Appeal Decision

Appeal No. 2018-5143

Appellant	Yamada Bee Company, Inc.
Patent Attorney	HASEGAWA, Yoshiki
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The case of appeal against the examiner's decision of refusal of Japanese Patent Application No. 2014-49007 entitled "PREVENTIVE COMPOSITION AND PREVENTIVE NUTRITIVE COMPOSITION FOR AGE-RELATED DISEASES AND LOW FUNCTIONAL CAPACITY" (publication of unexamined patent application, October 1, 2015; Japanese Unexamined Patent Application No. 2015-172021) has resulted in the following appeal decision.

Conclusion

The appeal of the case was groundless.

Reason

No. 1 History of the procedures

The present application was filed on March 12, 2014, and the history of the procedures is as follows:

September 29, 2017	: Notification of Reasons for Refusal
November 27, 2017	: Written Opinion
January 26, 2018	: Decision of Refusal
April 13, 2018	: Written Demand for Appeal and a Written Amendment

June 1, 2018 : Reconsideration Report
November 14, 2018 : Notification of Reasons for Refusal
January 16, 2019 : Written Opinion

No. 2 The Invention

Inventions according to Claims 1 to 3 of the present application are specified by matters described in Claims 1 to 3 in the scope of claims amended by the Written Amendment filed on April 13, 2018, and the invention according to Claim 1 (hereinafter, referred to as the "Invention") is as follows:

"[Claim 1]

A preventive composition for age-related diseases and low functional capacity comprising royal jelly, wherein

the age-related diseases and the low functional capacity are age-related muscle disorder or muscle weakness, and age-related bone diseases or bone density, and

the composition is used so that 600 to 14400 mg of royal jelly per day in terms of the weight of raw royal jelly is orally administered to a human."

No. 3 Reason for refusal

The reason for refusal notified by the body on November 14, 2018 was such that the Appellant should not be granted a patent under the provision of Article 29(2) of the Patent Act, since the Invention is such that a person ordinarily skilled in the art of the invention could have easily invented it on the basis of an invention described in the following Cited Document 1 and the matter described in Cited document 2 which were distributed within Japan or in a foreign country or made available to the public through electric telecommunication lines prior to the filing of the application.

Cited Document 1: Patent Publication for Japanese Patent No. 4908769 (issued on April 4, 2012)
Cited Document 2: "Food Science," KISHI, Naokuni, Food Science Co., Ltd., January 10, 2012, vol. 54, No. 2, p. 13.

No. 4 Judgment by the body

1 Description in Cited Documents and Cited Invention

(1) Regarding Cited Document 1

A Cited Invention 1 describes the following matters.

(1-A) [Scope of Claims]

[Claim 1]

An agent for preventing or improving age-related osteoporosis comprising royal jelly or extract therefrom as an active ingredient.

[Claim 2]

The agent for preventing or improving age-related osteoporosis of claim 1, further comprising an osteoclastic inhibitor and/or food materials having calcium supplementing action.

(1-B) [Problem to be solved by the invention]

[0007]

...it can be expected that activation of bone metabolism as a whole through promotion of bone formation realizes not only prevention and treatment of age-related osteoporosis and diabetic osteoporosis, but also effective preventive effect against general involutional osteoporosis including postmenopausal osteoporosis, resulting in great contribution in realizing a bright aging society.

[0008]

As a result of diligent research, the inventors of the present invention found that royal jelly has an action to promote bone formation. In addition, it was also found that royal jelly has an action to increase onset of procollagen 1α1 gene known as an important protein for bone matrix and at the same time a differentiation marker for osteoblast cells. Then, based on such knowledge, the inventors succeeded in completing the present invention.

[0009]

The objective of the present invention is to provide an agent for preventing or improving age-related osteoporosis that is useful for preventing osteoporosis by promoting bone formation.

(1-C) [Advantage of the Invention]

[0013]

According to the present invention, an agent for preventing or improving age-related osteoporosis that is useful for preventing osteoporosis can be provided by promoting bone formation.

