Chapter 3 Medicinal Inventions

In this chapter, the application of Examination Guidelines to patent applications relating to medicinal inventions is explained.

Determination of the matters which are not explained in this chapter is carried out according to Examination Guidelines.

Definition of Terms used in this Chapter

A medicinal invention here means "an invention of a product" which intends to provide a new medicinal use (Note 2) of a material (Note 1), based on the discovery of an unknown attribute of the material.

(Note 1) "A material" here means a component used as an active ingredient, including a compound, a cell, a tissue, or a chemical substance (or a group of chemical substances) whose chemical structure is not specified, such as an extract from a natural product, and combination thereof. Hereinafter, the material concerned is referred to as "a compound, etc."

(Note 2) "A medicinal use" here means the following (i) or (ii):

(i) an application to a specific disease;

(ii) an application to a specific disease in which dosage or administration such as a dosing time, a dosing procedure, a dosing amount or an administration site (hereinafter referred to as " dosage or administration") is specified.

See Examination Guidelines, Part II Description and Claims and Part III Patentability for the matters which are not explained in this chapter with respect to requirements for description and claims, and requirements for patentability.

1. Description and Claims

1.1 Requirements for Description

1.1.1 Enablement Requirement (Article 36(4)(i))

Determination of enablement requirement relating to medicinal inventions is carried out according to Examination Guidelines, Part II, Chapter 1, Section 1

Enablement Requirement.

Generally, medicinal invention belongs to a technical field where it is relatively difficult to understand how to make and use a product on the basis of their structures or names. Hence, normally one or more representative examples are necessary for the description to be stated such that a person skilled in the art can carry out the invention, unless a person skilled in the art can manufacture or obtain the compound, etc. and can also use the compound, etc. for the medicinal use in light of the common general knowledge as of the filing. In addition, the results of pharmacological study are usually required for supporting the medicinal use (see Examination Guidelines, Part II, Chapter 1, Section 1 Enablement Requirement 3.1(1)(iii)).

The ideas of the method for describing the results of pharmacological study sufficient to support pharmacological effects are described below.

(1) The Extent of the Description of the Results of Pharmacological Study

The results of pharmacological study are described for the purpose of confirming the pharmacological effects of the compound, etc. which is claimed as a medicinal invention. Hence, in principle, all of the followings should be made sufficiently clear as the results of pharmacological study: (i) which compound, etc. is applied to (ii) what pharmacological study system, (iii) what results are obtained, and (iv) what relevance the pharmacological study system has with the medicinal use of the claimed medicinal invention. It should be also noted that, in principle, the results of pharmacological study should be described with numerical data, but when the results cannot be described with numerical data due to the nature of the pharmacological study system, an objective description equivalent to numerical data may be accepted. An objective description equivalent to the numerical data is, for example, description of the objective observation results observed by a medical doctor. Furthermore, a clinical study, an animal experiment, and an in-vitro study are employed as the pharmacological study system.

(2) Examples of When Reasons for Refusal are Notified

(a) The results of pharmacological study not being described

Generally, it is difficult to predict whether the compound, etc. can be used for the specific medicinal use from only the structure and name of the compound, etc. Therefore, it still difficult for a person skilled in the art to predict whether the compound, etc. can be used for the specific medicinal use even when, although an

effective dose, a mode of administration and formulation method are described in the description, etc., the results of pharmacological study are not described. Accordingly, in such case, in principle, the reasons for refusal shall be notified.

(b) The compound, etc. that was used in the pharmacological study not being specified, and hence the compound, etc. of a claimed medicinal invention not being confirmed to have the pharmacological effect.

For example, when the compound, etc. used in the pharmacological study system described in the description as filed is merely provided as being "any of a plurality of the compounds, etc." without specifying which compound, etc. is actually used, this example corresponds to the above, in which, as described in "(1) The Extent of the Description of the Results of Pharmacological Study, " "(i) which compound, etc." was applied to the pharmacological study is not clear. Accordingly, the examiner should note that in many cases the pharmacological effect of the compound, etc. of the claimed medicinal invention cannot be confirmed to have the pharmacological effect.

(3) Arguments and/or explanation, etc. by applicant against the Reasons for Refusal

In response to a notice of reasons for refusal involving failure to comply with the enablement requirement, the applicant may present an argument, explanation, etc. by submitting a written opinion, certificate of experimental results, and the like.

For example, the applicant may, in a written opinion, point out the common general knowledge, etc. at the time of filing other than those that were taken into account by the examiner when making a determination, and argue that, in light of such common general knowledge, the statement in the description can be regarded to be clear and sufficient enough for a person skilled in the art to carry out the claimed invention. The applicant may also submit a certificate of experimental results to support such an argument presented in the written opinion (Cases 11 and 13).

However, when, due to an insufficient statement in the description, the statement in the description cannot be regarded to be clear and sufficient in such a manner as to enable a person skilled in the art to carry out the claimed invention even in light of the common general knowledge at the time of filing, the reason for refusal cannot be overcome even though the applicant submits a certificate of experimental results after filing of the application to make up for such a deficiency and thereby argues that the statement is clear and sufficient (Case 12 (Claim 2)).

1.2 Claims

1.2.1 Support Requirement (Article 36(6)(i))

Determination of support requirement relating to medicinal inventions is carried out according to Examination Guidelines, Part II, Chapter 2, Section 2 Support Requirement. Examples of the support requirement are as follows.

(1) While an invention of the antiemetic drug having an active ingredient A is claimed, neither a pharmacological study method nor the results, which could support the antiemetic use of the ingredient A, is described in the description, and furthermore, the antiemetic use of the ingredient A cannot be inferred from the common general knowledge as of the filing, the description cannot be regarded as describing the invention in such a way that a person skilled in the art could recognize that the problem of providing an antiemetic drug would be solved by the invention; therefore, the claimed invention is not described in the description.

(2) While an invention of a therapeutic agent for a specific use having a compound defined by a property as an active ingredient is claimed, the description supports the specific use with regard to only a few specific compounds claimed as an active ingredient, therefore, the details provided in the description can neither be expanded nor generalized to the scope of the claimed invention even in light of the common general knowledge at the time of filing

In response to a notice of reasons for refusal involving a violation of the support requirement, the applicant may present an argument, explanation, etc. by submitting a written opinion, certificate of experimental results, and the like.

For example, the applicant may, in a written opinion, point out the common general knowledge, etc. at the time of filing other than those that were taken into account by the examiner when making a determination, and argue that, in light of such common general knowledge, the details provided in the description can be expanded or generalized to the scope of the claimed invention. The applicant may also submit a certificate of experimental results to support such an argument presented in the written opinion (Cases 11 and 13).

However, when, due to an insufficient statement in the description, the details provided in the description can neither be expanded nor generalized to the scope of the claimed invention even in light of the common general knowledge at the time of filing, the reason for refusal cannot be overcome even though the applicant submits a

certificate of experimental results after filing of the application to make up for such a deficiency and thereby argues that the provided details can be expanded or generalized to the scope of the claimed invention (Case 12 (Claim 2)).

1.2.2 Clarity Requirement (Article 36(6)(ii))

Determination of support requirement relating to medicinal inventions is carried out according to Examination Guidelines, Part II, Chapter 2, Section 3 Clarity Requirement. In light of the purport of the provision of Article 36(5), various forms of expression may be used in a claim by an applicants to specify an invention for which a patent is sought.

