged with anti-human IgE. ... The results are reported in Table 1, below. As Table 1 clearly shows, the anti-allergic drugs disodium cromoglycate and nedocromil sodium failed to significantly inhibit human conjunctival mast cell degranulation. In contrast, Compound A (cis isomer) produced concentration-dependent inhibition of mast cell degranulation. (page 7, line 1 to page 9, line 7)

F Compound A may be administered to the eye by means of conventional topical ophthalmic formulations, such as solutions, suspensions, or gels. The preferred formulation for topical ophthalmic administration of Compound A is a solution. The solution is administered as eye drops. The preferred form of Compound A in the topical ophthalmic formulations of the present invention is the cis isomer. A general method of preparing the eye drops of the present invention is described below. Compound A and an isotonic agent are added to sterilized purified water, and if required, a preservative, a buffering agent, a stabilizer, a viscous vehicle, and the like are added to the solution and dissolved therein. The concentration of Compound A is 0.0001 to 5 w/v %, preferably 0.001 to 0.2 w/v %, and most preferably about 0.1 w/v %, based on the sterilized purified water. After dissolution, the pH is adjusted with a pH controller to be within a range which allows the use as an ophthalmologic medicine, preferably within the range of 4.5 to 8. ... The eye drops produced by the above method typically need only be applied to the eyes a few times a day in an amount of one to several drops at a time, although in more severe cases the drops may be applied several times a day. A typical drop is about 30 μl. (page 13, line 1 to page 14, line 13)

(2) In accordance with the above (1), it is found that the features of Present

Inventions are as described below.

A The Present Inventions relate to therapeutic and prophylactic topical use of Compound A for treating and/or preventing allergic eye diseases. (The above (1) A)

B Compound A has human conjunctival mast cell stabilizing activity, and may be applied as infrequently as once or twice a day in some cases. (The above (1) D)

C When the inhibitory effects of anti-allergic, mast cell stabilizing drugs on mast cells were obtained from human conjunctiva, Compound A (cis isomer) produced concentration-dependent inhibition of mast cell degranulation. (Table 1) (The above (1) E)

D A general method of preparing the eye drops of Present Inventions includes adding Compound A and an isotonic agent to sterilized purified water; and if required, adding a preservative, a buffering agent, a stabilizer, a viscous vehicle, and the like to the solution, and dissolving therein. The concentration of Compound A is 0.0001 to 5 w/v %, preferably 0.001 to 0.2 w/v %, and most preferably about 0.1 w/v %, based on the sterilized purified water. After dissolution, the pH is adjusted with a pH controller to be within a range which allows use as an ophthalmologic medicine, preferably within the range of 4.5 to 8. (The above (1) F)

2 Regarding Cited Invention 1

(1) Cited Document 1 (Exhibit Ko 1) has the following general descriptions.

A Impacts of various anti-allergic agents on antigen-induced and histamine-induced conjunctivitis were studied by use of guinea pigs. As a result, eye drops of chlorpheniramine, ketotifen and KW-4679 were found to exhibit stronger inhibitory effects on histamine-induced conjunctivitis compared to antigen-induced conjunctivitis. (Abstract in the middle section of page 603)

B Introduction

For the treatment of allergic conjunctivitis, drugs having an antihistaminic action such as chlorpheniramine or ketotifen, are widely used. (page 603, lines 1 to 4 of the left column)

C Experimental method

2. Quantification of conjunctivitis symptoms

The severity of conjunctivitis was defined as follows.

Score 1: mild hyperemia was exhibited.

Score 2: intense hyperemia was exhibited.

Score 3: mild to moderate edema was exhibited with hyperemia.

Score 4: outstanding edema was generated.

3. Release of histamine from conjunctiva

After 15 minutes of an eye drop of antigen, a conjunctiva was excised and weighed, and then, washed with a physiological saline solution. Thereafter, ... homogenized, ... centrifuged, and a supernatant thereof was cryopreserved. Then, ... thawed and centrifuged, and the histamine content in the supernatant was determined by HPLC (high performance liquid chromatography).

4. Measurement of histamine content in lacrimal fluid

After 15 minutes of administration of an eye drop of antigen, a physiological saline solution was instilled; and then, lacrimal fluid was collected, ... centrifuged, and the histamine content in the supernatant was measured by HPLC.