(1-D) [Best Mode for Carrying Out the Invention]

[0014]

An embodiment that embodies the bone formation promoter, the agent for preventing osteoporosis, and the collagen synthesis promoter of the present invention is explained below. Hereinafter, royal jelly is described in abbreviated form, RJ.

[0016]

Both raw RJ and dried RJ can be used as an active ingredient. ... RJ extract as an active ingredient is extracted by immersing raw RJ or dried RJ in a polar solvent such as alcohol. ...

[0020]

The agent for preventing osteoporosis is used as a pharmaceutical preparation, a quasi-pharmaceutical product, or a food or a drink.

As a pharmaceutical preparation, the agent is administered as an oral or parenteral drug. Tablet, capsule, powdered drug, syrup, health drink, etc. are conceivable as dosage forms for oral drugs. ... on the other hand, in the case of a food or a drink, the agent is orally taken in as a drink such as a health drink, or a food, such as a candy, rice cracker, cookie, or food formulation. ...

[0021]

Content of active ingredient in the pharmaceutical preparations, quasi-pharmaceutical products, and foods or drinks is preferably 0.001 to 100% by mass, more preferably 0.001 to 50% by mass, and still more preferably 0.01 to 30% by mass. If the content of active ingredient is less than 0.001% by mass, bone formation cannot be promoted sufficiently. In addition, it is preferable that the food or the drink is orally taken in regularly for preventing osteoporosis and it is especially preferable that the food or the drink is taken several times a day. Dose per day is not restricted, but, in terms of weight of royal jelly, it is preferably 0.001 to 30 g, more preferably 0.001 to 20 g, and still more preferably 0.001 to 10 g. If the amount of the food or the drink per day taken in is less than 0.001 g, effect of preventing osteoporosis cannot be sufficiently obtained. In contrast, if the amount taken in per day is over 30 g, while sufficient effect of preventing osteoporosis can be obtained, it is uneconomical because increase in preventive effect commensurate with increase in the amount of the agent taken in cannot be obtained.

(1-E) [Examples]

[0024] ...

<Evaluation of osteogenic potential by RJ>

(Example 1)

A mixed feed comprising RJ was prepared by adding 4% of RJ lyophilized powder produced in China to powdered feed for mice, rats, and hamsters CRF-1 (produced by Oriental Yeast Co., Ltd.).

[0025]

(Example 2)

2.5 L of 95% by volume ethanol was added to 1 kg of raw RJ produced in China, and, after stirring for 2 hours at room temperature, suction filtration was carried out. The obtained filtrate is hereinafter referred to as the primary extraction liquid. In addition, after extracting the primary extraction liquid, 2 L of 95% by volume ethanol was added to the residue and, after stirring for 2 hours at a room temperature, suction filtration was carried out. This filtrate is hereinafter referred to as the secondary extraction liquid. The primary and secondary filtrates were mixed together, and, after removing solvent by distillation under diminished pressure, added to CRF-1 in an amount of 4% to prepare mixed feed comprising RJ extract.

[0026]

(Test Example 1: Evaluation of osteogenic potential of normal mice)

C57BL mice (9-week old female) were purchased from SLC. After preliminary breeding with CRF-1 for 1 week, mice were divided into 4 groups (10 mice in each group), and 3 groups out of 4 were fed for 2 month and allowed to freely take in respectively normal feed consisting of CRF-1, mixed feed comprising 4% of RJ (Example 1), and mixed feed comprising 4% RJ extract (Example 2). During the testing period, there was no significant difference among groups in the amount of feed taken in. In addition, as a positive control, 17β estradiol (made by Sigma, #E8875) was subcutaneously administered to one group at the dose of 3 μg/kg/day for 2 months (5 days/week) while fed with normal feed.

[0027]

Two months later, mice of each group were slaughtered under ether anesthesia, and, after taking out and vacuum drying tibial bones, weight of the dried bone was measured. In addition, the dried bone was further subjected to ashing process for 3 hours at 600°C, and ashing weight was measured. Table 1 below shows the results of calculation of weight of the dried bone, and mean value ± standard deviation of ashing weight for mice of each group (10 mice in each group). In addition, Table 1 also shows the result of t-test of each group to the group of normal feed.