For example, in the case of "an invention of a product," various forms of expression such as operation, function, property, characteristics, method, use and others may be used to describe matters specifying the invention, in addition to the forms of expression such as a combination of products or a structure of the product. Therefore, applicants may describe claims using various expression forms so as to specify the medicinal invention for which a patent is sought.

On the other hand, in accordance with the provision of Article 36(6)(ii), an invention shall be described to be clearly identified from a single claim. Therefore, an examiner should note that the definition of an invention by applicant using the above various forms of expression is allowed so far as the invention can be clearly identified.

For example, when an active ingredient in a medicinal invention is defined by a function or characteristics, etc. in the claim, an examiner should note that the medicinal invention usually cannot be deemed clear if it is evident that the matter defined by the function or characteristics, etc. is not sufficiently specified from a technical perspective in light of the common general knowledge as of the filing, and the invention cannot be clearly identified from the statement of the claim even by taking into account the description and drawings (see Examination Guidelines, Part II, Chapter 2, Section 3 Clarity Requirement, 4.1.1(2)).

In case that the statement in the claim does not express a specific medicinal use but a general medicinal use, where the claim directed to a medicinal invention (for example, in case where the statement expresses not a “pharmaceutical agent for disease X consisting of...” but a “pharmaceutical agent consisting of...”), it should not be deemed a violation of Article 36(6)(ii) merely because the statement expresses a general use (i.e., merely because the scope of the claim is relatively broad) unless the expression

makes unclear the invention for which a patent is sought (see Examination Guidelines, Part II, Chapter 2, Section 3 Clarity Requirement, 2.3(2)).

A medicinal invention can be described in a claim as "an invention of a product" as follows:

Example 1: A medicine for disease Z containing an active ingredient A.
Example 2: A medicinal composition for disease Y containing an active ingredient B.
Example 3: A medicine for disease W containing active ingredients C and D in combination.
Example 4: A kit for disease V comprising an injection agent including an active ingredient E and an oral agent including an active ingredient F.

2. Patentability

2.1 Industrial Applicability (the main paragraph of Article 29(1))

Determination of support requirement relating to medicinal inventions is carried out according to Examination Guidelines, Part III, Chapter 1, Eligibility for Patent and Industrial Applicability.

A medicinal invention is defined by its medicinal use, and hence is intended to be applied for example, administered or spread to a human body. However, a medicinal invention is "an invention of a product," and therefore is not included in "methods of surgery, therapy or diagnosis of humans". Accordingly, a medicinal invention is identified as "an industrially applicable invention."

A medicinal invention defined by combination of two or more medicines, or defined by dosage or administration is also identified as "an industrially applicable invention."

2.2 Novelty (Article 29(1))

2.2.1 Basic Principles of Determination of Novelty related to Medicinal Invnetions

A medicinal invention is "an invention of a product" which intends to provide a new medicinal use of a compound, etc. based on the discovery of an unknown attribute

of such compound, etc. Therefore, the novelty of a medicinal invention is judged by the following two points:

(i) a compound etc. having a specific attribute;

(ii) a medicinal use based on such attribute

2.2.2 Determination Method for Novelty

(1) Identification of the claimed medicinal invention

The identification of the claimed invention shall be made based on the statement of the claim. Matters (terms) stated in the claim defining the claimed invention should be construed in the light of the statements in the description, the drawings and the common general technical knowledge as of the filing (see Examination Guidelines, Part III, Chapter 2, 3 Procedure of Determining Novelty and Inventive Step, 2).

(2) Identification of the cited invention

A medicinal invention consists of compounds etc. having a specific attribute and a medicinal use based on the attribute. Hence, in order to identify that there is a description or representation (hereinafter referred to merely as “a description”) of the medicinal invention in a publication or a web page, etc. (see Examination Guidelines, Part III, Chapter 2, Section 3 Procedure of Determining Novelty and Inventive Step, 3.1.1 (Note 2) and 3.1.2 (Note 3), hereinafter referred to as "a publication, etc."), both of the compounds, etc. and the medicinal use need to be described (or equivalent to be described) therein.

Unless the compound, etc. of the claimed medicinal invention is provided in the publication, etc. in a way that it is evident that a person skilled in the art can manufacture or obtain it based on the description of the publication, etc. and the common general technical knowledge as of the filing, it shall not be recognized that the medicinal invention is described in the publication, etc.

Also, unless the compound, etc. of the claimed medicinal invention is provided in the publication, etc. in a way that it is evident that a person skilled in the art can use it based on the description of the publication, etc. and the common general technical knowledge as of the filing, it shall not be recognized that the medicinal invention is described in the publication, etc. concerned (see Examination Guidelines, Part III, Chapter 2, Section 3 Procedure of Determining Novelty and Inventive Step, 3.1.1.(1)b).

For example, if a medicinal use is merely listed without any support in the

publication, etc. it shall not be recognized that the compound, etc. is provided in the publication, etc. in a way that it is evident that a person skilled in the art can use it for the medicinal use. Accordingly, it shall not be recognized that the medicinal invention is described in the publication, etc.

(3) Determination of novelty

Determination of novelty relating to medicinal inventions is carried out according to Examination Guidelines, Part III, Chapter 2, Section 1 Novelty, 2. Determination of Novelty and in this chapter, 2,2,1 Basic Principles of Determination of Novelty related to Medicinal Inventions, and is determined by the following (3-1) and (3-2)."

Hereinafter, "a cited invention" means a cited invention as provided in Article 29(1)

(3-1) Regarding the compound, etc. having a specific attribute

When the compound, etc. having a specific attribute of the claimed medicinal invention differs from the compound, etc. of a cited invention, the claimed medicinal invention involves novelty.

(3-2) Regarding the medicinal use based on a specific attribute

(3-2-1) Application to a specific disease

Even if the compound, etc. of the claimed medicinal invention does not differ from the compound, etc. of a cited invention, the claimed medicinal invention involves novelty when the claimed medicinal invention and the cited invention differ in medicinal use of applying to a specific disease based on the attribute of such compound, etc. (Cases 1 and 2).

For example, when the claimed invention is "a medicine for disease Z comprising an active ingredient A," and a cited invention is " a medicine for disease X comprising an active ingredient A," the claimed medicinal invention involves novelty if it becomes evident that disease X and disease Z are different diseases in the light of the common general technical knowledge as of the filing.

The determination of novelty relating to medicinal inventions is carried out as follows

(a) Even if the medicinal use of the claimed medicinal invention and the medicinal use of the cited invention are different in expression, novelty of the claimed medicinal

invention shall be denied when the medicinal use is determined corresponding to (i) or (ii) below in the light of the common general technical knowledge as of the filing;

(i) when the medicinal use can be derived from a working mechanism thereof;

(ii) when the medicinal use inevitably results from a closely related pharmacological effect.

