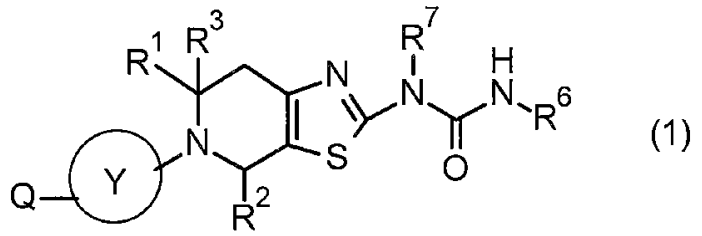
Claims

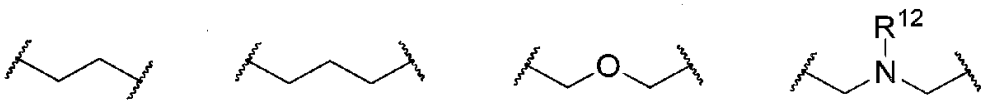
[Claim 1] A compound represented by Formula (1) or a pharmaceutically acceptable salt thereof,



(1)

wherein the symbols in Formula (1) have the following definitions,

R^1 and R^2 independently represent a hydrogen atom or a C1-C6 alkyl group and may be the same or different from each other, or R^1 and R^2 bond to each other to form a substituent and the substituent represents any group selected from the following groups,



R^{12} represents a C1-C6 alkyl group, a hydroxy C1-C6 alkyl group, a C1-C6 alkylcarbonyl group, a C1-C6 alkoxycarbonyl group, or a C1-C6 alkylsulfonyl group,

R^3 represents a hydrogen atom or a C1-C6 alkyl group,

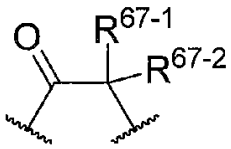
R^6 represents a C1-C6 alkyl group that may be substituted with one to three groups selected from a group G, a C3-C6 cycloalkyl group that may be substituted with one or two groups selected from the group G, or a 4- to 7-membered heterocyclic group that may be substituted with one or two groups selected from the group G,

the group G consists of a hydroxyl group, a halogen atom, an amino group, a halo-C1-C6 alkyl group, a hydroxy C1-C6 alkyl group, an amino C1-C6 alkyl group, a C1-C6 alkoxy group, a C1-C6 alkylsulfonyl group, a hydroxy C1-C6 alkoxy group, a C1-C6 alkylcarbonyl group, a carbamoyl group that may be substituted with one or two groups selected from a group J, a C3-C6 cycloalkyl group that may be substituted with one or two groups selected from the group J, a 4- to 7-membered heterocyclic group that may be substituted with one or two groups selected from the group J, or a 5- to 6-membered heteroaryl group that may be substituted with one or two groups selected from the group J,

the group J consists of a hydroxyl group, an oxo group, an amino C1-C6 alkyl group, an amino group, a C1-C6 alkyl group, and a C1-C6 alkylcarbonyl group,

R^7 represents a hydrogen atom, or

R^6 and R^7 bond to each other to form a substituent and the substituent represents a group shown below,



the group is oriented in either a rightward or leftward direction,

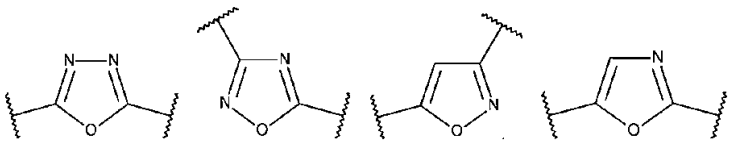
R^{67-1} and R^{67-2} independently represent a hydrogen atom, a C1-C6 alkyl group, a hydroxy C1-C6 alkyl group, a C1-C4 alkylene group, or a C1-C6 alkoxy C1-C6 alkyl group and may be the same or different from each other,

wherein Q represents a 1,3-benzoxazol-2-yl group that is substituted with one or two groups independently selected from the group consisting of a fluorine atom, a methyl group, a methoxy group, an ethoxy group, a dimethylamino group, and a methanesulfonyl group, and