(page 604, line 1 of the left column to line 2 of the right column)

D Experimental results

1. Effects on antigen-induced conjunctivitis

Figure 1 shows impacts of various anti-allergic agents on allergic conjunctivitis induced by instillation of an antigen liquid (20 mg/ml) on conjunctivas of guinea pigs. ... KW-4679 exhibited a significant inhibitory action at the concentrations of 10 and 100 ng/μl. ...

2. Effects on antigen-induced and histamine-induced conjunctivitis

Table 1 shows effects of various anti-allergic agents on antigen- and histamine-induced conjunctivitis in terms of the IC_{50} value. Chlorpheniramine, ketotifen, and KW-4679 exhibited stronger inhibitory effects on histamine-induced conjunctivitis than on antigen-induced conjunctivitis. ...

3. Action on histamine release from conjunctivas

As shown in Fig. 2, results show that ... the effects of chlorpheniramine, ketotifen, and KW-4679 were not significant.

4. Effects on the histamine content in lacrimal fluid

The histamine content in guinea pig lacrimal fluid before the instillation of antigen

was 1.7 ± 0.4 ng.ml; but after the instillation of antigen, the histamine content increased about fivefold (8.6 ± 0.8 ng/ml). Instillation of levocabastine and amlexanox 15 minutes before the application of antigen significantly inhibited an increase of the histamine content in lacrimal fluid, which was caused by antigen-antibody reaction. Chlorpheniramine, ketotifen, and KW-4679 did not show a significant effect.
(page 604, line 3 of the right column to page 605, line 19 of the left column)

E In view of the above findings, regarding chlorpheniramine, ketotifen, and KW-4679, it is speculated that the anti-histamine action mainly possessed by these drugs inhibited conjunctivitis caused by antigen-antibody reaction. (page 605, lines 26 to 29 of the left column)

F Meanwhile, it is speculated that levocabastine and amlexanox inhibit histamine release from conjunctivas, which is caused by antigen-antibody reaction. Then, when the effects of each drug on the histamine release from conjunctivas caused by antigen-antibody reaction were studied, these drugs were found to exhibit significant inhibitory effects. Chlorpheniramine, ketotifen, and KW-4679 were ineffective. (page 605, lines 29 to 34 of the left column)

(2) Invention described in Cited Document 1

In accordance with the above (1), it is found that Cited Document 1 discloses an eye drop, which contains KW-4679 for inhibiting allergic conjunctivitis. In addition, KW-4679 is a hydrochloride of "(Z)-11-(3-dimentylaminopropylidene)-6,11-dihydrodibenz[b,e]oxepin-2-acetic acid" (Z-form (cis-isomer) of Compound A) (see 1.2 in Exhibit Ko 2). Thus, KW-4679 described in Cited Document 1 corresponds to: "a pharmaceutically acceptable salt" of "11-(3-dimethylaminopropylidene)-6,11-dihydrodibenz[b,e]oxepin-2-acetic acid" of Present Invention 1; and "(Z)-11-(3-dimentylaminopropylidene)-6,11-dihydrodibenz[b,e]oxepin-2-acetic acid" (cis-isomer of Compound A) of Present Invention 2.

As described above, it is found that Cited Document 1 discloses an eye drop, which contains KW-4679 (a hydrochloride of a cis-isomer of Compound A) for inhibiting allergic conjunctivitis.

3 Regarding Ground for Rescission 1 (error in determining the inventive step based on Cited Invention 1)

(1) Comparison between Present Inventions and Cited Invention 1

Since Cited Invention 1 is as given in the above 2 (2), it is found that there exist Differences 1 to 4 described in the above II. 3 (2) between Cited Invention 1 and Present Inventions, and this is not disputed by the parties.

(2) Determination of Former Judgment that has become final and binding

Former Judgment (Exhibit Ko 84) has found the common technical knowledge at the time of the priority date of Present Patent as in the below-described A in the section subtitled "Ground for Rescission 3 (error in determining the inventive step based on the primary cited document or Exhibit Ko 1)." Based on that, Former Judgment has determined that: it was considered that a person ordinarily skilled in the art, who has learned of Cited Documents 1 and 2, could have easily conceived of using KW-4679 for "a stabilizing agent for human conjunctival mast cells"; and the determination of Secondary Trial Decision that the reasons for invalidation alleged by Plaintiff regarding the lack of inventive step based on Cited Document 1 as the primary cited document were groundless, was erroneous.