[Examples of (i) above]

(Cited invention) Bronchodilator

→ (Claimed medicinal invention) Antiasthmatic

(Cited invention) Vasodilator

→ (Claimed medicinal invention) Antihypertensive

(Cited invention) Coronary vasodilator

→ (Claimed medicinal invention) Therapeutic agent for angina

(Cited invention) Histamine release inhibitor

→ (Claimed medicinal invention) Antiallergic agent

(Cited invention) Histamine H-2 receptor antagonist

→ (Claimed medicinal invention) Therapeutic agent for gastric ulcer

[Examples of (ii) above]

(Cited invention) Cardiotonic

→ (Claimed medicinal invention) Diuretic

(Cited invention) Antiinflammatory

→ (Claimed medicinal invention) Analgesic

(Note) It is known in the field of medical treatment that there are certain compounds etc. having two or more medicinal uses inevitably. However, in the examples listed under (ii) above, it is also well known that all the compounds etc. having a first medicinal use coming under (ii) above do not have necessarily a second medicinal use. Accordingly, when the novelty of the claimed medicinal invention in such a case is considered, it is necessary to consider the common general technical knowledge as of the filing regarding the structure-activity correlation or the like of the compounds etc.

(b) When the medicinal use of the cited invention is expressed in a more specific concept of the medicinal use of the claimed medicinal invention, novelty of the claimed medicinal invention shall be denied.

[Examples]

(Cited invention) Antipsychotic

→ (Claimed medicinal invention) Agent acting on the central nervous system

(Cited invention) Therapeutic agent for lung cancer

→ (Claimed medicinal invention) Anticancer agent

(c) When the medicinal use of the cited invention is expressed as a generic concept of the medicinal use of the claimed medicinal invention, and the medicinal use of the claimed medicinal invention expressed as a more specific concept can be derived from the medicinal use of the cited invention based on the common general technical knowledge as of the filing, novelty of the claimed medicinal invention shall be denied.

(Note) A medicinal use expressed in a more specific concept cannot be derived only because a medicinal use expressed in a more specific concept is included in a medicinal use expressed in a generic concept or the medicinal use expressed in the more specific concept can be listed from a medicinal use expressed in a generic concept.

(d) When the medicinal use of the claimed medicinal invention is merely expressed as a newly discovered working mechanism in place of the medicinal use of the cited invention, and both medicinal uses are substantially indistinguishable, novelty of the claimed medicinal invention shall be denied.

[Example]

(Cited invention) antimicrobial

→ (Claimed medicinal invention) Inhibitor of bacterial cell membrane formation

(e) When there is no difference in component constitutions and medicinal use between the claimed medicinal invention and the cited invention, and a component contained in the claimed medicinal invention is expressed by merely defining the working mechanism of a part of the components of the cited invention by way of its use, novelty of the claimed medicinal invention shall be denied.

[Example]

(Cited invention) Dermal antiinflammatory analgesic comprising indomethacin and capsicum extract

→ (Claimed medicinal invention) Dermal antiinflammatory analgesic comprising indomethacin and capsicum extract, wherein the long-term stability improving agent is contained for indomethacin

(Note) As the component constitutions of the composition are the same, it is obvious that the components contained in the dermal antiinflammatory analgesic of both inventions perform the same working effect despite the subjective object for adding. Accordingly, even if the capsicum extract is defined as a stabilizer for improving long-term stability of the indomethacin, this cannot make the invention different from the invention described in the publication

(3-2-2) Application to a specific disease in which dosage or administration is specified

Even if the compounds etc. of the claimed medicinal invention do not differ from those of the cited invention, and there is also no difference in disease to which the invention is applied, the claimed medicinal invention involves novelty when there is a difference between the claimed medicinal invention and the cited invention in medicinal use in which the invention is applied to the specific disease in a specific dosage or administration based on the attribute of the compounds etc. thereof (Cases 3 to 5).

2.3 Inventive Step (Article 29(2))

2.3.1 Determination Method for Inventive Step relating to Medicinal Inventions

(1) Identification of the claimed medicinal invention

The claimed invention shall be identified in a similar manner as done in 2.2.2(1).

(2) Identification of an invention described in a publication, etc.

An invention described in a publication, etc. shall be identified in a similar manner as done in 2.2.2(2).

(3) Determination of inventive step

Determination of inventive step relating to medicinal inventions is carried out according to Examination Guidelines, Part III, Chapter 2, Section 2. Inventive Step.

2.3.2 Specific Examples of Determination of Inventive Step

When more than one of the following points of view can be applied, the determination shall be made from each of those points of view.

(1) Relevance between the medicinal use and the working mechanism

Even if the medicinal use of the claimed medicinal invention differs from that of the cited invention, when the relevance of the working mechanism between the two inventions can be derived from the state of the art as of the filing, an inventive step of the claimed medicinal invention shall usually be denied, unless there is another circumstance, such as a favorable effect, to affirm an inventive step.

(2) Diversion from a non-human veterinary use to a medicinal use to a human body

As for the claimed medicinal invention, in which a non-human, veterinary use of the compound, etc. in the cited invention for a similar or closely related disease is merely diverted to a medicinal use to a human body, even if the diversion concerned is not suggested in what is described in the cited invention, an inventive step of the claimed medicinal invention shall usually be denied, unless there is another circumstance, such as a favorable effect of the claimed medicinal invention, to affirm an inventive step.

Diversion from the medicinal use to a human body to a non-human veterinary use works the same way as well.

(3) A drug in which two or more medicinal components are combined

Optimizing the combination of two or more medicinal components in order to solve the problem well known to a person skilled in the art, such as to increase a drug effect or to reduce a side effect, is an exercise of ordinary creativity of a person skilled in the art. Hence, when the claimed medicinal invention is a mere combination of two or more publicly known medicinal components in order to solve the above problem, an inventive step of the claimed medicinal invention shall usually be denied.

For example, when the combination is the following (a) to (c), etc., an inventive step of the claimed medicinal invention shall usually be denied due to publicly known medicinal components (Cases 7 to 10):

(a) A combination of publicly known components having the same primary action;

(b) A combination with a publicly known secondary component by which a problem associated with the efficacy of a publicly known primary component can be overcome (for example, a combination of a primary component publicly known to have a side effect, and a secondary component publicly known to reduce such side

effect);

(c) A combination of components, each of which is publicly known to be therapeutically effective for any of various symptoms caused by the primary disease.

However, when there is another way to inferring the inventive step, such as, a favorable effect compared with each effect of the above publicly known medicinal components being remarkable by surpassing the extent that can be predicted from the state of the art as of the filing, the claimed medicinal invention involves an inventive step (Case 6).

A drug in which two or more medicinal components are combined can be expected to be claimed as "combination drug for the treatment of…," "composition for the treatment of…," "…medicine characterized in that … and …are combined," etc., there is no fundamental difference in any of the cases as the method of judgment.

(4) A drug characterized by the medicinal use in which the drug is applied to a specific disease by a specific dosage or administration

Optimizing a dosage or an administration in order to solve the problem well known to a person skilled in the art, such as to increase a drug effect, to reduce a side effect, or to improve compliance, is an exercise of ordinary creativity of a person skilled in the art. Hence, even if the claimed medicinal invention and cited invention are different in dosage or administration, for which the claimed medicinal invention is novel, while they are not different in disease to which the invention is applied, an inventive step of the claimed medicinal invention shall usually be denied when a favorable effect compared with the cited invention falls within the extent that can be predicted by a person skilled in the art (Case 5).

However, when there is another way to inferring the inventive step, such as, a favorable effect compared with the cited invention being remarkable by surpassing the extent that can be predicted from the state of the art as of the filing, the claimed medicinal invention involves an inventive step (Cases 3 and 4).

