Appeal decision

Appeal No. 2017-3343

Osaka, Japan
Appellant MAEDA, Kazuhisa

Patent Attorney MORITA, Takuo

The case of appeal against the examiner's decision of refusal for Japanese Patent application No. 2012-177717, titled "ADIPONECTIN PRODUCTION PROMOTING AGENT" [published on February 24, 2014, Japanese Unexamined Patent Application Publication No. 2014-34562] 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 August 10, 2012, for which a notice of Reasons for refusal was issued on May 17, 2016, and a Decision for refusal was issued on November 30 of the same year. In response, an appeal against the Examiner's Decision of Refusal was requested on March 6, 2017 together with a Written Amendment, and then a notice of reasons for refusal was notified by the body on February 9, 2018, and a written amendment was submitted on May 7 of the same year, followed by submission of a written statement on July 19 of the same year.

No. 2 The Invention

The inventions according to Claims 1 to 2 of the present application should be specified in the matters recited in Claims 1 to 2 of the Claims that have been amended by the written amendment on May 7, 2018. The invention according to Claim 1 (hereinafter referred to as "Present Invention 1") is set forth as below:

"[Claim 1]

An adiponectin production promoting agent consisting of a mixture to which a mulberry leaf extract and a mangosteen fruit rind extract are added in combination."

No. 3 Reasons for refusal by the body

The Reasons for refusal notified by the body on February 9, 2018 are summarized as follows: Present Invention 1 was easily conceivable by a person skilled in the art who had ordinary knowledge in the field of the art to which the invention

pertained on the basis of the inventions described in the following Cited Documents 1, 8, and 13 to 15 (hereinafter referred to as "a person skilled in the art"), and thus was not patentable under the provision of Article 29(2) of the Patent Act.

Cited Document 1: International Publication No. WO 2009-101698
Cited Document 8: National Publication of International Patent Application No. 2012-516842 (publication date: July 26, 2012)
Cited Document 13: International Publication No. WO 2010-109628
Cited Document 14: National Publication of International Patent Application No. 2009-518529
Cited Document 15: Japanese Unexamined Patent Application Publication No. 2007-63207

No. 4 Described matters in Cited Documents and Cited Invention

1. Cited Document 1
(1) Matters described in Cited Document 1
A. Described matter 1-1 (The scope of claims [1])
"A composition for suppressing fat accumulation comprising 1-deoxynojirimycin."

B. Described matter 1-2 ([0021])
"The composition of the present invention has a feature of comprising the above 1-deoxynojirimycin as an active ingredient. The composition of the present invention has an activity to suppress fat accumulation. The composition of the present invention promotes excretion of adiponectin and promotes fat metabolism and thereby having an activity to suppress fat accumulation. Therefore, the composition of the present invention can be used for the prevention and/or improvement of diseases and/or symptoms associated with excess fat accumulation."

C. Described matter 1-3 ([0027] to [0032])
"A composition comprising 1-deoxynojirimycin can be produced by a conventional method from mulberry plants. One embodiment is explained hereinafter.

First mulberry leaf is cleaned and then dried. Drying mulberry leaf may concentrate 1-deoxynojirimycin. ...

A process of drying mulberry leaf may be implemented by a method commonly used in the technical field. ...

Preferably, after drying mulberry leaf, an extraction is further conducted with water, hydrophilic organic solvent such as ethanol, or a mixed fluid thereof. ...

Subjecting the above extract to further drying may result in a composition with a further high content of 1-deoxynojirimycin. The drying method is not particularly limited, ... but drying and powdering may result in improved stability and facilitate handling.

A form of the composition of the present invention is not particularly limited as long as the composition includes 1-deoxynojirimycin. The composition may have a form of mulberry plant treated product such as mulberry leaf ground product, mulberry

leaf dried product, and mulberry leaf extract as well as a form of purified 1-deoxynojirimycin. ..."

D. Described matter 1-4 ([0033])
"In a case of preparing the composition of the present invention as a pharmaceutical composition, ... as long as it does not inhibit the effect of the present invention, additives and another publicly-known fat accumulation suppressant may be mixed."