A Common technical knowledge at the time of the priority date of Present Patent

(a) Common technical knowledge pertaining to research and development on drugs for inhibiting human allergic conjunctivitis

Anti-allergic agents are roughly classified into two categories by their action mechanisms: drugs having antagonism against various chemical mediators such as histamine produced and released from mast cells; and drugs having a release inhibitory action of those chemical mediators from mast cells. In research and development on drugs for inhibiting human allergic conjunctivitis, these two actions have been generally confirmed.

In research and development on drugs for inhibiting human allergic conjunctivitis, animal conjunctivitis models of rats or guinea pigs were created as a model similar to human allergic conjunctivitis, and used to assess effects of drugs such as the effect of instillation.

A package insert (in the section for "pharmacology") of an anti-allergic eyedrop for humans, which was sold at the time of the priority date of Present Patent, described that each active ingredient exhibited a conjunctivitis inhibitory action in animal conjunctivitis models of rats or guinea pigs; and exhibited a release inhibitory action of a chemical mediator such as histamine from peritoneal mast cells of rats or the like.
(page 83, line 18 to page 84, line 15)

(b) Heterogeneity of mast cells

At the time of the priority date of Present Patent, the histamine release inhibitory action of a drug against mast cells was sometimes varied depending on the species or the tissue of mast cells, and it was common technical knowledge that experimental results on mast cells of a certain tissue of a certain animal species did not always allow the prediction of experimental results on mast cells of other tissue of other animal species.

However, it is undeniable that: experimental results on the responsivity of a drug in human conjunctivitis sometimes exhibit the same tendency as experimental results on the responsivity of the drug in animal conjunctivitis models of rats or guinea pigs; and experimental results on mast cells in human conjunctivas sometimes exhibit the same tendency as experimental results on mast cells in a certain tissue of rats or guinea pigs. Regarding the heterogeneity of mast cells, the above goes no further than indicating that experimental results on mast cells in a certain tissue of a certain animal species do not always allow the prediction of experimental results on mast cells in other tissue of other animal species.

(page 85, line 25, page 86, line 7, page 87, lines 5 to 13)

B Whether or not the inventions after Secondary Correction could have been easily conceived of

(a) Cited Document 1 describes an eye drop containing KW-4679 (a hydrochloride of a cis-isomer of Compound A) for inhibiting allergic conjunctivitis. Further, Cited Document 1 describes that impacts of various anti-allergic agents on antigen-induced and histamine-induced conjunctivitis were studied by use of guinea pigs; and as a result of the study, instillation of KW-4679 was found to exhibit a significant inhibitory action on antigen-induced allergic conjunctivitis at concentrations of 10 and 100 ng/μl and to exhibit a stronger inhibitory effect on histamine-induced conjunctivitis compared to antigen-induced conjunctivitis.

In this connection, at the time of the priority date of Present Patent, in research and development on drugs for inhibiting human allergic conjunctivitis, animal conjunctivitis models of rats or guinea pigs were created as a model similar to human allergic conjunctivitis, and used to assess effects of drugs such as the effect of instillation. A package insert (the section for "pharmacology") of an anti-allergic eye drop for humans, which was sold at the time of the priority date of Present Patent, described that each active ingredient exhibited a conjunctivitis inhibitory action in

animal conjunctivitis models of rats or guinea pigs; and exhibited a release inhibitory action of a chemical mediator such as histamine from peritoneal mast cells of rats or the like. Considering the above, although Cited Document 1 fails to describe how KW-4679 acts on "human" conjunctival mast cells, it is considered that a person ordinarily skilled in the art, who has learned of Cited Document 1, would be motivated to attempt to use the eye drop containing KW-4679 for inhibiting allergic conjunctivitis described in Cited Document 1 as an eye drop for allergic eye diseases in humans.
(page 88, line 7 to page 89, line 2)

(b) Then, at the time of the priority date of Present Patent, in research and development on drugs for inhibiting human allergic conjunctivitis, it was common to confirm two actions of the drugs: an antagonistic action against various chemical mediators such as histamine produced and released from mast cells, and a release inhibitory action of these chemical mediators from mast cells. Therefore, in an attempt to use the eye drop containing KW-4679 described in Cited Document 1 as an eye drop for allergic eye diseases in humans, it is natural for a person ordinarily skilled in the art to study and confirm whether KW-4679 has the above two actions. (page 89, lines 3 to 11)