3. Cases

This chapter explains the application of examination on medicinal inventions, on the basis of specific cases.

(Points to note)

These cases are prepared for the purpose of explaining the application of examination on medicinal inventions. Therefore, it should be noted that the statement of claims, etc. in these cases are modified, e.g., simplified, to make the explanation of the medicinal invention more readily. Additionally, it should be noted that the absence of reasons for refusal other than those reasons for refusal being discussed in each case is not implied.

3.1 Cases relating to Determination of Novelty and Inventive Step

3.1.1 A therapeutic agent characterized by its medicinal use in which the drug is applied to a specific disease

[Case 1] An active ingredient is publicly known, and a medicinal use is novel.

Title of the invention

Therapeutic agent for Alzheimer's disease

The Claims

[Claim 1]

A therapeutic agent for Alzheimer's disease, comprising a compound A as an active ingredient.

Overview of the description

In this invention, the compound A that was known as an active ingredient in an antimicrobial agent has been found to reversibly inhibit acetylcholine esterase to suppress the degradation of acetylcholine.

In the working example, the results of pharmacological study are described to show that the compound A has a remarkable inhibitory activity on acetylcholine esterase and that the compound A reduced symptoms of Alzheimer's disease.

[Results of the prior art searches]

Although the compound A is already known as an active ingredient in an antimicrobial agent, no therapeutic agent for Alzheimer's disease having the compound A as an active ingredient therein is described in any prior art document. In addition, neither the existence of a structural similarity between the compound A and a compound having an inhibitory activity on acetylcholine esterase, nor the relevance of the mechanism of action of the compound A in an antimicrobial agent with the treatment of Alzheimer's disease have been revealed or suggested in any prior art document.

[Overview of reason for refusal]

None.

[Explanation]

It is evident that the medicinal use of the compound A (to treat Alzheimer's disease) is different from the medicinal use conventionally known (antimicrobial), and therefore, the medicinal invention of Claim 1 is a novel invention.

Moreover, there is no prior art document that provides a motivation to apply the compound A to treat Alzheimer's disease, such as the structural similarity between the compound A and a compound having an inhibitory activity on acetylcholine esterase, or the relevance of the mechanism of action of the compound A in an antimicrobial agent with the treatment of Alzheimer's disease, and therefore, the medicinal invention of Claim 1 involves an inventive step.

[Case 2] A tissue-derived biomaterial such as cells is publicly known, and a medicinal use is novel.

Title of the invention

Graft material to treat myocardial infarction

The Claims

[Claim 1]

A graft material to treat myocardial infarction comprising a cell sheet made of cells A.

Overview of the description

In this invention, it has been found that the cardiac function is recovered by implanting a cell sheet made of cells A to a site of myocardial infarction.

In the working example, the results of pharmacological study are described to show that the cardiac function is recovered and symptoms of myocardial infarction are reduced by implanting such cell sheet to the site of myocardial infarction in rats of a myocardial infarction model.

[Results of the prior art searches]

It is publicly known that the cells A are used to make a cell sheet, which is used as a graft material. However, no prior art document describes or suggests the implantation of such cell sheet to the site of myocardial infarction or the reduction of symptoms of myocardial infarction by such implantation.

Moreover, it is not possible to predict the recovery of the cardiac function or the reduction of symptoms of myocardial infarction by implanting the cells A from the state of the art as of the filing.

[Overview of reason for refusal]

None

[Explanation]

The medicinal use of the cell sheet made of the cells A (to treat myocardial infarction) is different from the medicinal use conventionally known, and therefore, the medicinal invention of Claim 1 is a novel invention.

Moreover, there is no prior art document publicly known that provides a

motivation to apply the cell sheet made of the cells A to treat myocardial infarction, such as the relevance of the cells A with the recovery of the cardiac function, and therefore, the medicinal invention of Claim 1 involves an inventive step.

[Remarks]

When, however, the claimed invention is the cells with a limited use, such as "The cells A to treat myocardial infarction", those cells are interpreted as the cells themselves, not having a limited use, because such limited use, in general, merely indicates the utility of the cells. Therefore, in this case, "the cells A to treat myocardial infarction" and the publicly known "cells A" that do not have a limited use shall not be recognized as different cells (see Examination Guidelines, Part III, Chapter 2, Section 4, 3. Expression Specifying the Product by its Use Application).

3.1.2 A therapeutic agent characterized by its medicinal use in which the drug is applied to a specific disease in a specific dosage or administration

[Case 3] A therapeutic agent which shows a remarkable effect by applying to a specific disease in a specific dosage or administration

Title of the invention

Antiasthmatic agent

The Claims

[Claim 1]

comprising the compound A characterized in that the compound A is administered in an amount of 30 to 40 μg/kg of body weight orally once every three months to a human.

[Overview of the description]

It has been known that the symptoms of asthma are reduced by administering the compound A in an amount of 1 μg/kg of body weight per day to an asthmatic patient orally every day. However, the reduction of the symptoms was provided only while the compound A was administered, and once the administration was discontinued, the symptoms recurred, and thus, the continuous daily administration of the compound A was required. Moreover, it was suggested that when the compound A was administered in an amount of 1 μg/kg of body weight per day orally every day, the side effect B frequently occurred.

In this invention, it has been found that, by administering the compound A in an amount of 30 to 40 μg/kg of body weight orally once every three months to an asthmatic patient, the symptoms of asthma are reduced for a long period of time, and also the occurrence rate of the side effect B is lower than that previously seen.

In the working example, the results of pharmacological study were described: when a single dose of the compound A was orally administered to each of the groups of asthmatic patients (body weight: 30 kg to 90 kg), in amount of 30 μg/kg of body weight, 35 μg/kg of body weight, and 40 μg/kg of body weight, respectively, the symptoms of asthma were reduced at least for three months in all treatment groups; no apparent difference in efficacy by body weight was also noted; and moreover, few occurrences of the side effect B were noted in all treatment groups in this study, the frequency of which was significantly lower than the frequency of the side effect B developed when the

compound A was conventionally administered in an amount of 1 μg/kg of body weight per day orally every day.

[Results of the prior art searches]

It is publicly known that the symptoms of asthma are reduced by administering the compound A in an amount of 1 μg/kg of body weight to an asthmatic patient orally every day and that the side effect B frequently occurs by such administration. However, no prior art document describes or suggests the administration of the compound A in an amount of 30 to 40 μg/kg of body weight orally once every three months.

Moreover, it is not possible to predict from the state of the art as of the filing that the symptoms of asthma would be reduced for at least three months by the oral single administration of the compound A in an amount of 30 to 40 μg/kg of body weight and that the occurrence rate of the side effect B would be lowered compared to the prior art.

[Overview of reason for refusal]

None

[Explanation]

In terms of dosage or administration of the compound A in the treatment of asthma, the dosage or administration of the claimed invention is different from the dosage or administration conventionally known, and therefore, the medicinal invention of Claim 1 is a novel invention.

Moreover, the reduction of the symptoms of asthma for at least three months and also the occurrence rate of the side effect B significantly lower than that developed by the daily oral administration of the compound A in an amount of 1 μg/kg of body weight per day are afforded by the single administration of the compound A in an amount of 30 to 40 μg/kg of body weight to an asthmatic patient, and are remarkable effects surpassing the extent predictable from the state of the art, and therefore, the medicinal invention of Claim 1 involves an inventive step.