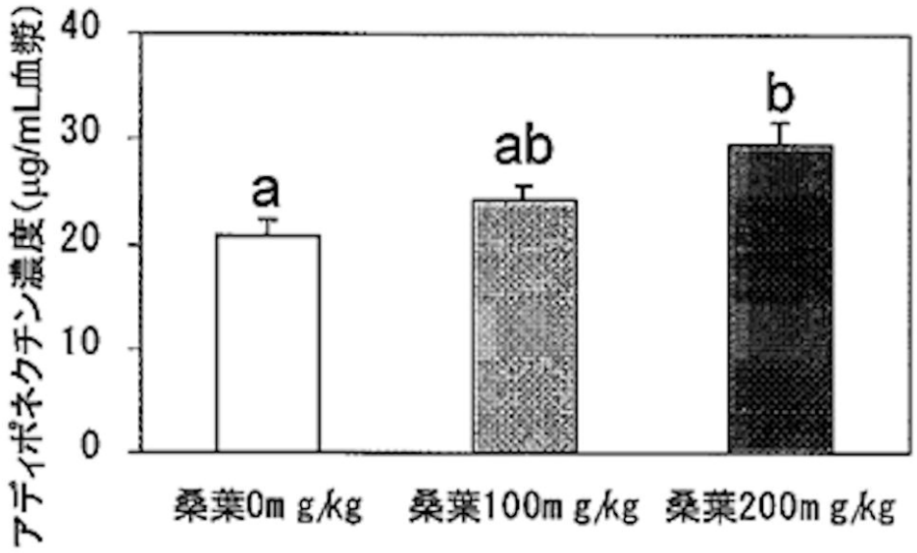
E. Described matter 1-5 ([0040] to [0042])
"Hereinafter, the present invention is further illustrated by examples, but the scope of the invention is not limited to the scope of the working examples.
Example
Method Leaves harvested from a young mulberry were washed with water, and after heated air drying (80 degree, 12 hours), they were ground. To 100 kg dried powder added was 1000 L solution of ethanol/water=20/80, and extracted. A filtrate was freeze-dried for use as a mulberry leaf extract (5 kg).

SD-based rats (4 week age, male) were preliminarily bred for one week, and mulberry leaf extract (containing about 0.5% of 1-deoxynojirimycin (DNJ)) was forcedly administered orally once daily on 5 pm for four weeks. Twenty-four rats were classified into three groups. Mulberry extract was dispersed into saline so that a dosage amount might become 0, 100, or 200 mg/kg body weight. After the completion of the test period, rat tissue (brain, heart, liver, renal, white adipose tissue surrounding epididymis) weights were measured. Fat compositions of plasma and liver, blood glucose level, and adiponectin were measured. Further, physiological function of DNJ believed to be an active ingredient of mulberry leaf was investigated by a test method similar to that performed on mulberry leaf extract. Rats were divided into two groups. DNJ dosage amount was set to 0.1 mg/kg body weight."

F. Described matter 1-6 ([0050])
"A blood concentration of adiponectin that promotes fat metabolism and anti-adiposeness effect was increased (FIG 3)."

G. Described matter 1-7 ([FIG 3])
"

[図3]



アディポネクチン濃度（μｇ／ｍＬ血漿） Adiponectin concentration (μg/ml plasma)
桑葉 Mulberry leaf
"

H. Described matter 1-8 ([0018])
"...
[FIG 3] A result of measuring adiponectin concentration in a rat plasma to which mulberry leaf extract was administered. The value was shown as an average ± standard deviation (n=6). A value shown with a different letter (a, b) has a statistically significant difference (P<0.05).
..."

(2) The invention described in Cited Document 1

The composition for suppressing fat accumulation comprising 1-deoxynojirimycin" of Cited Document 1 (Described matter 1-1) is to promote the excretion of adiponectin and suppress fat accumulation through the promotion of fat metabolism (Described matter 1-2). Thus the composition for suppressing fat accumulation corresponds to "a composition for promoting the excretion of adiponectin". Further, a form of the above composition is not particularly limited as long as it contains 1-deoxynojirimycin, including a form of a mulberry plant treated product such as mulberry leaf extract (Described matter 1-3). Thus it is obvious that the above composition encompasses the form of "mulberry leaf extract containing 1-deoxynojirimycin". Furthermore, in the working examples, mulberry leaf is subjected to extraction by the addition of ethanol/water=20/80, and the resultant filtrate is freeze-dried to produce a mulberry leaf extract. It is specifically described that, when this was orally administered to SD-based rats once daily for four weeks, blood adiponectin concentration was increased (Described matter 1-5 to 1-8).

In view of the foregoing, Cited Document 1 discloses an invention of "A composition for promoting the excretion of adiponectin, comprising a mulberry leaf extract obtained by subjecting a dried powder of mulberry leaf including 1-deoxynojirimycin to the extraction by the addition of ethanol/water=20/80, and subjecting a filtrate to freeze drying" (hereinafter referred to as "Cited Invention").