(c) In addition, Cited Document 2 describes that it is considered that PCA inhibitory action of Compound (I) represented by the general formula including Compound 20 (Compound A) is based on an action to inhibit the release of a chemical mediator such as histamine from skin mast cells. This description is not based on an experiment that confirms a histamine release inhibitory action, but it states a hypothesis that Compound (I) has a release inhibitory action on a chemical mediator such as histamine from mast cells as one of pharmacological actions. For verifying this hypothesis, the above description is a motivation to confirm whether Compound A has a release inhibitory action on histamine or the like from mast cells. (page 89, lines 12 to 23)

(d) In addition to the circumstance of the above (b), at the time of the priority date of Present Patent, it was common technical knowledge that: the histamine release inhibitory action of a drug on mast cells is sometimes varied depending on the species or the tissue of mast cells; and experimental results on mast cells in a certain tissue of a certain animal species do not always allow the prediction of experimental results on mast cells in other tissue of other animal species. Considering the common technical

knowledge, the fact that Cited Document 1 describes that KW-4679 did not have a histamine release inhibitory action in the experiments using animal conjunctivitis models of guinea pigs cannot be a ground to deny a motivation to confirm whether KW-4679 has an inhibitory action on histamine release from human conjunctival mast cells (page 90, line 17 to page 91, line 8)

(e) In view of the above, there is a motivation for a person ordinarily skilled in the art, who has learned of Cited Documents 1 and 2, to attempt to apply the eye drop containing KW-4679 for inhibiting allergic conjunctivitis described in Cited Document 1 as an eyedrop for allergic eye diseases in humans. In attempting the application, it should be said that there is a motivation to confirm that KW-4679 has antagonism against histamine or the like produced and released from human conjunctival mast cells and has an inhibitory action on histamine release from human conjunctival mast cells. Thus, it would be easily conceivable to confirm that KW-4679 has an inhibitory action on histamine release from human conjunctival mast cells (human conjunctival mast cell stabilizing action) and to use it for a human conjunctival mast cell stabilizing agent.

Therefore, the determination of Secondary Trial Decision states that the invention-specifying matter "human conjunctival mast cell stabilization" in the inventions after Secondary Correction was not conceived through a motivation based on Cited Documents 1 and 2; and the reasons for invalidation alleged by Plaintiff regarding the lack of inventive step based on Cited Document 1 as the primary cited document were groundless, but the determination is erroneous.
(page 91, lines 9 to 23)

(3) Determination of Present Trial Decision

Present Trial Decision states that: due to the binding effect of final Former Judgment (Article 33, paragraph (1) of Administrative Case Litigation Act), a person ordinarily skilled in the art who has learned of Cited Documents 1 and 2 could have easily conceived of both of Differences 1 and 2 and Difference 3 is merely design matters; however, the facts that: Compound A has an excellent stabilizing effect (high histamine release inhibition ratio) on "human conjunctival mast cells"; and AL-4943A (cis-isomer of Compound A) has a very wide range of concentration for providing a maximum histamine release inhibition ratio were particularly outstanding effects that a person ordinarily skilled in the art could not have predicted based on Cited Documents

1 and 3, and the common technical knowledge as of the priority date of Present Patent. In determining the inventive step, these should be taken into consideration as advantageous effects compared to Cited Invention 1, and the JPO determined that a person ordinarily skilled in the art could not have easily conceived of Present Inventions.

(4) Regarding the effects of Present Inventions

A Whether an invention is easily conceivable should be determined based on whether the invention has an unpredictable and outstanding effect in addition to whether there is a motivation or obstruction for applying a secondary cited invention to a primary cited invention. Moreover, in order to consider the effect of the invention, the effect has to be stated in the description; or even if the effect is not stated in the description, the effect has to be presumed by a person ordinarily skilled in the art based on the description or drawings. Regarding the effects of Present Inventions, Present Description discloses the following points.