[Case 4] A therapeutic agent which shows a remarkable effect by applying to a specific disease in a specific dosage or administration

Title of the invention

Therapeutic agent for ovarian cancer

The Claims

[Claim 1]

A therapeutic agent for ovarian cancer comprising the compound A as an active ingredient characterized in that the compound A is administered in an amount of 100 to 120 μg/kg of body weight per administration to the specific site Z in the brain in a human.

[Overview of the description]

The compound A has been known to have an effect of growth suppression on ovarian cancer when administered intravenously to a human, but has also been known to have hepatotoxicity as a side effect.

In this invention, it has been found that the blood concentration of the hormone Y secreted from the pituitary gland changes by the administration of the compound A to the specific site Z in the brain in a human, and as a result, the ovarian cancer significantly reduces in size compared to the treatment by the conventional intravenous administration.

In the working example, the results of pharmacological study are described to show that the blood concentration of the hormone Y secreted from the pituitary gland changes by the administration of the compound A to the specific site Z in the brain in a human, and as result, the ovarian cancer further reduces in size compared to the treatment by the conventional intravenous administration. Other results of pharmacological study are also described to show that when administered to the specific site Z in the brain, the compound A does not move to the liver, and thus has no hepatotoxicity.

[Results of the prior art searches]

It is publicly known that the compound A has an effect of growth suppression on ovarian cancer when administered intravenously to a human and has a side effect of hepatotoxicity. However, no prior art document describes or suggests that the compound A intravenously administered moves into the brain through the blood-brain barrier and that the ovarian cancer further reduces in size by the administration of the compound A to the specific site Z in the brain in a human compared to the intravenous administration.

Moreover, it is not possible to predict that the reduction in size of the ovarian

cancer would be provided without a side effect of hepatotoxicity by the administration of the compound A to the specific site Z in the brain in a human from the state of the art as of the filing.

[Overview of reason for refusal]
None

[Explanation]

In terms of dosage or administration of the compound A in the treatment of ovarian cancer, the dosage or administration of the claimed invention (the administration to the specific site Z in the brain) is different from the dosage or administration conventionally known (intravenous administration), and therefore, the medicinal invention of Claim 1 is a novel invention.

Moreover, no development of the side effect of hepatotoxicity and also the further reduction in size of the ovarian cancer compared to the treatment by the intravenous administration are afforded by the administration of the compound A to the specific site Z in the brain, and are remarkable effects surpassing the extent predictable from the state of the art, and therefore, the medicinal invention of Claim 1 involves an inventive step.

[Case 5] A therapeutic agent which is applying to a specific disease in a specific dosage or administration

Title of the invention

Antitussive agent

The Claims

[Claim 1]

An antitussive agent comprising the compound A characterized in that the compound A is administered in an amount of 400 to 450 μg/kg of body weight per administration orally once a day to a human.

[Overview of the description]

It was known that an antitussive effect was provided by administering the compound A in an amount of 160 μg/kg of body weight per administration orally three times a day to a human. In contrast, it has been found that the administration of the compound A in an amount of 400 to 450 μg/kg of body weight per administration orally once a day to a human provides an antitussive effect better than that previously provided in this invention.

In the working example, the results of pharmacological study are described to show that an antitussive effect is increased by the administration of the compound A in an amount of 400 μg/kg of body weight per administration orally once a day to a patient compared to the administration of the compound A in an amount of 160 μg/kg of body weight per administration orally three times a day. It is described that compliance is also improved because of the decreased frequency of administration per day.

[Results of the prior art searches]

It is publicly known that an antitussive effect is provided by administering the compound A in an amount of 160 μg/kg of body weight per administration orally three times a day. Moreover, the level of the increase in antitussive effect and compliance described in the description of the claimed invention falls within the extent predictable from the state of the art as of the filing.

[Overview of reason for refusal]

It is publicly known that an antitussive agent, the active ingredient of which is the compound A, is orally administered. In general, making dosage or administration of a

drug preferred in order to solve a problem well known to a person skilled in the art, such as to increase a drug effect or to improve compliance, is an exercise of ordinary creativity of a person skilled in the art, and thus, the determination of the preferred dosage or administration of the compound A can be readily done with experiments by a person skilled in the art.

Moreover, a person skilled in the art would commonly predict that a drug effect or compliance can be increased by making dosage or administration preferred, and in the claimed invention, the level of the increase thereof cannot be recognized to be remarkable surpassing the extent predictable from the state of the art as of the filing.

[Measures of the applicant]

In general, the reasons for refusal above shall not be overcome.

[Remarks]

To what level the effect is "remarkably surpassing the extent predictable from the state of the art as of the filing" shall be determined on a case-by-case basis in consideration of what is disclosed in the description of the claimed invention, the results of prior art search, the common general knowledge as of the filing, and the like.

3.1.3 A therapeutic agent characterized by a combination of materials having specific attributes

[Case 6] A therapeutic agent which shows a remarkable effect by a combination of active ingredients

Title of the invention

Composition to treat diabetes

The Claims

[Claim 1]

A composition to treat diabetes comprising a compound A and a compound B in a ratio of 5:1 to 4:1 by weight

[Overview of the description]

In this invention, it has been found that the use of the combination of the compound A and the compound B in a specific ratio provides a reduction of side effects, such as body weight gain, which were seen with use of the compound A alone.

In the working example, the results of pharmacological study are described to show that the use of the combination of the compound A and the compound B in a specific ratio provides the reduction of the side effects.

[Results of the prior art searches]

It is publicly known that each of the compound A and the compound B is used to treat diabetes. However, no prior art document describes a medicinal composition to treat diabetes in which the compound A and the compound B are combined. Moreover, from the state of the art as of the filing, it is not possible to predict that the side effects such as body weight gain would be reduced with the use of a combination of the compound A and the compound B in a specific ratio.

[Overview of reason for refusal]

None

[Explanation]

The results of pharmacological study, etc. demonstrate that the use of the combination of the compound A and the compound B in a specific ratio provides the

effect in reducing the side effects, which surpasses the extent predictable from the state of the art as of the filing, and therefore, the invention of Claim 1 involves an inventive step.

[Case 7] A combination of components those having the same primary action publicly known

Title of the invention

Liquid agent to regulate intestinal functions

The Claims

[Claim 1]

A liquid agent to regulate intestinal functions characterized by comprising 1 g to 30 g of a dietary fiber and 1 x 106 to 1 x 108 of the bacteria YY.

[Overview of the description]

In this invention, a dietary fiber and the bacteria YY, each of which regulates intestinal functions, are combined to make an agent having the enhanced regulation of intestinal functions. Additionally, in the description, the results of pharmacological study are provided in which the agent to regulate intestinal functions having this combination was used. However, no results of the pharmacological study with the dietary fiber alone or the bacteria YY alone are provided.

[Results of the prior art searches]

It is publicly known that when the dietary fiber is given in an amount of 1 g to 30 g or the bacteria YY is given in an amount of 1 x 106 to 1 x 108, intestinal functions are regulated. It is also publicly known that such bacteria and a dietary fiber are made to co-exist in order to maintain in the body the bacterial action of regulating intestinal functions to enhance the regulation of intestinal functions.