2. Regarding Cited Document 8
(1) Described matters in Cited Document 8
A. Described matter 8-1 (Example 5 ([0169]))
"Garcinia mangostana methanol extract (AR933): A fruit skin of Garcinia mangostana dried in the shade (1 kg) was ground into coarse powder, and extracted with methanol (5 L) for two hours at 60 to 65°C. A solvent was separated from the raw materials by filtration. Extraction process was repeated three times using methanol (2*3L and 1*2L). The combined extracts were subjected to ultrafiltration, and condensed under reduced pressure, and precipitated at a room temperature. The separated solid was filtrated to obtain a dried powder (165 g, α-mangosteen: 32% and γ-mangosteen: 3%)."

B. Described matter 8-2 (Example 23 ([0195] to [0197]))
"Inhibition of PPAR-γ, ADRP, CD36, aP2, B3AR, and perilipin in 3T3-L1 adipocytes by the composition 1B:

Experimental Protocol: Mouse pre-adipocyte 3T3-L1 cells were maintained in Dulbecco's modified Eagle medium (DMEM) to which 2 mM glutamine, 4.5 g/L glucose, and 10% fetal bovine serum were added. Equal number of cells was plated in each well of 24-well culture plates. Cells were pre-treated for 2 hours in any one of 5 μg/ml LI/DD-II/054A/01, AR933, or the composition 1B, followed by the addition of differentiation medium comprising 500 nM insulin, 1.0 uM dexamethazone, and 0.5 mM isobutylmethylxanthin (IBMX) over 48 hours. Thereafter, cells were further incubated in the presence or absence of composition 1B by use of post differentiation medium (DMEM including 100 nM insulin). Finally, cells were harvested, and washed with chilled phosphate buffer solution, and lysed with the lysis buffer. The protein extracts were clarified for 20 minutes at 14000 g. Protein content was measured by the Bradford method using Coomassie Brilliant Blue, and cell lysate was divided in aliquots until use, and stored at -80°C. The modulation of adiposite differentiation markesr such as Peroxisome proliferator activation factor receptor-γ (PPAR-γ), CD36, and adipose cell fatty acid binding protein (aP2); and intracellular fat droplet surface related protein, perilipin expression were assayed by immunoblotting assay.

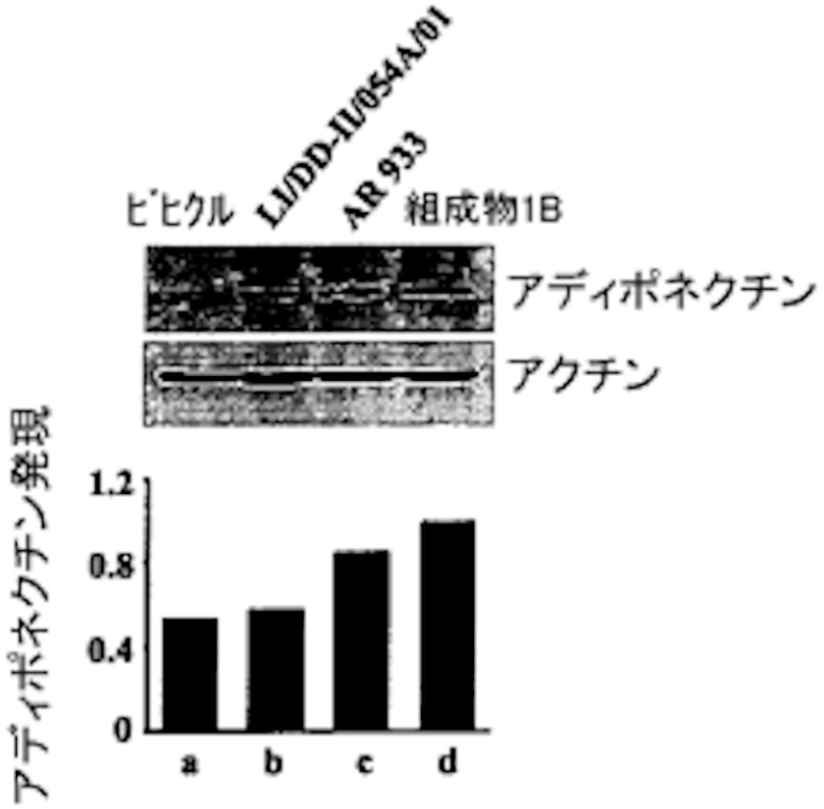
The inhibition of protein expression of biomarker molecule adipocyte in presence or absence of the composition 1B was evaluated in immunoblotting assay. Briefly, eqal amount of cell lysate proteins were resolved in 7.5% SDS-PAGE; and then proteins were transferred to nitrocellulose membrane. After blocking non-specific sites, membrane was incubated together with any one of anti-PPAR-γ, anti-CD36, anti-aP2, anti-β3AR, anti-ADRP, or anti-perilipin antibody. Finally, a specific immunoreactive band was developed by West-pico Chemical fluorescence substrate (Pierce Biotechnology, IL, USA), and an immunoblotting images were recorded by Kodak Image Station (Kodak, USA). Band intensities were calculated by

densitometry, and normalized by the actin expression in each sample. The data is summarized in FIG 6."