(a) Compound A has human conjunctival mast cell stabilizing activity, and may be applied as infrequently as once or twice a day in some cases. In addition to its mast cell stabilizing activity, Compound A also possesses significant antihistaminic activity. Thus, in addition to a prophylactic effect, Compound A will also have a therapeutic effect. (page 6, lines 26 to 29)

(b) The inhibitory effects of reported anti-allergic, mast cell stabilizing drugs on mast cells obtained from human conjunctiva ... were tested according to the following experimental method. ... As Table 1 clearly shows, the anti-allergic drugs disodium cromoglycate and nedocromil sodium failed to significantly inhibit human conjunctival mast cell degranulation. In contrast, Compound A (cis isomer) produced concentration-dependent inhibition of mast cell degranulation. (page 7, line 13 to page 9, line 7, Table 1)

(c) A general method of preparing the eye drops of the present invention is described below. ... The concentration of Compound A is 0.0001 to 5 w/v%, preferably 0.001 to 0.2 w/v%, and most preferably about 0.1w/v %, based on the sterilized purified water. After dissolution, the pH is adjusted with a pH controller to be within a range which allows use as an ophthalmologic medicine, preferably within the range of 4.5 to 8. ... The eye drops produced by the above method typically need only be applied to the eyes a few times a day in an amount of one to several drops at a time, although

in more severe cases the drops may be applied several times a day. A typical drop is about 30 μl. (page 13, line 5 to page 14, line 13)

B According to these descriptions, it should be said that in the experiments (wherein a drug is given to a cell group prepared by culturing conjunctival mast cells and the histamine release inhibition ratio from the cells is measured) described in Present Description, a person ordinarily skilled in the art having learned of Present Description perceives that: Compound A (cis-isomer) has recorded inhibition ratios of histamine release from human conjunctival tissue mast cells of 29.6% at 300 μM, 47.5% at 600 μM, 66.7% at 1000 μM, and 92.6% at 2000 μM; the inhibition ratio increased along with an increase of concentration within the concentration range from 30 μM to 2000 μM; a high histamine release inhibition ratio of 66.7% was exhibited at 1000 μM; a high ratio of 92.6% was kept even at 2000 μM, which was a twofold concentration of the above; and, in contrast, disodium cromoglycate and nedocromil sodium known as anti-allergic drugs failed to significantly inhibit histamine release from human conjunctival tissue mast cells within the concentration range up to 2000 μM.

Meanwhile, the Present Description does not have such a statement of suggestion that explains that Compound A has a high histamine release inhibitory effect in a wide range of concentration exceeding 2000 μM along with an experimental result wherein the histamine release inhibition ratio of Compound A is measured at a concentration exceeding 2000 μM. Even considering the state of the art as of the priority date of Present Patent, there is no evidence that is sufficient to identify that a person ordinarily skilled in the art could presume the above effect. Therefore, in determining whether or not Present Invention 1 has an outstanding effect, the histamine release inhibitory effect of Compound A at a concentration exceeding 2000 μM cannot be taken into consideration as the effect of Present Invention 1. In this connection, Exhibit Ko 39 distributed after the priority date of Present Patent describes that: the same experimental method as in the above experiments described in the Present Description was used; the inhibition ratio increased in a dose-dependent manner even when the concentration (dose) of AL-4943A (cis-isomer of Compound A) reached about 2000 μM; and an inhibition ratio of about 90% was exhibited when the concentration was increased to 10000 μM. However, since a person ordinarily skilled in the art cannot presume from the Present Description that concentration-dependent inhibition is caused at a concentration exceeding 2000 μM, the contents of Exhibit Ko 39 should not be taken into consideration in determining whether Present Invention 1 has an outstanding effect.

C Regarding the effect of Present Invention 1

According to Former Judgment, which has become final and binding, it is found that a person ordinarily skilled in the art, who has learned of Cited Documents 1 and 2, could have confirmed that KW-4679 has an inhibitory action of histamine release from human conjunctival mast cells (human conjunctival mast cell stabilization action) and could have easily conceived of the idea to apply it to the use as a human conjunctival mast cell stabilizing agent. Regarding this point, there is no conflict between the parties. Therefore, it cannot be said that the effect itself that Compound A has a histamine release inhibitory action from human conjunctival mast cells is an outstanding effect that is unpredictable to a person ordinarily skilled in the art.