[Overview of reason for refusal]

It is publicly known that when the dietary fiber is given in an amount of 1 g to 30 g or the bacteria YY is given in an amount of 1 x 106 to 1 x 108, intestinal functions are regulated. It is also publicly known that such bacteria and a dietary fiber are made to co-exist in order to maintain in the body the bacterial action of regulating intestinal functions to enhance the regulation of intestinal functions. Hence, combining 1 x 106 to 1 x 108 of the bacteria YY that regulates intestinal functions and 1g to 30g of a dietary fiber that also regulates intestinal functions to prepare an agent for regulating intestinal functions could be readily done by a person skilled in the art. Moreover, during such preparation, making an agent in a liquid formulation for such as the ease of

administration can be done by a person skilled in the art, if necessary. Yet it is not possible to make the efficacy of such agent notable.

[Measures of the applicant]

In this example, in the description, the results of pharmacological study with the agent of the claimed invention to regulate intestinal functions, in which the dietary fiber and the bacteria YY are combined, are provided, and also the enhanced regulation of intestinal functions is described. Therefore, in a written opinion, etc., the applicant, while showing the results of the experiments in which either of the dietary fiber and the bacteria YY alone is given as described in the cited inventions, is allowed to assert and demonstrate that the agent to regulate intestinal functions, in which the dietary fiber and the bacteria YY are combined, affords a more favorable effect than that provided by the cited inventions. However, unless such effect surpasses the extent predictable from the state of the art as of the filing, the reasons for refusal shall be preserved.

[Case 8] A combination of a primary component publicly known to have a side effect and a secondary component publicly known to suppress such side effect

Title of the invention

Agent to treat paclitaxel responsive tumor

The Claims

[Claim 1]

An agent to treat paclitaxel responsive tumor comprising paclitaxel in combination with an effective amount of the compound X to suppress vomiting caused by the administration of paclitaxel.

[Overview of the description]

In this invention, it has been found that when paclitaxel is used in combination with the compound X, a paclitaxel responsive tumor can be treated while the side effect of vomiting upon the administration of paclitaxel is suppressed.

In the working example, the results of pharmacological study are described to show that the use of paclitaxel in combination with the compound X suppresses the side effect.

[Results of the prior art searches]

It is publicly known that paclitaxel is a remarkable antitumor agent, but because vomiting occurs as a side effect upon its administration, paclitaxel is used in combination with a secondary component to suppress vomiting. On the other hand, the compound X is generally well known to suppress vomiting. In addition, the effect to suppress vomiting described in the description of the claimed invention falls within the extent predictable from the state of the art as of the filing.

[Overview of reason for refusal]

Paclitaxel is known to be used in combination with a secondary component to suppress the side effect of vomiting caused by the administration of paclitaxel, and the compound X is also generally well known as a component to suppress vomiting. Hence, in order to suppress the side effect of vomiting caused by the administration of paclitaxel, its use in combination with the compound X can be readily assumed by a person skilled in the art. Yet a notable effect more than expected has not been provided by such use.

[Measures of the applicant]

In general, the reasons for refusal above shall not be overcome.

[Case 9] A combination of a publicly known primary component with a publicly known secondary component by which the problem related to the efficacy of the primary component can be solved.

Title of the invention

Combination preparation of antiinflammatory and analgesic agents

The Claims

[Claim 1]

A combination preparation of antiinflammatory and analgesic agents comprising the compound X and compound Y added thereto at 1 to 100 weight parts and 0.2 to 20 weight parts, respectively, based on 100 weight parts of a total amount of diclofenac or its salt and acetaminophen.

[Overview of the description]

In this invention, it has been shown that in a combination preparation of antiinflammatory and analgesic agents comprising a combination of diclofenac or its salt and acetaminophen, the addition thereto of the compound X and the compound Y can increase the pain threshold and in addition extend the duration of action when the analgesic action is tested.

In the working example, the results of pharmacological study are described to show that the above effects are provided by adding the compound X and the compound Y in a specific ratio to diclofenac or its salt and acetaminophen.

[Results of the prior art searches]

The combination preparation of an antiinflammatory and analgesic agents comprising a combination of diclofenac or its salt and acetaminophen is publicly known, and it is also known that the so-called ceiling effect is seen in these nonsteroidal antiinflammatory and analgesic drugs, in which an increase in dosing at a certain level or more no longer provides an increase in analgesic effects but only results in an increase in side effects.

In general, it is publicly known that the addition of the compound X and the compound Y to a nonsteroidal antiinflammatory and analgesic drug can increase the pain threshold as much as the claimed invention can and in addition can extend the duration of action as much as the claimed invention can when the analgesic action is tested.

[Overview of reason for refusal]

A nonsteroidal antiinflammatory and analgesic drug comprising a combination of diclofenac or its salt and acetaminophen is publicly known, and it is known that the addition of the compound X and the compound Y to a nonsteroidal antiinflammatory and analgesic drug can increase the pain threshold and extend the duration of action when the analgesic action is tested. Thus, in order to increase the pain threshold and extend the duration of action in a nonsteroidal antiinflammatory and analgesic drug comprising a combination of diclofenac or its salt and acetaminophen, addition of the compound X and the compound Y thereto could be readily devised by a person skilled in the art, and also it is recognized that the range of ratios of the components to add therein could be optimized with experiments by a person skilled in the art. Yet it is not possible to make its effect notable.

[Measures of the applicant]

In general, the reasons for refusal above shall not be overcome.

[Case 10] A combination of components, each of which is publicly known to have an effect, respectively, on any of various symptoms caused by the primary disease

Title of the invention

Therapeutic agent for AIDS

The Claims

[Claim 1]

A therapeutic agent for AIDS characterized by comprising a combination of azidothymidine (AZT), which is an anti-HIV agent, and a compound Z.

[Overview of the description]

In this invention, it has been shown that, in order to treat AIDS that develops following the HIV infection, the use of the combination of an anti-HIV agent AZT, and the compound Z, which is effective to treat pneumonia developed as an aspect of AIDS, is effective in suppressing the progress of HIV and in treating pneumonia.

[Results of the prior art searches]

It is publicly known that azidothymidine (AZT) can be used as a therapeutic agent for AIDS. It is also known that pneumonia develops as an aspect of AIDS. Moreover, the effects of suppressing the growth of HIV and treating pneumonia described in the description of the claimed invention falls within the extent predictable from the state of the art as of the filing.

[Overview of reason for refusal]

It is known that azidothymidine (AZT) is useful as a therapeutic agent for AIDS, and it is also known that pneumonia tends to develop as an aspect of AIDS. Moreover, the compound Z is commonly used to treat pneumonia.

Therefore, when an AIDS patient is treated, the intent of use of the combination of an anti-HIV agent AZT and the compound Z, for the purpose of treating pneumonia developed as an aspect of AIDS, while suppressing the growth of HIV, which is the cause of AIDS, is no more than ordinary creativity exercisable by a person skilled in the art. Moreover, the use of both agents in combination has not provided a notable effect more than expected.

[Measures of the applicant]

In general, the reasons for refusal above shall not be overcome.