C. Described matter 8-3 (Example 25 ([0200]))
"Modulation of adiponectin by LI/DD-II/054A/01, AR933, and the composition 1B: The modulation of adiponectin protein in 3T3-L1 adipocytes by LI/DD-II/054A/01, AR933, or the composition -1B was evaluated in Western immunoblotting assay. A procedure of cell culture, treatment protocol, and immunoblotting assay was the same as the one described in Example 23. FIG 8 summarizes the enhancement of adiponectin protein expression in 3T3-L1 mature adipocytes by the composition 1B or its individual components such as LI/DD-II//054A/01 or AR933."

D. Described matter 8-4 ([0051])
"...
[FIG 8] shows a representative immunoblotting showing overexpression of adiponectin protein in 3T3-L1 adipocytes treated with 5 μg/ml LI/DD-II/054A/01, AR933, or the composition 1B. Protein expression was analyzed by densitometry, and normalized with the actin expression. The bar diagram in each panel shows a normalized protein expressions in arbitrary units. In a bar diagrams, the bars represent protein expressions in cells treated with vehicle control (a), LI/DD-II/054A/01(b), AR933(c), and the composition 1B(d).
..."

E. Described matter 8-5 (FIG 8)
"



アディポネクチン発現	Adiponectin Expression
アディポネクチン	Adiponectin
アクチン	Actin
ビヒクル	Vehicle
組成物１Ｂ	Composition 1B

"

3. Regarding Cited Document 13

(1) Described matters in Cited Document 13

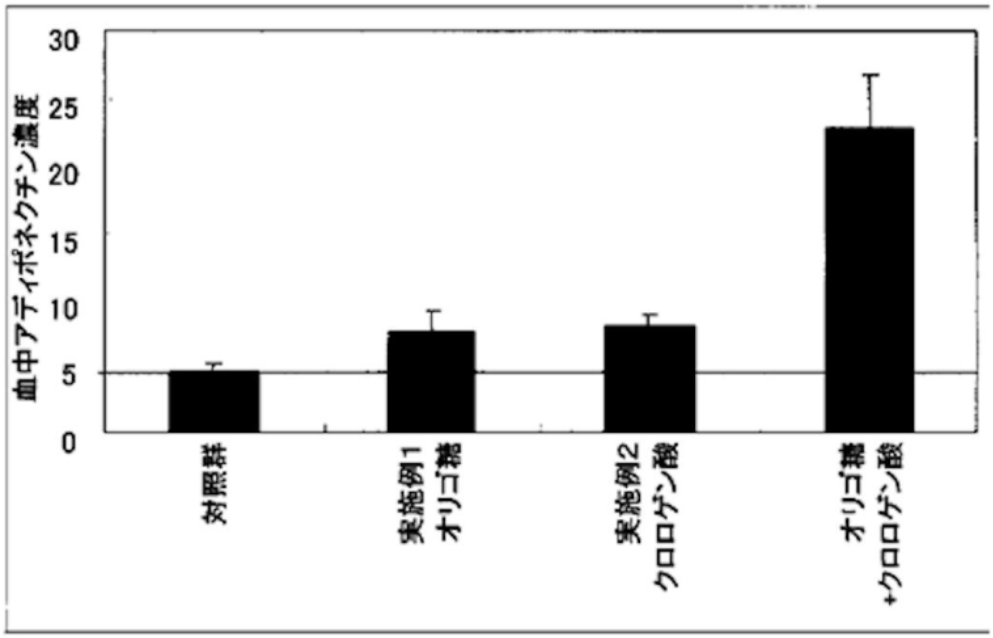
A. Described matter 13-1 (Claim 1)

"A pharmaceutical composition for promoting adiponectin production, comprising a sugar with a polymerization degree of 2 to 10 in which mannose unit occupies 50% or more on a number basis, and chlorogenic acids."

B. Described matter 13-2 (FIG 1)

"

[図1]



血中アディポネクチン濃度　　Blood adiponectin concentration
対照群　Control group
実施例１　オリゴ糖　　Example 1 Oligosaccharides
実施例２　クロロゲン酸　　Example 2 Chlorogenic acid
オリゴ糖　＋クロロゲン酸　　Oligosaccharides + Chlorogenic acid
"

4.　Cited Document 15
(1) Described matters in Cited Document 15
A.　Described matter 15-1 ([Claim 1])
"An adiponectin production promoter comprising one kind or two or more kinds of extracts selected from Chinese mushroom, Pleurotus citrinopileatus, Cantharellus cibarius, and Ganoderma Iucidem."