In addition, although neither Cited Document 1 nor Cited Document 2 contains any clear statement regarding whether Compound A has a histamine release inhibitory action from human conjunctival mast cells or regarding the level of the effect in the case where Compound A has that action, Exhibit Ko 20, etc. disclose that, before the priority date of Present Patent, a compound other than Compound A was used for 11 or 30 patients with Japanese cedar pollinosis, and ophthalmic challenge tests with an antigen (allergic reaction challenge tests by instillation of a cedar antigen solution) were conducted, then the histamine release inhibitory ratio in lacrimal fluid was measured 5 minutes and 10 minutes after instillation of an eye drop, and as a result, the ratios described below are recorded and disclosed. (i) In the case of a 0.0003% procaterol hydrochloride eye drop, the ratio was 79.0% on average 5 minutes after challenge and 82.5% on average 10 minutes after challenge; in the case of a 0.001% procaterol hydrochloride eye drop, the ratio was 81.6% on average 5 minutes after challenge and 89.5% 10 minutes after challenge; and in the case of a 0.003% procaterol hydrochloride eye drop, the ratio was 81.7% on average 5 minutes after challenge and 90.7% 10 minutes after challenge (Exhibit Ko20). (ii) In the case of 0.05% ketotifen eye drop, the ratio was 67.5% on average 5 minutes after challenge and 67.2% on average 10 minutes after challenge (Exhibit Ko 32). (iii) In the case of a 2% disodium cromoglycate eye drop, the ratio was 73.8% on average 5 minutes after challenge and 67.5% on average 10 minutes after challenge (Exhibit Ko 34). (iv) In the case of a 0.25% pemirolast potassium eye drop, the ratio was 71.8% on average 5 minutes after challenge and 61.3% on average 10 minutes after challenge; and in the case of a 0.1% pemirolast potassium eye drop, the ratio was 69.6% on average 5 minutes after challenge and 69.0% on average 10 minutes after challenge (Exhibit Ko 37).

In view of the forgoing, it is found that the state of the art of a person ordinarily skilled in the art as of the priority date of Present Patent shows, in addition to Compound A, there existed several compounds that exhibit a high histamine release inhibition ratio of about 70% to about 90% by instillation of a predetermined concentration of eye drop; and among them, some of the compounds keep a high histamine release inhibitory effect over the range of 2.5-time to 10-time concentrations.

As described above, as of the priority date of Present Patent, it was known that compounds that exhibit a high inhibitory effect against histamine release from human conjunctival mast cells were present other than Compound A. Considering these circumstances, it cannot be said that the histamine release inhibitory effect of a human conjunctival mast cell stabilizing agent containing Compound A of Present Invention 1 described in Present Description is an outstanding effect that goes beyond the scope that can be predicted by a person ordinarily skilled in the art based on the state of the art at that time. Further, in determining whether or not Present Invention 1 has an outstanding effect, the contents of Exhibit Ko 39 cannot be taken into consideration as mentioned in the above B. However, even if the contents thereof are taken into consideration, it cannot be said that the histamine release inhibitory effect of a human conjunctival mast cell stabilizing agent containing Compound A of Present Invention 1, which is described in Exhibit Ko 39, is an outstanding effect that goes beyond the scope that can be predicted by a person ordinarily skilled in the art based on the state of the art at that time in consideration of the facts that: there existed several compounds exhibiting a high histamine release inhibition ratio in addition to Compound A as described above, on the priority date of Present Patent; and some of them keep a high histamine release inhibitory effect over the range of 2.5-time to 10-time concentrations.

Therefore, it cannot be said that the effect of Present Invention 1 is an outstanding effect that is hard to predict on the premise of the structure of Present Invention 1, which could have been easily conceived of by a person ordinarily skilled in the art based on Cited Inventions 1 and 2, and the determination of Present Trial Decision on the effect of Present Invention 1 is erroneous.

D Regarding Present Invention 2

Present Invention 2 is an invention wherein the invention-specifying matter that Compound A "inhibits histamine release from human conjunctival mast cells by 66.7% or more" is added to Present Invention 1.

Then, it cannot be said that the matter "inhibits histamine release from human conjunctival mast cells by 66.7% or more" is an outstanding effect that is hard to predict on the premise of the structure of Present Invention 2, which could have been easily conceived of based on Cited Inventions 1 and 2 due to the same reason as in the above C, and thus, the determination of Present Trial Decision on the effect of Present Invention 2 is erroneous.

(5) Regarding the allegation of Defendants

A Defendants allege that: Cited Document 1 has a description that effects of each drug on histamine release from conjunctivas, which is caused by antigen-antibody reaction, were studied and KW-4679 (a hydrochloride of a cis-isomer of Compound A) was ineffective; and thus, the effect that could have been predicted as stabilizing human conjunctival mast cells by a person ordinarily skilled in the art has merely such a degree that human conjunctival mast cells are not stabilized at all as described in Cited Document 1, or "possibly 5%, 10%, or somewhat may be stabilized."

