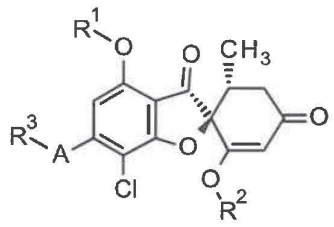
Statements of invention

[Claim 1]

A compound of general formula (1) or a pharmacologically acceptable salt thereof:

[Formula 1]



(1)

wherein the symbols in the formula are defined below:

R^1: a C1-C6 alkyl group or a hydroxyC1-C6 alkyl group,

R^2: a C1-C6 alkyl group,

A: a 5-membered aromatic heterocycle having bonds and having 1-4 atoms selected from the group consisting of a nitrogen atom, an oxygen atom and a sulfur atom, or an oxygen atom, and

R^3: if A is a 5-membered aromatic heterocycle having bonds and having 1-4 atoms selected from the group consisting of a nitrogen atom, an oxygen atom and a sulfur atom, then R^3 is a C1-C6 alkyl group, a hydroxyC1-C6 alkyl group or a C1-C6 alkoxyC1-C6 alkyl group; and if A is an oxygen atom, then R^3 is a hydroxyC1-C6 alkyl group or a C1-C6 alkoxyC1-C6 alkyl group.

[Claim 2]

A compound or a pharmacologically acceptable salt thereof according to Claim 1, wherein R^1 is a methyl group, an ethyl group or a hydroxyethyl group.

[Claim 3]

A compound or a pharmacologically acceptable salt thereof according to Claim 1 or 2, wherein R^2 is a methyl group.

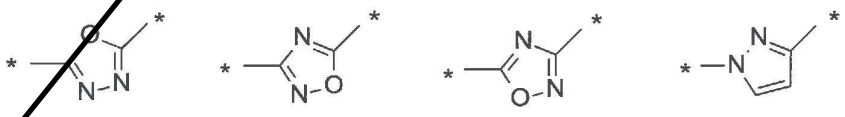
[Claim 4]

A compound or a pharmacologically acceptable salt thereof according to any one of Claims 1 to 3, wherein A is a 5-membered aromatic heterocycle having bonds and having 1-4 atoms selected from the group consisting of a nitrogen atom, an oxygen atom and a sulfur atom; and R^3 is a methyl group, an ethyl group, a hydroxyC1-C3 alkyl group or a methoxyC1-C3 alkyl group.

[Claim 5]

A compound or a pharmacologically acceptable salt thereof according to any one of Claims 1 to 4, wherein A is a 5-membered aromatic heterocycle having bonds selected from the following group:

[Formula 2]



wherein * represents a bond.

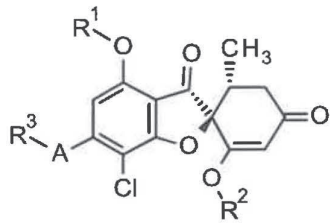
[Claim 6]

A compound or a pharmacologically acceptable salt thereof according to any one of Claims 1 to 3, wherein A is an oxygen atom.

[Claim 7]

A compound of general formula (1) or a pharmacologically acceptable salt thereof:

[Formula 3]



(1)

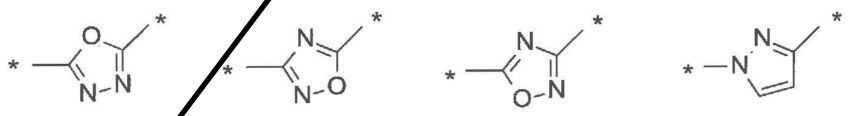
wherein the symbols in the formula are defined below:

R^1: a methyl group, an ethyl group or a hydroxyethyl group,

R^2: a methyl group,

A: a 5-membered aromatic heterocycle having bonds selected from the following group:

[Formula 4]



wherein * represents a bond, and

R^3: a methyl group, an ethyl group or a hydroxyC1-C3 alkyl group.