B.　Described matter 15-2 ([0013])
"The above extract has excellent adiponectin production promoting effect, and may be utilized as an adiponectin production promoter.　Diseases preventable or improvable by adiponectin production promotor may include diabetes, dyslipidemia, arterial sclerosis, and fatty liver.　The adiponectin production promotor of the present invention may be expected to exert the effects of the prevention or improvement of such diseases as well as the prevention and improvement of adiposeness."

No. 5 Comparison between Present Invention 1 and Cited Invention

A comparison is made between Present Invention 1 and Cited Invention.

First, it is obvious from [0024] of the specification of the present application "Extraction used herein does not particularly limit the extraction method, but an example of a method may include a method of immersing raw materials into a solvent for extraction and after filtration, obtained as a filtrate. Filtrate may be ... powdered or further purified. .. The solvent to be used in extraction is not particularly limited, but may include, as a preferable example, a polar solvent selected from the group consisting of ... methanol, ethanol, ... and water, or a mixed solvent thereof. ... Extraction solvent may be preferably ethanol, or a combination of water and ethanol, in terms of safety" and "mulberry leaf extract" of Present Invention 1 may be extracted with an extraction solvent of a mixed fluid of ethanol/water. Thus "mulberry leaf extract obtained by subjecting a dried powder of mulberry leaf including 1-deoxynojirimycin to the extraction by the addition of ethanol/water=20/80, and subjecting a filtrate to freeze drying" corresponds to "mulberry leaf extract" of Present Invention 1. Further, promoting the excretion of adiponectin is equivalent to the promotion of adiponectin production.

Therefore, they have a common point of "adiponectin production promoter including mulberry leaf extract", and have the following different feature.

(Different Feature 1)

Present Invention 1 further adds "mangosteen fruit skin extract", whereas Cited Invention does not add "mangosteen fruit skin extract".

No. 6 Judgment

1. Regarding Different Feature 1

Cited Document 1 specifically discloses that adiponectin level in plasma was significantly increased (Described matters 1-7 and 1-8) in an administered group of 200 mg/kg mulberry leaf extract ("mulberry leaf 200 mg/kg" of Described matter 1-7) as compared to an administered group of 0 mg/kg mulberry leaf extract ("mulberry leaf 0 mg/kg" of Described matter 1-7; i.e., corresponding to "a control group") when a mulberry leaf extract was orally administered to SD-based rats once daily for four weeks in an amount of 0, 100, or 200 mg/kg (Described matter 1-5).

Further, Cited Document 8 specifically discloses that when mouse pre-adipocyte 3T3-L1 cell was pretreated with mangosteen fruit skin methanol extract (AR933) (Described matters 8-2 and 8-3), cells treated with mangosteen fruit skin methanol extract (AR933) ("c" of Described matter 8-5) showed significant increase of adiponectin protein expression in 3T3-L1 mature adipocyte as compared to vehicle control ("a" of Described matter 8-5, corresponding to "control group" to which adiponectin production promoter is not administered.) (Described matter 8-5). Here, mangosteen fruit skin methanol extract (AR933) of Cited Document 8 is extracted from a fruit skin; i.e., coarse powder of fruit skin, of Garcinia mangostana (mangosteen) dried in the shade (Described matter 8-1). Thus it corresponds to "magosteen fruit skin extract" of Present Invention 1 from the description of [0024] of the specification of the present application as pointed out in the above No. 5. Further, "significant increase in the expression of adiponectin protein" of Cited Document 8 represents "adiponectin production promotion".

As seen above, Cited Document 1 and Cited Document 8 specifically disclose that each of mulberry leaf extract and mangosteen fruit skin methanol extract solely showed a significant adiponectin production promoting effect as an adiponectin production promoter as compared to the control (to which adiponectin production promoter is not administered).

Further, it is well known that adiponectin production promoter is used as a pharmaceutical (see, if necessary, [0021] of Cited Document 1 (Described matter 1-2), and Claim 1 of Cited Document 13 (Described matter 13-1), [0013] of Cited Document 15 (Described matter 15-2)). It is recognized that it was common as of the filing in the technical field of pharmaceuticals to use a plurality of active ingredients having a similar effect in combination, and it was actually a well-known technique for a person skilled in the art to use a plurality of adiponectin production promoters in combination (see, if necessary, the above Described matters 13-1, 13-2, and 15-1). In addition, Cited Document 1 discloses that another publicly known fat accumulation suppressant may be mixed in the Cited Invention (Described matter 1-4), and further discloses that the promotion of adiponectin excretion may suppress fat accumulation (Described matter 1-2). In view of this, Cited Document 1 also suggests the combined use of mulberry leaf extract with another adiponectin production promoter for promoting the adiponectin production.

