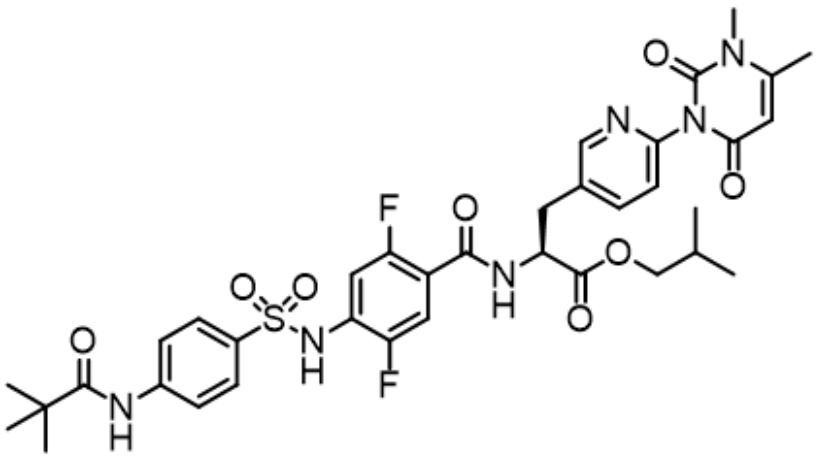
Publication No. 2021-169476, for tetrahydro-pyrazolopyrimidinone compounds in Published Japanese Translation of PCT International Application No. 2022-540780, and for ω3 polyunsaturated fatty acids in Japanese Patent Application Publication No. 2021-107433.

It has been reported that a sulfonamide derivative represented by the following formula (1), a pharmaceutically acceptable salt thereof, or an active metabolite thereof has an α4 integrin inhibiting action and is useful as a pharmaceutical agent for use in treating or preventing inflammatory bowel diseases and the like (International Publication No. WO2017/135472). However, findings regarding membrane permeability or absorbability of this compound, which has a molecular weight of 500 or more, have not been satisfactory.



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Summary

Problems to be solved

Even compounds having molecular weights of 500 or more have various physical properties such as solubility and membrane permeability, and it is not clear that using SEDDS can ameliorate the absorbability of a compound. In addition, it has not been clear what component may be combined with a compound to prepare SEDDS that can ameliorate solubility and membrane permeability.

Regarding the sulfonamide derivative represented by the above formula (1), a

pharmaceutically acceptable salt thereof, or an active metabolite thereof, the studies of the present inventors revealed that there is room for ameliorating a blood exposure amount in the case of simply orally administering a powder or a suspension of this compound. That is, a further improvement in membrane permeability and absorbability has been desired.

The present disclosure has been found out by the present inventors earnestly studying in view of such situations, and one of objects of the present disclosure is to provide a pharmaceutical composition comprising a sulfonamide derivative represented by a formula (1), a pharmaceutically acceptable salt thereof, or an active metabolite thereof, and having an improved absorbability at the time of oral administration.

The present inventors have conducted various studies in order to solve the above problems, and found that absorbability of the sulfonamide derivative represented by the formula (1), a pharmaceutically acceptable salt thereof, or an active metabolite thereof can be ameliorated by preparing a self-emulsifying composition comprising: the sulfonamide derivative represented by the formula (1), a pharmaceutically acceptable salt thereof, or an active metabolite thereof; and at least two solubilizers, thus completing the disclosure.

Non-limiting examples of the present disclosure provide the following technical ideas.

[1] A self-emulsifying composition comprising: a sulfonamide derivative represented by the following formula (1), a pharmaceutically acceptable salt thereof, or an active metabolite thereof; and at least two solubilizers

d-α-tocopherol PEG-1000 succinate.

[6] The self-emulsifying composition according to any one of the [2], [4], and [5], wherein

a content of the surfactant is 0.1 times or more relative to % by mass of the sulfonamide derivative represented by the formula (1) or a pharmaceutically acceptable salt thereof, and

a content of the auxiliary surfactant is 10 times or less relative to the sulfonamide derivative represented by the formula (1) or a pharmaceutically acceptable salt thereof.