3.2 Cases relating to Determination of Description Requirements

[Case 11]

Title of the invention

Antiasthmatic drug

The Claims

[Claim 1]

An antiasthmatic drug comprising the compound A as an active ingredient characterized in that the compound A is used by orally administering at a dose of from 10 μg/kg body weight to 100 μg/kg body weight once every three months to a human.

Overview of the description

Asthma is a chronic inflammatory disease in the respiratory tract, and requires routine administration of a therapeutic agent over a long period of time. The compound A is publicly known as an antiasthmatic drug, and usually administered orally at a dose of about 10 μg/kg body weight once a day. Since missing a dose of an antiasthmatic drug which needs to be taken every day over a long period of time increases the risk of asthmatic attacks, it has been desired to decrease the frequency of the administration as well as to suppress asthmatic symptoms. It has also been known that the chronic administration of the compound A may cause a side effect, the reduction of which has been desired. Then, it has been found that the compound A, even when administered at a dose of from 10 μg/kg body weight to 100 μg/kg body weight orally once every three months to a human, is also useful as an antiasthmatic drug.

In the working example, the results of pharmacological study are stated: when a single dose of the compound A was orally administered to each of the groups of asthmatic patients (body weight: from 30 kg to 90 kg) at a dose of 100 μg/kg body weight, the symptoms of asthma were reduced at least for three months in all treatment groups; and no side effect was reported during the study.

[Overview of reason for refusal]

• Article 36(4)(i) (Enablement Requirement) / Article 36(6)(i) (Support Requirement): Claim 1

The invention claimed in Claim 1 is an invention for an antiasthmatic drug comprising the compound A as an active ingredient, wherein the compound A is used at

a dose of from 10 μg/kg body weight to 100 μg/kg body weight administered orally once every three months to a human. On the other hand, an antiasthmatic drug is usually administered routinely so that asthmatic attacks can be continuously suppressed as long as it is taken. In this respect, the dosage and administration established for the compound A at the time of filing was to provide it as an oral antiasthmatic drug at a dose of about 10 μg/kg body weight once a day; however, the common general knowledge is that, when the frequency of the administration of a therapeutic agent which is administered once a day is decreased, such as, to once every three months, the dosage of the therapeutic agent is in general increased, and therefore, it is difficult to predict that the effect of the drug supposed to be administered once a day would be preserved by administering it at an interval of three months at a similar dosage to that administered once a day. In addition, the description discloses the therapeutic effect on asthma for three months provided by the oral administration of the compound A only at a dose of 100 μg/kg body weight.

Thus, it is compelled to doubt whether the compound A, even when administered at a lower dosage (e.g., only one tenth of "100 μg/kg body weight", i.e., "10 μg/kg body weight"), is therapeutically effective in asthma for three months, that is, could continuously suppress asthmatic attacks. Therefore, it cannot be strictly asserted that the invention claimed in Claim 1 can be used as an antiasthmatic drug administered orally at a dose of the compound A in the entire range of from 10 μg/kg body weight to 100 μg/kg body weight once three months to a human.

Consequently, the description is not stated in a clear and sufficient manner to enable a person skilled in the art to carry out the invention claimed in Claim 1.

Moreover, the problem to be solved by the invention claimed in Claim 1 is to provide an antiasthmatic drug characterized by the administration of the compound A by the above dosage and administration. However, as mentioned above, it is compelled to doubt whether the compound A, even when administered at a lower dose than that of 100 μg/kg body weight, is therapeutically effective in asthma for three months, that is, could continuously suppress asthmatic attacks.

Accordingly, the description cannot be interpreted as supporting, when the compound A is orally administered once three months to a human, the same therapeutic effect confirmed by its administration at a dose of 100 μg/kg body weight being afforded by its administration at a dose in the entire range of from 10 μg/kg body weight to 100 μg/kg body weight.

Therefore, the details provided in the description can be neither expanded nor

generalized to the scope of the invention claimed in Claim 1, and thus, the invention claimed in Claim 1 exceeds the extent of disclosure in the description.

[Measures of the applicant]

If the applicant sets forth the common general knowledge that, even when a dosage of the compound A is different by about tenfold, the therapeutic effect is not unexpected at all in this technical field and also submits a certificate of experimental results in which, for example, a symptom of asthma was shown to be reduced for three months when a single dose of 10 μg/kg body weight of the compound A was orally administered, then, the reasons for refusal would be overcome.

(Supplemental explanation)

In this Case, based on the common general knowledge that it is difficult to predict that the effect of the drug supposed to be administered once a day would be preserved by administering it at an interval of three months at a similar dosage, it is doubtful whether the antiasthmatic drug which is administered once a day is effective when orally administered at a dose of less than 100 μg/kg body weight once every three months. On the other hand, as for an active ingredient in a drug, it is also the common general knowledge that, in general, even when a dosage is different by about tenfold, total disappearance of the therapeutic effect cannot be always expected; and based on that, the effectiveness as a therapeutic agent even at a dose of from 10 μg/kg body weight to 100 μg/kg body weight may possibly be acknowledged.

Although which of these pieces of the common general knowledge was not known to be applicable, the applicant sets forth the latter common general knowledge and submits the certificate of experimental results, so that the applicability of the latter common general knowledge is validated. Thus, the reasons for refusal would be overcome.

It should be noted that this Case is the case where the lower and upper limits of the dosage is different by about tenfold and the working example of said upper limit of the dosage is described in the description, while the common general knowledge regarding a dosage different by about tenfold is set forth and the certificate of experimental results of said lower limit of a dosage is also submitted.

[Case 12]

Title of the invention

Therapeutic agent comprising an oligonucleotide

The Claims

[Claim 1]

A therapeutic agent comprising the oligonucleotide X consisting of a base sequence set forth in SEQ ID NO: 1 as an active ingredient, for tumors, ischemia, immunodeficiency, epilepsy, hyperlipidemia, hypertension, Parkinson's disease, baldness, hair loss, diabetes mellitus, muscular dystrophy, infections, acne, calculi or osteoporosis.

Overview of the description

Kinases, enzymes for protein phosphorylation, play a major role in signal transduction pathways in the body. Conventionally, it has been known that there are numerous types of kinases such as kinase A and kinase B.

Recently, the protein Y was discovered in the tumor model animals in which the expression of the protein Y was increased, and the analysis of the amino acid sequence thereof revealed that the protein Y was a novel protein comprising a kinase-like domain therein. Hence, it can be expected that the antisense oligonucleotide X consisting of a base sequence complementary to a part of the nucleic acid coding for the protein Y would suppress the expression of the protein Y, thereby, providing therapeutic effects on a wide variety of diseases in which kinases may be involved. Those diseases may include tumors, ischemia, immunodeficiency, epilepsy, hyperlipidemia, hypertension, Parkinson's disease, baldness, hair loss, diabetes mellitus, muscular dystrophy, infections, acne, calculi and osteoporosis.

In the working example, the results of pharmacological study are stated: when the oligonucleotide X was prepared and administered in the tumor model animals, the expression of the protein Y was suppressed, and the tumor size was reduced.
(Note: it is not confirmed whether or not the protein Y has a kinase activity.)