[Claim 8]

A compound or a pharmacologically acceptable salt thereof selected from the following group:

(2S,5'R)-7-chloro-6-(2-hydroxyethoxy)-3',4-dimethoxy-5'-methyl-spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione,

(2S,5'R)-7-chloro-3',4-dimethoxy-6-(2-methoxyethoxy)-5'-methyl-spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione,

(2S,5'R)-7-chloro-3',4-dimethoxy-5'-methyl-6-(1-methylpyrazol-3-yl)spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione,

(2S,5'R)-7-chloro-6-(1-ethylpyrazol-3-yl)-3',4-dimethoxy-5'-methyl-spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione,

(2S,5'R)-7-chloro-3',4-dimethoxy-5'-methyl-6-(5-methyl-1,3,4-oxadiazol-2-yl)spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione,

(2S,5'R)-7-chloro-3',4-dimethoxy-5'-methyl-6-(3-methyl-1,2,4-oxadiazol-5-yl)spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione,

(2S,5'R)-7-chloro-3',4-dimethoxy-5'-methyl-6-(5-methyl-1,2,4-oxadiazol-3-yl)spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione,

(2S,5'R)-7-chloro-6-[5-(1-hydroxy-1-methyl-ethyl)-1,3,4-oxadiazol-2-yl]-3',4-dimethoxy-5'-methyl-spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione,

(2S,5'R)-7-chloro-6-[5-[(1S)-1-hydroxyethyl]-1,3,4-oxadiazol-2-yl]-3',4-dimethoxy-5'-methyl-spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione,

(2S,5'R)-7-chloro-6-[5-[(1R)-1-hydroxyethyl]-1,3,4-oxadiazol-2-yl]-3',4-dimethoxy-5'-methyl-spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione,

(2S,5'R)-7-chloro-4-ethoxy-6-[5-(1-hydroxy-1-methyl-ethyl)-1,3,4-oxadiazol-2-yl]-3'-methoxy-5'-methyl-spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione,

(2S,5'R)-7-chloro-4-ethoxy-6-[5-[(1S)-1-hydroxyethyl]-1,3,4-oxadiazol-2-yl]-3'-methoxy-5'-methyl-spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione,

(2S,5'R)-7-chloro-6-[3-(1-hydroxyethyl)-1,2,4-oxadiazol-5-yl]-3',4-dimethoxy-5'-methyl-spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione,

(2S,5'R)-7-chloro-4-(2-hydroxyethoxy)-3'-methoxy-5'-methyl-6-(5-methyl-1,3,4-oxadiazol-2-yl)spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione,

(2S,5'R)-7-chloro-4-(2-hydroxyethoxy)-3'-methoxy-5'-methyl-6-(3-methyl-1,2,4-oxadiazol-5-yl)spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione, and

(2S,5'R)-7-chloro-4-(2-hydroxyethoxy)-3'-methoxy-5'-methyl-6-(5-methyl-1,2,4-oxadiazol-3-yl)spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione.

[Claim 9]

A pharmaceutical composition containing a compound or a pharmacologically acceptable salt thereof according to any one of Claims 1 to 8, as an active ingredient.

[Claim 10]

A pharmaceutical composition according to Claim 9, for preventing and/or treating an inflammatory disease. [Claim 11]

A pharmaceutical composition according to Claim 10, wherein the inflammatory disease is a disease selected from the group consisting of rheumatoid arthritis, systemic lupus erythematosus, scleroderma, bronchial asthma, asthmatic bronchitis, diffuse interstitial pneumonia, chronic obstructive pulmonary disease, ulcerative colitis, Crohn's disease, acute hepatitis, chronic hepatitis, fulminant hepatitis, autoimmune hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis, alcoholic hepatitis, non-alcoholic steatohepatitis, cirrhosis, peripheral neuritis, ankylosing spondylitis, eczema (acute, subacute, chronic), contact dermatitis, sunlight (ultraviolet light) dermatitis, radiation dermatitis, atopic dermatitis, seborrheic dermatitis, psoriasis vulgaris, arthropathic psoriasis, psoriatic erythroderma, pustular psoriasis, lichen planus, erythema, rosacea, urticaria, alopecia areata, pemphigus, erythroderma, acne vulgaris, pressure sore, wound, burn, conjunctivitis, keratitis, scleritis, acute/chronic otitis media, perennial allergic rhinitis, hay fever, sinusitis, laryngitis, esophagitis, refractory stomatitis, glossitis, acute/chronic salivary gland inflammation, angular cheilitis, cheilitis, Behcet's disease, multiple sclerosis, Type I diabetes, Type II

diabetes, atherosclerosis, pancreatitis and chronic heart failure.