However, in Former Judgment, which has become final and binding, it is found that it was common technical knowledge as of the priority date of Present Patent that: the histamine release inhibitory action of a drug on mast cells is sometimes varied depending on the species or the tissue of mast cells; and experimental results on mast cells in a certain tissue of a certain animal species do not always allow the prediction of experimental results on mast cells in other tissue of other animal species. In accordance with the evidence (Exhibit Ko 7, 10, 13 to 18, 23, 41, 42, 101 to 103, and 127 to 129), it is found that the above common technical knowledge existed as of the priority date of Present Patent. Further, Former Judgment states that the description of Cited Document 1 that KW-4679 did not exhibit a histamine release inhibitory action in the experiment using animal conjunctivitis models of guinea pigs cannot be a ground to deny a motivation to confirm whether KW-4679 has a histamine release inhibitory action from human conjunctival mast cells; and therefore, it determines that it would have been easily conceivable to apply KW-4679 to the use as a human conjunctival mast cell stabilizing agent. Considering the above common technical knowledge, it is not acceptable that a person ordinarily skilled in the art predicts that Compound A of Present Inventions has no histamine release inhibitory effect as of the priority date of Present Patent only based on the description of Cited Document 1 that KW-4679 did not exhibit a histamine release inhibitory action in the experiment using animal conjunctivitis models of guinea pigs. Even if the effect is produced, it is not acceptable that the skilled person predicts that the inhibition ratio is at most 5% or

10%. The allegation of Defendants is contrary to the above finding and determination of Former Judgment, which has become final and binding.

B Defendants allege that,
since the experiments described in Exhibit Ko 20, etc. are in vivo and conducted under experimental conditions completely different from those for Present Invention 2, they cannot be comparative to Present Invention 2; regarding some of the compounds described in Exhibit Ko 20, etc., Exhibit Otsu 1 describes experimental results that are measured in comparison with the compound of Present Invention 2 under the same experimental conditions as those for Present Invention 2, in which the compound of Present Invention 2 exhibits a remarkably stronger human conjunctival mast cell stabilizing effect than those compounds; in the in vivo tests described in Exhibit Ko 20, etc., it is quite difficult to make generally correct quantification, evaluation, and comparison, and the validity on the experimental conditions/methods is still doubtful; and thus, the outstanding effect of Present Invention 2 cannot be denied based on the experimental results described in Exhibit Ko 20, etc. The written opinion of Dr. Shigeaki Ohno (Exhibit Otsu 3) has portions in line with the above allegation.

However, the experimental methods described in Exhibit Ko 20, etc. are a method wherein a drug is administered to actual eyes of humans (patients with Japanese cedar pollinosis) (in vivo experiment), and they are completely different from the experimental methods described in Present Description or Exhibit Otsu 1 wherein a drug is administered to cell groups prepared by culturing human conjunctival mast cells (in vitro experiment). Thus, even when experimental results obtained by both experiments on the histamine release inhibition ratios of a specific compound are inconsistent, it cannot be said that the inconsistency directly indicates that the experimental results of Exhibit Ko 20, etc. generally lack credibility and that the experimental results cannot be taken into consideration in finding the state of the art as of the priority date of Present Patent.

Further, the experimental methods described in Exhibit Ko 20, etc. are as described above, and no particularly illogical point resides in them as a method for measuring an inhibition ratio of histamine release from human conjunctival mast cells. The allegation of Defendants fails to point out which portion of the experimental methods, experimental results, and others described in Exhibit Ko 20, etc. has a technical problem and lacks objective support, and thus, it cannot be adopted.

(6) Summary

Hence, Ground for Rescission 1 is grounded.

4 Conclusion

As described above, the Present Trial Decision shall be rescinded without making the determination on other points, and the judgment is made as in the main text.

An additional remark is made on the examination of the Present Trial.