Consequently, a person skilled in the art would have easily conceived of further adding mangosteen fruit skin methanol extract known to have adiponectin production promoting effects in combination with mulberry leaf extract comprising 1-deoxynojirimycin in the Cited Invention on the basis of well-known technique as of the filing of the present application as shown in the described matter of Cited Documents 1 and 8 and Cited Documents 13 and 15.

2. Effects of Present Invention 1

A person skilled in the art would expect from the description of Cited Documents 1 and 8 that the combined use of mulberry leaf extract and mangosteen fruit skin extract that have excellent adiponectin production promoting effect solely would improve adiponectin production promoting effect as compared to a case of sole use of each extract (cause the so-called "additive effect").

Further, in addition, in order to find that an adiponectin production promotor of Present Invention 1 according to the combined use of both extracts (hereinafter, "adiponectin production promotor" may be sometimes referred to as only "an agent") involves an inventive step over an agent described in Cited Documents 1 and 8, it is necessary to clarify from the description of the specification of the present application that an adiponectin production promoting effect (so-called "synergistic effect") is caused, beyond an adiponectin production promoting effect to be expected from the combined use of agents that contain either one of mulberry leaf extract or mangosteen fruit skin extract (the above "additive effect").

Here, there are differences in the measurement method and measurement condition between an adiponectin production promoting effect of an agent that contains either one of mulberry leaf extract or mangosteen fruit skin extract shown in Cited document 1 or 8 and an adiponectin production promoting effect of an agent that contains both extracts as shown in the specification of the present application. Therefore, the adiponectin production promoting effect of Cited Document 1 or 8 and

the adiponectin production promoting effect of an agent that contains both extracts as shown in the specification of the present application cannot be directly compared. The specification of the present application discloses a test result for an adiponectin production promoting effect of an agent that contains either one of mulberry leaf extract or mangosteen fruit skin extract in addition to a test result for an adiponectin production promoting effect caused by the combined use of both extracts. The test result can be seen as equivalent to the test result for an agent described in Cited document 1 or 8, in that the test result is directed to an agent that contains only mulberry leaf extract or only mangosteen fruit skin extract.

In view of this, consideration is given to the description of the specification.
(1-1) Regarding
- Variation of supernatant adiponectin level (ng/ml) of fat cell culture by the addition of both mulberry leaf extract and mangosteen fruit skin extract of Present Invention 1 to a medium ("Adiponectin production test using cells", [0036] to [0041], [Table 15] to [Table 17]),
and
- Variation of serum adiponectin level (μg/ml) due to oral administration of mulberry leaf extract and mangosteen fruit skin extract to subjects ("in vivo test",
[Table 20])
the specification of the present application discloses the following data A to D as data for a test result showing an adiponectin production promoting effect caused by an agent of Present Invention 1:
(In the following, "case N" (N is a number) represents individual subjects, and data with the same number are construed as data derived from the same subject. Further, numerical value in parentheses represents a variation of adiponectin level after the addition or oral administration of mulberry leaf extract and magosteen fruit skin extract as compared to an adiponectin level of the control group (In an "adiponectin production test using cells", a group to which only a solvent (water or DMSO) was added without an adiponectin production promoter. In an "in vivo test", at the start of oral administration of adiponectin production promoter.))

A [Table 15] (case 32) Control group ->
Mulberry leaf extract 10 μg/ml and
Mangosteen fruit skin extract 1 μg/ml addition group
1 "Day 10" 18.08 -> 18.93 [+0.85]
2 "Day 12" 8.1 -> 9.81 [+1.71]

B [Table 16] (case 37) Control group ->
Mulberry leaf extract 10 μg/ml and
Mangosteen fruit skin extract 1 μg/ml addition group
1 "Day 10" 14.09 -> 14.82 [+0.73]
2 "Day 12" 11.87 -> 13.1 [+1.23]

C [Table 17] (case 48) Control group ->
Mulberry leaf extract 10 μg/ml and
Mangosteen fruit skin extract 1 μg/ml addition group

1 "Day 10" 2.69 -> 2.47 [-0.22]
2 "Day 12" 0.57 -> 0.90 [+0.33]

D [Table 20] (Mulberry leaf extract 600 mg and Mangosteen fruit skin extract 400 mg/day oral administration)
(case 37):
2011/8/24 (at the start of uptake) -> 2011/10/12
-> 2011/11/30
(case 39):
2011/10/5 (at the start of uptake) -> 2011/10/18
-> 2011/11/24
1 (case 37) 9.55 -> 10.18 [+0.63]
-> 9.77 [+0.22]
2 (case 39) 3.21 -> 3.93 [+0.72]
-> 5.52 [+2.31]