[Claim 12]

A pharmaceutical composition according to Claim 10, wherein the inflammatory disease is a disease selected from the group consisting of rheumatoid arthritis, systemic lupus erythematosus, bronchial asthma, acute hepatitis, autoimmune hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis, alcoholic hepatitis, nonalcoholic steatohepatitis, ankylosing spondylitis, contact dermatitis, sunlight (UV) dermatitis, atopic dermatitis, seborrheic dermatitis, psoriasis vulgaris, arthropathic psoriasis, psoriatic erythroderma, pustular psoriasis, lichen planus, erythema, rosacea, alopecia areata, pemphigus, erythroderma, acne vulgaris, pressure sore, wound, burn, sinusitis, laryngitis, esophagitis, refractory stomatitis, glossitis, acute/chronic salivary gland inflammation, angular cheilitis, cheilitis and Behcet's disease.

[Claim 13]

A pharmaceutical composition according to Claim 10, wherein the inflammatory disease is a disease selected from the group consisting of rheumatoid arthritis, systemic lupus erythematosus, autoimmune hepatitis, alcoholic hepatitis, nonalcoholic steatohepatitis, ankylosing spondylitis, atopic dermatitis, psoriasis vulgaris, arthropathic psoriasis, psoriatic erythroderma,

pustular psoriasis, lichen planus, pressure sore, wound, refractory stomatitis, glossitis and Behcet's disease.

[Claim 14]

A compound or a pharmacologically acceptable salt thereof according to any one of Claims 1 to 8, for treating an inflammatory disease.

[Claim 15]

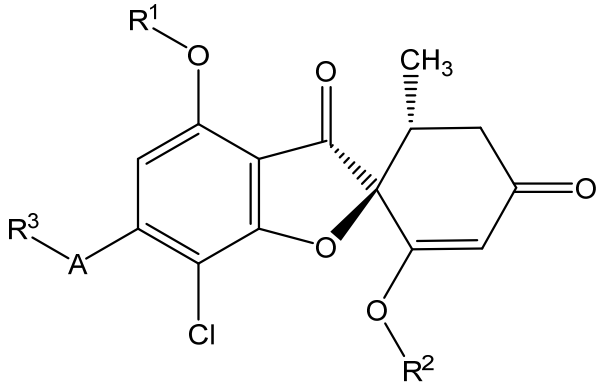
A method for administering an effective amount of a pharmaceutical composition according to Claim 9, for preventing and/or treating an inflammatory disease.

[Claim 16]

A TNF-α inhibitor containing a compound or a pharmacologically acceptable salt thereof according to any one of Claims 1 to 8, as an active ingredient.

CLAIMS

1. Use of a compound of general formula (1) or a pharmacologically acceptable salt thereof:



(1)

in the preparation of a medicament for the treatment of an inflammatory disease in a subject; wherein the symbols in the formula are defined below:

R^1: a C1-C6 alkyl group or a hydroxyC1-C6 alkyl group,

R^2: a C1-C6 alkyl group,

A: a 5-membered aromatic heterocycle having bonds and having 1-4 atoms selected from the group consisting of a nitrogen atom, an oxygen atom and a sulfur atom, or an oxygen atom, and

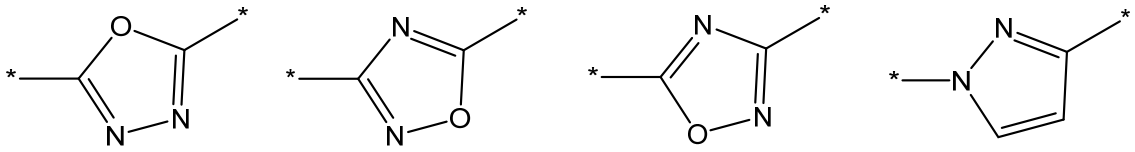
R^3: if A is a 5-membered aromatic heterocycle having bonds and having 1-4 atoms selected from the group consisting of a nitrogen atom, an oxygen atom and a sulfur atom, then R^3 is a C1-C6 alkyl group, a hydroxyC1-C6 alkyl group or a C1-C6 alkoxyC1-C6 alkyl group; and if A is an oxygen atom, then R^3 is a hydroxyC1-C6 alkyl group or a C1-C6 alkoxyC1-C6 alkyl group.