...

[0029]

Two months later, mice of each group were slaughtered under ether anesthesia,

and, after taking out tibial bones, weight of dried bone and ashing weight were measured. Table 1 below shows the results of calculation of weight of the dried bone and mean value ± standard deviation of ashing weight for mice of each group (10 mice in each group). In addition, Table 1 also shows the result of t-test of each group to the group of normal feed.

[0030]

[Table 1]

試験例1	乾燥骨重量(g)	灰化重量(g)
通常飼料	0.0309±0.0017	0.0190±0.0012
実施例1	0.0320±0.0020	0.0199±0.0013 *
実施例2	0.0323±0.0012 **	0.0201±0.0008 **
17βエストラジオール	0.0333±0.0010 ***	0.0209±0.0008 ***
比較例1(卵巣切除)		
偽手術	0.0307±0.0017	0.0187±0.0010 ***
通常飼料	0.0300±0.0013	0.0175±0.0008
実施例1	0.0308±0.0012 *	0.0177±0.0006
17βエストラジオール	0.0323±0.0010 ***	0.0197±0.0006 ***

*:P<0.1
**:P<0.05
***:P<0.01

試験例１　Test Example 1
乾燥骨重量　Weight of dried bone
灰化重量　Ashing weight
通常飼料　Normal feed
実施例　１　Example 1
実施例　２　Example 2
１７β エストラジオール　17β estradiol
比較例１（卵巣切除）　Comparative Example 1 (removal of ovary)
偽手術　Placebo surgery

[0031]

As shown in Table 1, ... in Test Example 1, increasing tendency of ashing weight was observed by feeding with mixed feed comprising RJ (Example 1), and a significant increase in ashing weight was observed by feeding with mixed feed comprising RJ extract (Example 2). Accordingly, action of the mixed feed comprising RJ of Example 1 and the mixed feed comprising RJ extract to suppress increased bone resorption (namely, postmenopausal osteoporosis) is not large, and, rather, these mixed feeds were excellent in suppression of decrease in bone formation; namely, in preventing and improving age-related osteoporosis. Judging from the above, both of RJ and RJ extract deliver

excellent effects in preventing osteoporosis through promotion of bone formation, and, at the same time, can deliver excellent effects in preventing and improving age-related osteoporosis.

[0032]

Furthermore, in the Examples, weight of dried bone and ashing weight were measured using the tibia bone, which has small variation in weight of bone during measuring compared to the femur, etc. and can exactly reflect increase/decrease of the weight of bone of the individual as a whole. Because of this, it is very important that increase in weight of the tibia bone (especially, ashing weight) in Examples 1 and 2 of Test Example 1 does not mean that weight of only a specific bone increased, but means that bone weight of the individual as a whole physiologically increased. It seems that weight of dried bone shown in Table 1 should be referred to just for reference, because it is a sum of ashing weight and weight of organic substances such as protein, and a large variation was observed between mice in a same group, and, in addition, normally problem in osteoporosis is density of bone (ashing weight).

B According to above A, Cited Document 1 describes that both royal jelly and extracts therefrom exhibit excellent effect of preventing and improving age-related osteoporosis, since a tendency to increase or a significant increase in ashing weight of tibia bone was recognized in groups in which normal mice were allowed to freely take mixed feed comprising 4% royal jelly or mixed feed comprising 4% royal jelly extract for 2 months, compared to the group fed with normal feed (Excerpt 1-E), and that the preventive agent for osteoporosis is used as a pharmaceutical preparation, a quasi-pharmaceutical product, or a food or a drink, and, preferably, the food or drink should be orally taken regularly for preventing osteoporosis and intake per day in terms of weight of royal jelly should preferably be 0.001 to 30 g (Excerpt 1-D).

Then, it is recognized that Cited Document 1 describes the following invention (hereinafter, referred to as "Cited Invention").

"An agent for preventing or improving age-related osteoporosis comprising royal jelly or extracts therefrom used so that preferably 0.001 to 30 g in terms of royal jelly is orally taken in as an intake per day."

(2) Regarding Cited Document 2

Cited Document 2 describes the following matter.