In a suit against a trial decision on a case for an invalidation trial of a patent, when the judgment for rescission of the trial decision becomes final and binding, trial examiners further make another examination and another trial decision on the case for the trial in accordance with the provision of Article 181, paragraph (2) of the Patent Act, and the binding effect of the judgment for rescission is placed on the other examination and the other trial decision to be made in accordance with the provision of Article 33, paragraph (1) of the Administrative Case Litigation Act. Then, since this binding effect is over the found facts and the legal determination, which are needed to deduce a main text of the judgment, the trial examiners are not allowed to make findings and determinations that conflict with the findings and determinations in the judgment for rescission. Therefore, in another trial procedure, the trial examiners should not permit the repetition of the same allegation as the previous one that the findings and determinations in reasons of the judgment reached by the binding effect of the judgment for rescission are erroneous, or the provision of new proof for supporting the above allegation. Further, when the judgment states that the findings and determinations of the trial decision that the invention could not have been easily conceived of is erroneous, as the invention could have been easily conceived of by a person ordinarily skilled in the art based on a specific cited document before the filing of the patent application, and the judgment for rescission of the trial decision has become final, the trial examiners are not allowed to determine that the invention could not have been easily conceived of by a person ordinarily skilled in the art based on the same cited document before the filing of the patent application, since the binding effect of the judgment is placed on the other trial procedure (see the third Petty Bench Judgment of the Supreme Court, 1988 (Gyo-Tsu), 10, April 28, 1992, Minshu Vol. 46, No. 4, at 245).

In the section subtitled "Ground for Rescission 3 (error in determining the inventive step based on Exhibit Ko 1 as the primary cited document), Former Judgment states that it has been found that a person ordinarily skilled in the art having learned of Cited Documents 1 and 2 could have confirmed that KW-4679 has a

histamine release inhibitory action (human conjunctival mast cell stabilizing action) from human conjunctival mast cells and could have easily conceived of applying KW-4679 to the use for a human conjunctival mast cell stabilizing agent; and thus, Former Judgment rescinds Secondary Trial Decision that the reasons for invalidation regarding the lack of inventive step based on Cited Document 1 as the primary cited document were groundless. In particular, Invention 1 after Secondary Correction, which was examined through Secondary Trial Decision and Former Judgment, is the same as Present Invention 1 examined through Present Trial Decision; and although the cited documents were the same, Present Trial Decision has found that Present Invention 1 could not have been easily conceived of by a person ordinarily skilled in the art based on Cited Documents 1 and 2 and thus, Present Inventions has an inventive step.

Whether an invention is easily conceivable should be determined based on whether the invention has an unpredictable and outstanding effect in addition to whether there is a motivation or obstruction for applying a secondary cited invention to a primary cited invention. Then, the parties were enabled to allege and prove the fact confirming the conceivability based on a specific cited document, and also the fact denying it through Secondary Trial Decision and the suit against the trial decision. Former Judgment has become final without alleging or proving the above, and then, at the resumed procedure of Present Trial, the parties were allowed to allege and prove that Present Invention 1 that is not corrected and is the same as in the previous suit could not have been easily conceived of by a person ordinarily skilled in the art based on Cited Documents 1 and 2 that are the same as those in the previous suit. This leads to the possibility that the case goes back and forth endlessly between the JPO and the court and is against the principle judicial economy; and it has to be said that a problem is raised in light of the purpose of the provision of Article 33, paragraph (1) of the Administrative Case Litigation Act.

Intellectual Property High Court, 4th Division

Presiding judge:	TAKABE Makiko
Judge:	YAMAKADO Masaru
Judge:	KATASE Akira

Attachment

List of figures and tables of the present description

Table 1

Compound effect on Histamine Release from

Human Conjunctival Tissue Mast Cells upon anti-Human IgE Challenge

Compound	Dose (μM)	Treatment (min.)	Inhibition (%)
Cromolyn sodium	1000	15	-15.4
	300	15	-6.9
	100	15	-1.2
	30	15	1.8
	10	15	10.5
Cromolyn sodium	1000	1	-9.4
	300	1	-1.8
	100	1	1.2
	30	1	0.1
	10	1	-0.9
Nedocromil sodium	1000	15	7.2
	300	15	11.3
	100	15	28.2°
	30	15	15.2
	10	15	9.2
	3	15	13.2
	1	15	10.7
	0.3	15	3.7
	0.1	15	8.7
Nedocromil sodium	1000	1	-1.1
	300	1	4.0
	100	1	6.7
	30	1	-0.9
	10	1	-6.5
	3	1	0.8
	1	1	4.8
	0.3	1	8.8
	0.1	1	17.4
Compound A	2000	15	92.6°
	1000	15	66.7°
	500	15	47.5°

	300	15	29.6°
	100	15	13.0
	30	15	-3.9

*p<0.05, Dunnett's t-test