2. The use according to claim 1, wherein R^1 is a methyl group, an ethyl group or a hydroxyethyl group.

3. The use according to claim 1 or claim 2, wherein R^2 is a methyl group.

4. The use according to any of claims 1 to 3, wherein A is a 5-membered aromatic heterocycle having bonds and having 1-4 atoms selected from the group consisting of a nitrogen atom, an oxygen atom and a sulfur atom; and R^3 is a methyl group, an ethyl group, a hydroxyC1-C3 alkyl group or a methoxyC1-C3 alkyl group.

5. The use according to any of claims 1 to 4, wherein A is a 5-membered aromatic heterocycle having bonds selected from the following group:



wherein * represents a bond.

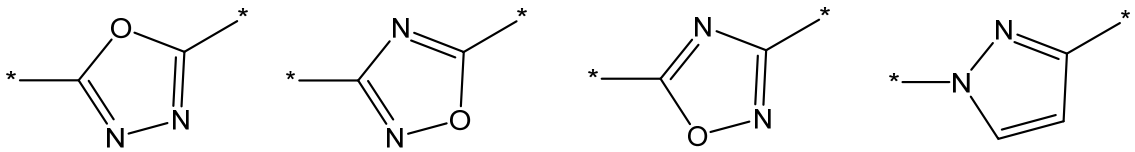
6. The use according to claim 1, wherein A is an oxygen atom.

7. The use according to claim 1, wherein the symbols in the formula are defined below:

R^1: a methyl group, an ethyl group or a hydroxyethyl group,

R^2: a methyl group,

A: a 5-membered aromatic heterocycle having bonds selected from the following group:



wherein * represents a bond, and

R^3: a methyl group, an ethyl group or a hydroxyC1-C3 alkyl group.

8. The use according to claim 1, wherein the compound or a pharmacologically acceptable salt thereof selected from the following group:

(2S,5'R)-7-chloro-6-(2-hydroxyethoxy)-3',4-dimethoxy-5'-methyl-spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione,

(2S,5'R)-7-chloro-3',4-dimethoxy-6-(2-methoxyethoxy)-5'-methyl-spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione,

(2S,5'R)-7-chloro-3',4-dimethoxy-5'-methyl-6-(1-methylpyrazol-3-yl)spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione,