"Health/natural food

Results of study of honey-bee products were published

The YAMADA BEE COMPANY INC. held on December 21, in Okayama city, "Grant for research on honey-bees - health seminar." In the seminar, researchers chosen for the grant delivered lectures on new possibility of products by honey-bees.

Associate Professor NIU, Kaijun from Graduate School of Biomedical Engineering, Tohoku University delivered a lecture on suppressing effect of royal jelly on muscle weakness. The Associate Professor investigated using mice to determine whether royal jelly and enzymatically degraded royal jelly suppresses age-related muscle weakness. As a result, it has been proved that royal jelly suppresses muscle weakness and enhances muscle strength. It was found that, in humans, grasping power is enhanced and walking speed is increased. It was stated that, judging from these results, it is expected that enzymatically degraded royal jelly is useful for maintaining muscle strength, moving the body smoothly and, for aged persons, having a self-subsistent life" (p. 13, middle paragraph, l. 12 to lower paragraph, l. 10).

2 Comparison

Comparing the Invention and Cited Invention, the "agent for preventing or improving age-related osteoporosis" of Cited Invention corresponds to "preventive composition" of the Invention in which "age-related disease and low functional capacity" is "age-related bone diseases or reduced bone density."

In addition, since Cited Invention relates to an agent for preventing or improving "age-related" osteoporosis, it is used so that a "human" orally takes it, which corresponds to "used ... orally administered to a human" of the Invention.

Then, since it is understood that "royal jelly" of "in terms of weight of royal jelly" of Cited Invention has not been subjected to any special processing, it corresponds to "raw royal jelly" of the Invention.

Therefore, the Corresponding Feature and Different Features between the Invention and Cited Invention are as shown below.

<Corresponding Feature>

"A preventive composition comprising royal jelly for age-related disease and low functional capacity, wherein the age-related disease and low functional capacity are age-related bone diseases or reduced bone density, and the composition is used to be orally administered to a human."

<Different Feature 1>

While age-related disease and low functional capacity are "age-related muscle disorder or muscle weakness" in addition to "age-related bone diseases or reduced bone density," that is, "age-related muscle disorder or muscle weakness, and age-related bone diseases or reduced bone density" in the Invention, they are age-related osteoporosiss that correspond to "age-related bone diseases or loss in bone density," and "age-related muscle disorder or loss in muscle strength" is not specified in Cited Invention.

<Different Feature 2>

While the dose per day for royal jelly is 600 to 14400 mg in terms of amount of raw royal jelly in the Invention, it is preferably 0.001 to 30 g in Cited Invention.

3 Judgment

(1) Regarding Different Feature 1

Cited Document 2 that is a magazine named "Food Science" describes, in its column for "Health/natural foods," the content of the lecture by Associate Professor NIU, Kaijun from Graduate School of Biomedical Engineering, Tohoku University delivered in "Grant for research on honey-bees - health seminar" held in Okayama city, and the content of the lecture is as follows: "(The Associate Professor) investigated using mice to determine whether royal jelly and enzymatically degraded royal jelly suppress age-related muscle weakness. As a result, it has been proved that royal jelly suppresses muscle weakness and enhances muscle strength. It was found that, in a humans, grasping power is enhanced and walking speed is increased. (It was stated that,) judging from these results, it is expected that enzymatically degraded royal jelly is useful for maintaining muscle strength, moving the body smoothly and, for aged persons, having a self-subsistent life."

It is understood that, judging from the results from mice, "in a human, grasping power is enhanced" in the above description is the result of suppression of muscle weakness and enhancement of muscle strength in a human.

In addition, judging from the fact that the Associate Professor stated that the experiments using mice were carried out for determining "whether ... suppresses age-related muscle weakness" and that " it is expected ... for aged persons, having a self-subsistent life," a person skilled in the art who read the description in Cited Document 2 can understand that royal jelly or enzymically degraded royal jelly has effect to suppress age-related muscle weakness and enhance muscle strength.