[7] The self-emulsifying composition according to any one of the [2] and [4] to [6], wherein a ratio of the surfactant to the auxiliary surfactant is 1:1 to 1:8.

[8] The self-emulsifying composition according to any one of the [2] and [4] to [7], wherein the surfactant comprises propylene glycol monocaprylate.

[9] The self-emulsifying composition according to any one of the [2] and [4] to [8], wherein the auxiliary surfactant comprises polyoxyl 40 castor oil, polyoxyl 35 castor oil, or polyoxyethylene castor oil.

[10] The self-emulsifying composition according to any one of the [1] to [9], further comprising a cosolvent.

[11] A self-emulsifying drug delivery system in a form of a formulation suitable for oral administration, comprising the self-emulsifying composition according to any one of the [1] to [10].

[12] The self-emulsifying drug delivery system according to the [11], wherein the formulation is a capsule.

Moreover, as different examples of the present disclosure, the following technical ideas are also provided.

[2-1] A treatment agent or prevention agent for a disease, comprising a self-emulsifying composition comprising: a sulfonamide derivative represented by a formula (1), a pharmaceutically acceptable salt thereof, or an active metabolite thereof; and at least two solubilizers.

[2-2] The treatment agent or prevention agent according to the [2-1], wherein the

Crohn's disease.

[2-12] The self-emulsifying composition according to the [3], wherein the fatty acid or a derivative thereof is an amide ester of a fatty acid, an ester of a fatty acid and a hydroxy acid, a sugar ester or a sugar ester derivative of a fatty acid, an ester of a fatty acid and a propylene glycol, an ester of a fatty acid and a glycerol, an ester of a fatty acid and a polyglycerol, an ester of a fatty acid and an ethylene glycol, an ester of a fatty acid and a polyethylene glycol, or an ester of a fatty acid and a macrogol glycerin.

Furthermore, as different examples of the present disclosure, the following technical ideas are also provided.

[3-1] A self-emulsifying composition comprising: a sulfonamide derivative represented by a formula (1), a pharmaceutically acceptable salt thereof, or an active metabolite thereof; and at least two solubilizers, wherein a total content of the solubilizers is 10% by mass or more and 90% by mass or less relative to a total mass of the self-emulsifying composition.

[3-2] The self-emulsifying composition according to the [3-1], wherein the total content of the solubilizers is 20% by mass or more and 90% by mass or less relative to the total mass of the self-emulsifying composition.

[3-3] The self-emulsifying composition according to the [3-1], wherein the total content of the solubilizers is 30% by mass or more and 90% by mass or less relative to the total mass of the self-emulsifying composition.

[3-4] The self-emulsifying composition according to the [3-1], wherein the total content of the solubilizers is 40% by mass or more and 90% by mass or less relative to the total mass of the self-emulsifying composition.

[3-5] The self-emulsifying composition according to any one of the [3-1] to [3-4], wherein the solubilizers comprise at least one surfactant, and a content of the surfactant is 5% by mass or more and 85% by mass or less relative to the total mass of the self-emulsifying composition.