[Overview of reason for refusal]

• Article 36(4)(i) (Enablement Requirement) / Article 36(6)(i) (Support Requirement): Claim 1

It is stated in the description that the oligonucleotide X can provide therapeutic

effects on a wide variety of diseases in which kinases may be involved, via suppression of the expression of the protein Y comprising the kinase-like domain, and that said disease include tumors, ischemia, immunodeficiency, epilepsy, hyperlipidemia, hypertension, Parkinson's disease, baldness, hair loss, diabetes mellitus, muscular dystrophy, infections, acne, calculi and osteoporosis. However, the therapeutic effect of the oligonucleotide X was specifically confirmed only on tumors.

On the other hand, the common general knowledge at the time of filing was that it was difficult to predict a physiological activity of a protein only on the basis of its partial commonality among amino acid sequences and, thus, it could not be sufficiently evident that a protein would function as a protein kinase only because said protein comprised a kinase-like domain in its amino acid sequence. On top of that, kinases were known as enzymes for protein phosphorylation and responsible for various physiological effects via diverse signal transduction pathways in the body and it was known that there were numerous types of kinases such as kinase A and kinase B, each of those kinases providing a different activity in the respective signal transduction pathway in the body. Therefore, it was also the common general knowledge that an antisense nucleotide that inhibited a certain kinase could not be expected to globally provide therapeutic effects on a battery of diseases in which kinases might be involved. In this respect, in the description, the protein Y was not confirmed to actually have a kinase activity, and the relevance of the protein Y with the diseases excepting the tumors was not confirmed as well. Therefore, even when the common general knowledge at the time of filing is consulted, it cannot be recognized what types of diseases the oligonucleotide X with suppressing effect on the expression of such protein Y is useful for treating.

Accordingly, it is not evident from the description of the present application that the oligonucleotide X has therapeutic effects on the diseases excepting the tumors.

Consequently, the description is not stated in a clear and sufficient manner to enable a person skilled in the art to carry out the invention claimed in Claim 1.

Moreover, the problem to be solved by the invention claimed in Claim 1 is to provide a therapeutic agent comprising the oligonucleotide X as an active ingredient, to treat tumors, ischemia, immunodeficiency, epilepsy, hyperlipidemia, hypertension, Parkinson's disease, baldness, hair loss, diabetes mellitus, muscular dystrophy, infections, acne, calculi or osteoporosis. However, as mentioned above, it is not evident that the oligonucleotide X has therapeutic effects on the diseases excepting the tumors.

Accordingly, the details provided in the description can be neither expanded nor generalized to the scope of the invention claimed in Claim 1 which includes therapeutic agents even for the diseases excepting tumor, and thus, the invention claimed in Claim 1 is not the invention stated in the description.

[Measures of the applicant]

For example, it can be expected that the applicant amends the claims as shown below and submits a certificate of experimental results demonstrating the therapeutic effect of the oligonucleotide X on osteoporosis (e.g., an effect of the oligonucleotide X to increase the bone density);

[Claim 1]

A therapeutic agent comprising the oligonucleotide X consisting of a base sequence set forth in SEQ ID NO: 1 as an active ingredient, for tumors..

[Claim 2]

A therapeutic agent comprising the oligonucleotide X consisting of a base sequence set forth in SEQ ID NO: 1 as an active ingredient, for osteoporosis.

In this case, the reasons for refusal regarding Claim 1 would be overcome.

On the other hand, as for Claim 2, the above amendment may be made on the basis that the statement on osteoporosis exists literally in the claims or in the description. However, when the applicant does not set forth the common general knowledge or the like at the time of filing other than one that was taken into account by the examiner at all, but only submits the certificate of experimental results demonstrating the therapeutic effect of the oligonucleotide X on osteoporosis, then, the reasons for refusal would not be overcome in light of the common general knowledge at the time of filing and the extent of the description, as mentioned above.

[Case 13]

Title of the invention

A drug to treat tumors

The Claims

[Claim 1]

A drug to treat tumors comprising a keratan sulfate salt of an isoquinoline alkaloid selected from A, B or C as an active ingredient.

Overview of the description

A, B and C have isoquinoline backbone in their chemical structures and are publicly known as isoquinoline alkaloids. While A was known to be useful as a drug to treat tumors, it has been found that the therapeutic effect on tumors is enhanced by converting A into a keratan sulfate salt thereof.

In the working example, the results of pharmacological study are stated: keratan sulfate salts of A and B were prepared, and the enhanced therapeutic effect thereof on tumors compared to that of the hydrochloride salt of A was confirmed by using the cancer-bearing model animals.

[State of the art (cited inventions, well-known art, etc.)]

The literature X publicly known at the time of filing discloses that the hydrochloride salt of C showed no therapeutic effect on tumors in the study using the cancer-bearing model animals.

(Note: it is not known whether or not the hydrochloride salt of B has the therapeutic effect on tumors.)

[Overview of reason for refusal]

• Article 36(4)(i) (Enablement Requirement) / Article 36(6)(i) (Support Requirement): Claim 1

In Claim 1 of the present application, the drug to treat tumors comprising a keratan sulfate salt of isoquinoline alkaloids of A, B or C as an active ingredient is comprehensively stated. However, in the working example, it is only for the keratan sulfates salts of A and B that the therapeutic effect on tumors was confirmed.

On the other hand, the literature X publicly known at the time of filing discloses that the hydrochloride salt of C showed no therapeutic effect on tumors in the study

using the cancer-bearing model animals. Although the keratan sulfate salt of C is not disclosed in the literature X, since it is recognized as the common general knowledge that a physiological activity of a salt of a given compound could be similar to that of another salt of said compound, it could be rationally inferred that the keratan sulfate salt of C, similar to the hydrochloride salt thereof, had no therapeutic effect on tumors.

Accordingly, as for the invention claimed in Claim 1, it cannot be readily recognized that the embodiment using the keratan sulfate salt of C as an active ingredient can be used as a drug to treat tumors, and therefore, the description is not stated in a clear and sufficient manner to enable a person skilled in the art to carry out the invention claimed in Claim 1.

Moreover, the therapeutic effect on tumors disclosed in the description can be readily neither expanded nor generalized to the scope of the invention claimed in Claim 1 which comprises C as an option, and therefore, the invention claimed in Claim 1 exceeds the extent of disclosure in the description.

[Measures of the applicant]

If the applicant sets forth a common general knowledge that the same salts of compounds having a similar chemical structure could be similar in their physiological activity, argues that the keratin sulfate salt of C is not completely ineffective against tumor therapy even though the hydrochloride salt of C is ineffective against tumor therapy, based on said common general knowledge, and submits a certificate of experimental results to demonstrate that the keratan sulfate of C also has a similar therapeutic effect on tumors, then, the reason for refusal would be overcome.

(Supplemental explanation)

The examiner rationally infers that the keratan sulfate salt of C has no therapeutic effect on tumors based on the literature X and the common general knowledge that a physiological activity of a salt of a given compound could be similar to that of another salt of said compound. On the other hand, it is also the common general knowledge that the same salts of compounds having a similar chemical structure could be similar in their physiological activity, and therefore, the latter common general knowledge may possibly be applicable to the keratan sulfate salt of C.

Although which of these pieces of the common general knowledge was not known to be applicable, the applicant sets forth the latter common general knowledge and submits the certificate of experimental results demonstrating the therapeutic effect

of the keratin sulfate salt of C on tumors, so that the applicability of the latter common general knowledge is validated. Thus, the reasons for refusal would be overcome.