(1-2) Further, [Table 2] to [Table 6], [0074], second paragraph
"... Case 37 not shown in Table was ... Case 39 was ... high." and [Table 21] discloses
- Regarding the variation of supernatant adiponectin level (ng/ml) of adipocyte culture by the addition of any one of mulberry leaf extract or mangosteen fruit skin extract of the present invention ("Adiponectin production test using cells", [Table 2] to [Table 6]), and
- Variation of serum adiponectin level (μg/ml) due to oral administration of only mangosteen fruit skin extract to subjects ("in vivo test", [0072], [0074] second sentence, [Table 21]),
the following data E to K are described:
(Regarding "case N", the same can apply to the above. Further, a numerical value in parentheses represents a variation of adiponectin level after the addition or oral administration of mulberry leaf extract only or magosteen fruit skin extract only as compared to an adiponectin level of the control group. (In an "adiponectin production test using cells", a group to which only a solvent (water or DMSO) was added without adiponectin production promoter. In an "in vivo test", at the start of oral administration of an adiponectin production promoter.))

Further, the addition or oral administration of any one of extracts of these E to K corresponds to the use of an adiponectin production promotor including mulberry leaf extract (Cited Document 1) or mangosteen fruit skin extract (Cited Document 8) described in Cited Document 1 or Cited Document 8.

E [Table 2] (case 37) Control -> Mulberry leaf extract
10 μg/ml additive group
1 "Day 10" 10.78 -> 12.16 [+1.38]
2 "Day 12" 5.27 -> 5.68 [+0.41]

F [Table 3] (case 45) Control group -> Mulberry leaf extract
10 μg/ml additive group

1 "Day 10" 8.51 -> 9.09 [+0.58]
2 "Day 12" 2.37 -> 2.95 [+0.58]

G [Table 4] (case 45) Control group -> Mangosteen fruit skin extract
1 μg/ml addition group
1 "Day 10" 7.97 -> 8.92 [+0.95]
2 "Day 12" 1.79 -> 3.06 [+1.27]

H [Table 5] (case 49) Control group -> Mangosteen fruit skin extract
1 μg/ml addition group
1 "Day 10" 18.61 -> 14.21 [-4.40]
2 "Day 12" 4.37 -> 9.71 [+5.34]

I [Table 6] (case 51) Control -> Mangosteen fruit skin extract
1 μg/ml addition group
1 "Day 10" 14.32 -> 15.03 [+0.71]
2 "Day 12" 3.22 -> 6.06 [+2.84]

J [0074] Second sentence
(Mangosteen fruit skin extract 400 mg/day oral administration) at the start of intake ->
After 3 months
1 (case 37) 9.08 -> 8.43 [-0.65]
2 (case 39) 6.63 -> 7.17 [+0.54]

K [Table 21] "Measurement result of amount of adiponectin in human serum (average of four persons)"
(Mangosteen fruit skin extract 400 mg/day oral administration) at the start of intake ->
After 3 months
16.9 ± 1.4 -> 7.8 ± 1.0 [+0.9 ± SE]

(2)a. However, there are no comparative control data in the above (1-2) appropriate for both the case of adding only mulberry leaf extract and the case of adding mangosteen fruit skin extract in the respective subjects adopted in a combined test ((1-1)) of mulberry leaf extract and mangosteen fruit skin extract of Present Invention 1 (case 32, case 37, case 48 in adiponectin production test (A to C) using cells; case 37, case 39 in in vivo test (D)).
(In addition, case 37 includes data for single addition of mulberry leaf extract ((1-2)E) corresponding to the combined use group of both extracts ((1-1)B) in an adiponectin production test using cells; however, there are no data for single addition of mangosteen fruit skin extract. There are data for single oral administration of mangosteen fruit skin extract corresponding to the combined use of both extracts ((1-1)D1) in vivo test ((1-2)J1). There are no data for single oral administration of mulberry leaf extract.

Further, regarding case 39 of (1-1)D2, there are data for single oral administration of mangosteen fruit skin extract in the corresponding in vivo test ((1-2)J2); however, there are no data for single oral administration of mulberry leaf extract.)