Therefore, it can be deemed that a person skilled in the art could have easily conceived to make the composition of Cited Invention whose active ingredient is royal

jelly for use of not only preventing or improving age-related osteoporosis but also concurrently suppressing age-related muscle weakness and enhancing muscle strength, and to make Cited Invention include a matter specifying the invention of the Invention according to Different Feature 1.

(2) Regarding Different Feature 2

A Intake per day (synonymous with "dose per day") of royal jelly in Cited Invention is "preferably 0.001 to 30 g" and overlaps with the Invention in the range of "600 to 14400 mg."

On the other hand, Cited Document 2 does not indicate any concrete numerical value with respect to the dose of royal jelly that has an action to suppress age-related loss in muscle strength and enhance the same.

B As examined for Different Feature 1, however, in the case in which the composition of Cited Invention is used not only for preventing or improving age-related osteoporosis but also concurrently for suppressing age-related muscle weakness and enhancing muscle strength, it can be deemed that the dose per day that a person skilled in the art tries first is the range of "preferably 0.001 to 30 g" according to Cited Invention.

Then, a person skilled in the art could have easily set the dose per day to the range of 600 to 14400 mg (0.6 to 14.4 g) that is a numerical range within the range of "preferably, 0.001 to 30 g," in the light of the fact that Cited Document 1 describes that, below 0.001 g, the effect of preventing osteoporosis cannot be exerted sufficiently, and that, above 30 g, it is uneconomical because increase in preventive effect commensurate with increase in intake is not obtained (Excerpt 1-D), taking into consideration preventing effect against the osteoporosis, degree of exertion of the action to suppress age-related loss in muscle strength, and enhancement of the same and economical factor.

(3) Regarding the Effect

A person skilled in the art could have easily predicted from the descriptions in Cited Documents 1 and 2 that royal jelly can prevent not only age-related reduced bone density but also muscle weakness.

It cannot be recognized particularly prominent that royal jelly can prevent age-related muscle weakness with a dose at the same level as that for preventing age-related reduced bone density.

Examples in the present specification show that the effects in the cases in which royal jelly was administered to residents in seniors' homes with doses of 3600 mg/day

(low dose group) and 14400 mg/day (high dose group), but no test for the dose close to the lower limit value of the Invention, 600 mg/day, has been carried out and no comparison with any dose exceeding 14400 mg/day has been made. Therefore, no critical significance can be found in "600 to 14400 mg" of the Invention.

Accordingly, the effect of the Invention cannot be deemed to be a particularly prominent one that a person skilled in the art could not have predicted.

(4) Summary

According to the above, a person skilled in the art could have easily invented the Invention based on matters described in Cited Documents 1 and 2.

4 The Appellant's allegation

(1) In the Written Opinion filed on January 16, 2019, the appellant Alleges as follows:

"Invention 1 specifies both uses, 'use for preventing age-related muscle disorder or muscle weakness' and 'use for preventing age-related bone diseases or reduced bone density,' and, at the same time, presupposing application to both uses, specifies dosage and administration of royal jelly. Namely, both of these (uses and dosage and administration) can be deemed as a coherent constitution that cannot be separated from problem-solving point of view.

Accordingly, the different feature between Invention 1 and Cited Invention should be acknowledged for a unit of a coherent constitution. To be concrete, it should be as the following Different Feature A.

<Different Feature A>

While Invention 1 specifies that 'a composition for preventing both of age-related muscle disorder or muscle weakness, and age-related bone diseases or reduced bone density, wherein the composition is used so that 600 to 14400 mg per day of royal jelly in terms of the amount of raw royal jelly is orally administered to a human,' Cited Invention specifies 'An agent for preventing or improving age-related osteoporosis which is used so that preferably 0.001 to 30 g in terms of the weight of royal jelly is orally taken.'"

"Neither Cited Document 1 nor Cited Document 2 describes any use of royal jelly in two uses, 'use for preventing age-related muscle disorder or muscle weakness' and 'use for preventing age-related bone diseases or reduced bone density', and, still less, dosage and administration for royal jelly on the premise of application to both uses; namely, 'the composition is used so that 600 to 14400 mg per day of royal jelly in terms of the amount of raw royal jelly is orally administered to human' is not suggested.