(2S,5'R)-7-chloro-6-(1-ethylpyrazol-3-yl)-3',4-dimethoxy-5'-methyl-spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione,
(2S,5'R)-7-chloro-3',4-dimethoxy-5'-methyl-6-(5-methyl-1,3,4-oxadiazol-2-yl)spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione,
(2S,5'R)-7-chloro-3',4-dimethoxy-5'-methyl-6-(3-methyl-1,2,4-oxadiazol-5-yl)spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione,
(2S,5'R)-7-chloro-3',4-dimethoxy-5'-methyl-6-(5-methyl-1,2,4-oxadiazol-3-yl)spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione,
(2S,5'R)-7-chloro-6-[5-(1-hydroxy-1-methyl-ethyl)-1,3,4-oxadiazol-2-yl]-3',4-dimethoxy-5'-methyl-spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione,
(2S,5'R)-7-chloro-6-[5-[(1S)-1-hydroxyethyl]-1,3,4-oxadiazol-2-yl]-3',4-dimethoxy-5'-methyl-spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione,
(2S,5'R)-7-chloro-6-[5-[(1R)-1-hydroxyethyl]-1,3,4-oxadiazol-2-yl]-3',4-dimethoxy-5'-methyl-spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione,
(2S,5'R)-7-chloro-4-ethoxy-6-[5-(1-hydroxy-1-methyl-ethyl)-1,3,4-oxadiazol-2-yl]-3'-methoxy-5'-methyl-spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione,
(2S,5'R)-7-chloro-4-ethoxy-6-[5-[(1S)-1-hydroxyethyl]-1,3,4-oxadiazol-2-yl]-3'-methoxy-5'-methyl-spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione,
(2S,5'R)-7-chloro-6-[3-(1-hydroxyethyl)-1,2,4-oxadiazol-5-yl]-3',4-dimethoxy-5'-methyl-spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione,
(2S,5'R)-7-chloro-4-(2-hydroxyethoxy)-3'-methoxy-5'-methyl-6-(5-methyl-1,3,4-oxadiazol-2-yl)spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione,
(2S,5'R)-7-chloro-4-(2-hydroxyethoxy)-3'-methoxy-5'-methyl-6-(3-methyl-1,2,4-oxadiazol-5-yl)spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione, and
(2S,5'R)-7-chloro-4-(2-hydroxyethoxy)-3'-methoxy-5'-methyl-6-(5-methyl-1,2,4-oxadiazol-3-yl)spiro[benzofuran-2,4'-cyclohex-2-ene]-1',3-dione.

9. The use according to any of claims 1 to 8, wherein the inflammatory disease is a disease selected from the group consisting of rheumatoid arthritis, systemic lupus erythematosus, scleroderma, bronchial asthma, asthmatic bronchitis, diffuse interstitial pneumonia, chronic obstructive pulmonary disease, ulcerative colitis, Crohn's disease, acute hepatitis, chronic

hepatitis, fulminant hepatitis, autoimmune hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis, alcoholic hepatitis, non-alcoholic steatohepatitis, cirrhosis, peripheral neuritis, ankylosing spondylitis, eczema (acute, subacute, chronic), contact dermatitis, sunlight (ultraviolet light) dermatitis, radiation dermatitis, atopic dermatitis, seborrheic dermatitis, psoriasis vulgaris, arthropathic psoriasis, psoriatic erythroderma, pustular psoriasis, lichen planus, erythema, rosacea, urticaria, alopecia areata, pemphigus, erythroderma, acne vulgaris, pressure sore, wound, burn, conjunctivitis, keratitis, scleritis, acute/chronic otitis media, perennial allergic rhinitis, hay fever, sinusitis, laryngitis, esophagitis, refractory stomatitis, glossitis, acute/chronic salivary gland inflammation, angular cheilitis, cheilitis, Behcet's disease, multiple sclerosis, Type I diabetes, Type II diabetes, atherosclerosis, pancreatitis and chronic heart failure.

10. The method according to any one of claims 1 to 9, wherein the inflammatory disease is a disease selected from the group consisting of rheumatoid arthritis, systemic lupus erythematosus, bronchial asthma, acute hepatitis, autoimmune hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis, alcoholic hepatitis, nonalcoholic steatohepatitis, ankylosing spondylitis, contact dermatitis, sunlight (UV) dermatitis, atopic dermatitis, seborrheic dermatitis, psoriasis vulgaris, arthropathic psoriasis, psoriatic erythroderma, pustular psoriasis, lichen planus, erythema, rosacea, alopecia areata, pemphigus, erythroderma, acne vulgaris, pressure sore, wound, burn, sinusitis, laryngitis, esophagitis, refractory stomatitis, glossitis, acute/chronic salivary gland inflammation, angular cheilitis, cheilitis and Behcet's disease.

11. The use according to any one of claims 1 to 10, wherein the inflammatory disease is a disease selected from the group consisting of rheumatoid arthritis, systemic lupus erythematosus, autoimmune hepatitis, alcoholic hepatitis, nonalcoholic steatohepatitis, ankylosing spondylitis, atopic dermatitis, psoriasis vulgaris, arthropathic psoriasis, psoriatic erythroderma, pustular psoriasis, lichen planus, pressure sore, wound, refractory stomatitis, glossitis and Behcet's disease.