In such circumstances where not both comparative control test results for the addition or oral administration of mangosteen fruit skin extract only and the

comparative control result for the addition or oral administration of mulberry leaf extract only are disclosed, it cannot be seen at all from the increase in adiponectin level as shown in the respective subjects for the test of (1-1)A to D that the effect goes beyond the increase in adiponectin level that can be expected from the test result for the use of either one.

b. Further, regarding the adiponectin production test using cells showing all three test data of a single addition of mulberry leaf extract, a single addition of mangosteen fruit skin extract, and the addition of both extracts, setting aside the subjects, comprehensively taking data of (1-1)A to C and (1-2)E to I into account, the extent of adiponectin production promotion caused by the combined use of both extracts is not at a level that a person skilled in the art cannot expect. Specifically, in view of each maximum value (A2, B2, C2) of the increase of adioponectin level in data of the combined use group ((1-1)A to C) of both extracts in a test using adipocyte, the maximum increase in adiponectin level caused by the combined use of both extracts falls within a range of *1:+0.33 (C2) to +1.71 (ng/ml) (A2); i.e. at most +1.71, whereas each maximum increase in adiponectin level caused by the single addition of mulberry leaf extract falls within a range of *2: +0.58 (F1, F2) to +1.38(E1), in view of each maximum value (E1, F1, F2) of the increase of adioponectin level in data of the single addition group of mulberry leaf extract ((1-2)E to F). Further, each maximum increase in adiponectin level caused by the single addition of mangosteen fruit skin extract falls within a range of *3: +1.27(G2) to +5.34(H2), in view of each maximum value (G2, H2, I2) of the increase of adioponectin level in data of the single addition group of mangosteen fruit skin extract. In view of these numerical values, a degree of the increase in adiponectin production caused by the combined use of mulberry leaf extract and mangosteen fruit skin extract of the above *1 is not particularly excellent as compared to a degree of the increase in adiponectin production caused by either one of mulberry leaf extract or mangosteen fruit skin extract of the above *2 and *3.

(3) As per the consideration of (1-1), (1-2), and (2), it cannot be said that the description of the specification of the present application including the test results of the above (1-2) and (1-2) clarifies that the combined use of mulberry leaf extract and mangosteen fruit skin extract according to Present Invention 1 causes an excellent adiponectin production promoting effect that goes beyond the scope that can be expected from an agent including either one of each extract (corresponding to an agent of Cited Documents 1 and 8) in every subject.

(4) Appellant's allegation

Appellant alleges in the written statement on July 19, 2018 that "Regarding the invention of Claim 1, the combined addition of mulberry leaf extract and mangosteen fruit skin extract may result in an excellent result in adiponectin production test as per described in the paragraph 0063 and later of the specification." (2. First paragraph)

Specifically, Appellant cites a part of data in [Table 15] to [Table 17] ("(1) Adiponectin production test using cells (a combination in Claim 1)" and [Table 20] and [Table 21] and [0074] ("(2) adiponectin production in vivo test of mangosteen fruit skin extract") in and after [0064] of the specification of the present application, and alleges that

"As aforementioned, an excellent adiponectin producing effect (synergistic effect) caused by the combined use of mulberry leaf extract and mangosteen fruit skin extract ... is disclosed in the specification. This is a synergistic effect based on an excellent effect unexpected from the conventional publicly-known documents. The comparison and construction of these experimental data shows that the invention recited in Claims 1 and 2 after the Amendment involves an inventive step. ..." (Final paragraph. Underlined by the body).

However, in the above written statement Appellant only cites each of a part of data of [Table 15] to [Table 17] and [Table 20] as a ground for the above "synergistic effect" of Present Invention 1. Appellant fails to conduct "comparison and construction of these experimental data" as Appellant alleges.

Specifically, a specific and reasonable explanation involving the comparison with an appropriate comparative control data was not at all given in the written statement as to in what point a person skilled in the art can recognize from these cited data that the combined use of mulberry leaf extract and mangosteen fruit skin extract of Present Invention 1 causes unexpected adiponectin production promotion compared to a degree of the increase in adiponectin production expected from a test result in a case of using either one of mulberry leaf extract or mangosteen fruit skin extract.

Therefore, the Appellant's allegation in the written statement cannot rebut the determination by the body as shown in the above (1-1) to (3).

3 Summary

As described above, Present Invention 1 was easily conceivable by a person skilled in the art on the basis of the inventions described in Cited Documents 1 and 8 and the well-known technique as of the filing as shown in Cited Documents 13 and 15.

No. 7 Closing

Present Invention 1 was easily conceivable by a person skilled in the art on the basis of the inventions described in Cited Documents 1 and 8 and the well-known technique as of the filing as shown in Cited Documents 13 and 15, and thus cannot be granted a patent under the provision of Article 29(2) of the Patent Act.

Therefore, the present application should be rejected without considering the invention according to Claim 2 of the present application.

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

October 23, 2018

Chief administrative judge: SEKI, Masatatsu
Administrative judge: INOUE, Akiko
Administrative judge: OKUBO, Motohiro