Accordingly, it can never be deemed that a person skilled in the art could have easily conceived to adopt the constitution according to Different Feature A based on the inventions described in Cited Documents 1 and 2."

(2) Then, above allegation is examined below.

A Judging from the use, it is understood that the agent for preventing or improving of Cited Invention is used as a pharmaceutical preparation and a health food product for the purpose of drug efficacy.

It is common technical knowledge in the field that, generally, in the process of developing pharmaceutical preparations, after sufficiently evaluating drug efficacy, risk, possible side effects, etc. from the result of non-clinical studies such as safety trial using animals, clinical trials are carried out only for medicinal substances for which it has been judged that use as a pharmaceutical agent can be expected, and the dose is determined from a viewpoint of drug efficacy or side effects through clinical trials by gradually increasing dose (if necessary, refer to the notification from the Ministry of Health, Pharmaceutical Affairs Bureau, Chief of New Drug Division addressed to the department responsible for health field of each prefecture, "Regarding general guidelines for clinical evaluation of new drugs," June 29, 1992), and the common technical knowledge applies also to the process of developing health food products for the purpose of drug efficacy.

As explained above, generally, in the process of developing pharmaceutical preparations or health food products, it is found that a certain substance has a specific "drug efficacy" and then a "dose" suitable for delivering the "drug efficacy" is studied, and, in developing a pharmaceutical preparation or a health food product expecting multiple drug efficacies, study on dose is inevitably carried out within the range in which the multiple drug efficacies can be delivered.

Based on such procedures for developing a pharmaceutical preparation or a health food product, in the Notification of Reasons for Refusal the body acknowledged "drug efficacy (use)" and "dose" as Different Features 1 and 2 in comparison of the Invention with Cited Invention, then examined first the point whether multiple drug efficacies (use) could have been conceived for the composition comprising royal jelly or extracts therefrom according to Cited Invention (Different Feature 1), and, based on that, examined whether "dose" could be set on the premise that the composition has multiple drug efficacies (uses) (Different Feature 2).

Judging from descriptions in the present specification: "The purpose of the present invention is ... to provide a preventive composition and preventive nutritive composition for age-related diseases and low functional capacity suitable for administration to a

human" ([0006]), "As a result of diligent research, the inventors of the present invention found that, if royal jelly is administered to a human, in accordance with the dose, age-related disease and low functional capacity are effectively prevented, and succeeded to complete the present invention" ([0007]), "although it differs depending on purpose of administration, method of administration, conditions of the object of administration, ... in terms of the amount of raw royal jelly, 600 to 14,400 mg per day, ... more preferably 3600 to 14400 mg per day of royal jelly is used by oral administration" ([0025]), it can be deemed that the inventors of the Invention first found that royal jelly can effectively prevent age-related disease and low functional capacity, and, after that, found the range of effective dose. The process of development of the Invention is consistent with the above process of examining on Different Feature 1 and Different Feature 2.

Therefore, in the present case, wherein two different features, Different Features 1 and 2, are acknowledged and they are judged in sequence on easily-conceivable property, no inappropriate point can be found, such as, inventive step is denied without properly judging on easily-conceivable property because, by acknowledging different features divided into small units inordinately.

B Even if the judgment is made after integrating Different Features 1 and 2 and acknowledging the result of integration as Different Feature A as alleged by the Appellant, it is easy to apply Cited Invention to the both uses, and, since it can be deemed that a person skilled in the art can appropriately set the dose within the range described in Cited Document 1, there is no change in the fact that a person skilled in the art could have easily adopted the constitution of the Invention according to Different Feature A in Cited Invention.

C Accordingly, above allegation by the Appellant cannot be accepted.

No. 5 Closing

As explained above, since a patent shall not be granted for the Invention under the provision of Article 29(2) of the Patent Act, the present application should be refused, without need to examine inventions according to other claims.

Therefore, the appeal decision shall be made as described in the conclusion.

March 18, 2019

Chief administrative judge: MITSUMOTO, Minako
Administrative judge: FUJIWARA, Hiroko
Administrative judge: MAEDA, Kayoko