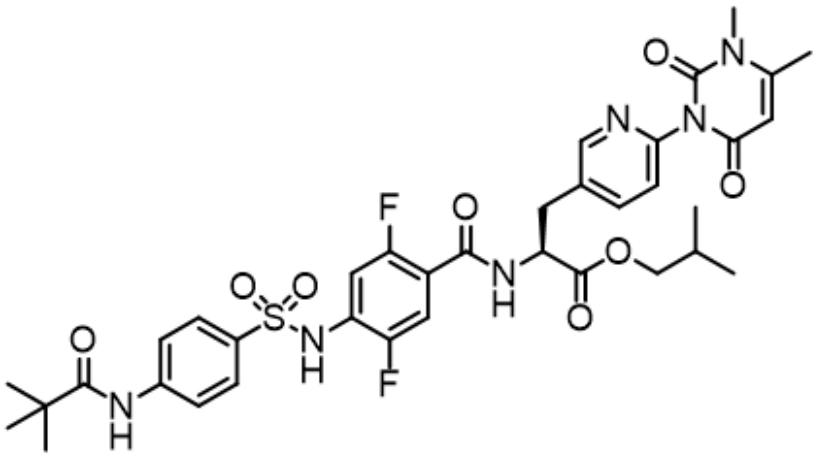
[3-6] The self-emulsifying composition according to any one of the [3-1] to [3-4], wherein the solubilizers comprise at least one surfactant, and a content of the surfactant is 10% by mass or more and 80% by mass or less relative to the total mass of the

[3-16] The self-emulsifying composition according to the [2] or [4], a mass ratio of the sulfonamide derivative represented by the formula (1) or a pharmaceutically acceptable salt thereof to the surfactant is 1:1 to 1:8.

[3-17] The self-emulsifying composition according to the [2] or [5], a mass ratio of the sulfonamide derivative represented by the formula (1) or a pharmaceutically acceptable salt thereof to the auxiliary surfactant is 1:1 to 1:8.

[3-18] A self-emulsifying composition comprising 10 to 1000 mg of a sulfonamide derivative represented by a formula (1), a pharmaceutically acceptable salt thereof, or an active metabolite thereof.

In an aspect of the present disclosure, there is provided a self-emulsifying composition comprising: a sulfonamide derivative represented by the following formula (1), a pharmaceutically acceptable salt thereof, or an active metabolite thereof; and at least two solubilizers



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In another aspect of the present disclosure, there is provided a self-emulsifying drug delivery system in a form of a formulation suitable for oral administration, comprising the self-emulsifying composition as disclosed herein.

By providing a self-emulsifying composition comprising at least two solubilizers in addition to the sulfonamide derivative represented by the formula (1), a pharmaceutically acceptable salt thereof, or an active metabolite thereof, the present disclosure is capable of ameliorating absorbability of this compound, a

pharmaceutically acceptable salt thereof, or an active metabolite thereof.

Brief Description of Drawings

Fig. 1 is a graph showing a correlation between logarithmic values (Tube method Log($AUC_{0\text{-}2.25}$)) of AUC of a Tube method and logarithmic values (rat PO/PK Log(AUC)) of AUC of blood plasma concentrations.

Fig. 2 is a graph showing a correlation between logarithmic values (Tube method Log($AUC_{0\text{-}2.25}$)) of AUC of the Tube method and dissolution rates (%) at pH 2.4.

Fig. 3 is a graph showing a correlation between logarithmic values (Tube method Log($AUC_{0\text{-}2.25}$)) of AUC of the Tube method and dissolution rates (%) at pH 6.4.

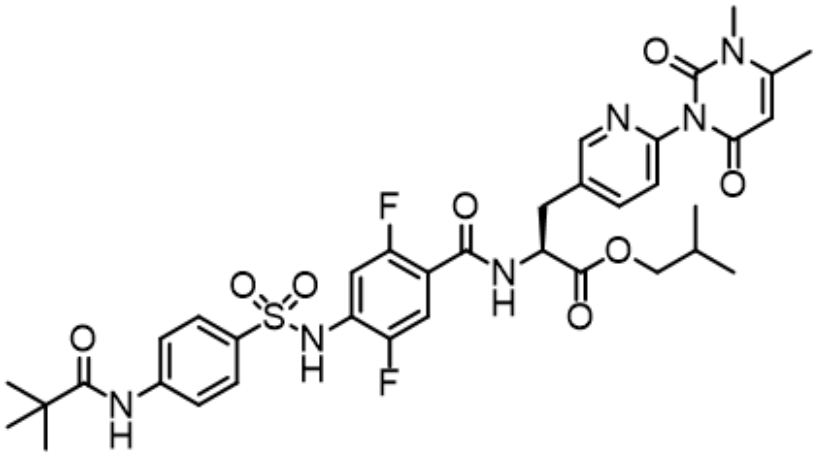
Description of Embodiments

Hereinafter, the present disclosure will be described in detail. Note that the embodiments described below are one aspects of the present disclosure and are not intended to limit the scope of the present disclosure.

What is claimed is:

Claim 1

A self-emulsifying composition comprising: a sulfonamide derivative represented by the following formula (1), a pharmaceutically acceptable salt thereof, or an active metabolite thereof; and at least two solubilizers



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Claim 2

The self-emulsifying composition according to claim 1, wherein the at least two solubilizers comprise at least one surfactant and at least one auxiliary surfactant.

Claim 3

The self-emulsifying composition according to claim 1, wherein the solubilizers comprise at least two selected from a cyclodextrin or a derivative thereof, bile acid or a derivative thereof, a fatty alcohol, a fatty acid or derivatives thereof, and a tocol derivative.

Claim 4

The self-emulsifying composition according to claim 2, wherein the surfactant comprises at least one selected from the group consisting of polyglyceryl-2 dioleate, polyglyceryl-3 dioleate, polyglyceryl-10 trioleate, propylene glycol monolaurate,

propylene glycol monocaprylate, glyceryl monocaprylate, glyceryl monolaurate, glyceryl dilaurate, and glyceryl monolinoleate.

Claim 5

The self-emulsifying composition according to claim 2, wherein the auxiliary surfactant comprises at least one selected from the group consisting of polyoxyl 40 castor oil, polyoxyl 35 castor oil, PEG-25 trioleate, PEG-60 corn glycerides, PEG-60 almond oil, PEG-40 palm kernel oil, PEG-50 castor oil, PEG-50 hydrogenated castor oil, PEG-60 hydrogenated castor oil, PEG-8 caprylic/capric glycerides, lauroyl polyoxyl-32 glycerides, linoleoyl polyoxyl-6 glycerides, oleoyl polyoxyl-6 glycerides, stearoyl polyoxyl-32 glycerides, PEG-6 caprylic/capric glycerides, polyglyceryl-10 monooleate, polyglyceryl-10 laurate, polyglyceryl-15 hydroxystearate, α-tocopherol PEG-400 succinate, α-tocopherol PEG-1000 succinate, dl-α-tocopherol PEG-1000 succinate, and d-α-tocopherol PEG-1000 succinate.

Claim 6

The self-emulsifying composition according to any one of claims 2, 4, and 5, wherein

a content of the surfactant is 0.1 times or more relative to % by mass of the sulfonamide derivative represented by the formula (1) or pharmaceutically acceptable salt thereof, and

a content of the auxiliary surfactant is 10 times or less relative to the sulfonamide derivative represented by the formula (1) or pharmaceutically acceptable salt thereof.

Claim 7

The self-emulsifying composition according to any one of claims 2, 4, and 5, wherein a ratio of the surfactant to the auxiliary surfactant is 1:1 to 1:8.

Claim 8

The self-emulsifying composition according to claim 2 or 4, wherein the surfactant comprises propylene glycol monocaprylate.

Claim 9

The self-emulsifying composition according to claim 2 or 5, wherein the auxiliary surfactant comprises polyoxyl 40 castor oil, polyoxyl 35 castor oil, or polyoxyethylene castor oil.

Claim 10

The self-emulsifying composition according to claim 1 or 2, further comprising a cosolvent.

Claim 11

A self-emulsifying drug delivery system in a form of a formulation suitable for oral administration, comprising the self-emulsifying composition according to claim 1 or 2.

Claim 12

The self-emulsifying drug delivery system according to claim 11, wherein the formulation is a capsule.