Y represents a single bond; or

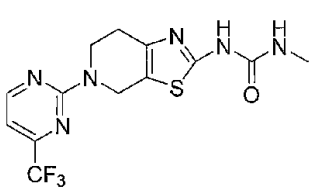
wherein Q represents a cyclohexyl group that is substituted with two fluorine atoms, a phenyl group that is substituted with a fluorine atom or a cyclopropylcarbonyl group, or a pyridyl group that is substituted with one group selected from the group consisting of a methoxy group, an ethoxy group, and a difluoromethoxy group, and

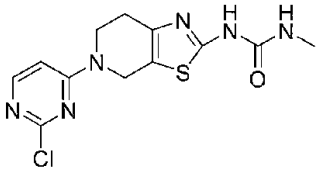
Y represents any group selected from the following groups, oriented in either a rightward or lefrward direction:



, and

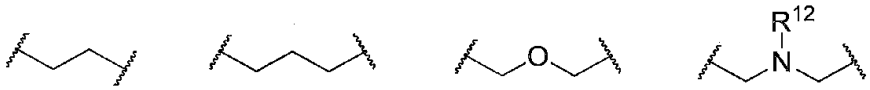
the following compounds or pharmaceutically acceptable salts thereof are excluded





[Claim 2] The compound or the pharmaceutically acceptable salt thereof according to claim 1,

Wherein both R^1 and R^2 represent a hydrogen atom, or R^1 and R^2 bond to each other to form a substituent and the substituent represents any group selected from the following groups,

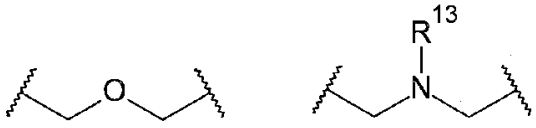


R^{12} represents a methyl group, a hydroxyethyl group, an acetyl group, a methoxycarbonyl group, or a methanesulfonyl group, and

R^3 represents a hydrogen atom or a methyl group.

[Claim 3] The compound or the pharmaceutically acceptable salt thereof according to claim 1,

wherein both R^1 and R^2 represent a hydrogen atom, or R^1 and R^2 bond to each other to form a substituent and the substituent represents any group selected from the following groups,



R^{13} represents an acetyl group or a methoxycarbonyl group, and

R^3 represents a hydrogen atom.

[Claim 4] The compound or the pharmaceutically acceptable salt thereof according to claim 1,

wherein both R^1 and R^3 represent a methyl group, and

R^2 represents a hydrogen atom.

[Claim 5] The compound or the pharmaceutically acceptable salt thereof according to any one of claims 1 to 4,

wherein R^6 represents any group selected from a C1-C6 alkyl group, a hydroxy C1-C6 alkyl group, a hydroxy C3-C6 cycloalkyl group, a C1-C6 alkoxy C1-C6 alkyl group, a tetrahydrofuranyl group, a tetrahydropyranyl group, and a dioxanylmethyl group, and

R^7 represents a hydrogen atom.

[Claim 6] The compound or the pharmaceutically acceptable salt thereof according to any one of claims 1 to 4,

wherein R^6 represents any group selected from a methyl group, an isobutyl group, a 2-hydroxy-1-methylethyl group, a 2-hydroxy-2-methylpropyl group, a 3-hydroxybutyl group, a 2-hydroxycyclopentyl group, a 4-hydroxycyclohexyl group, a 2-methoxypropyl group, a 3-tetrahydrofuranyl group, a 4-tetrahydropyranyl group, and a 1,4-dioxan-2-ylmethyl group, and R^7 represents a hydrogen atom.

[Claim 7] The compound or the pharmaceutically acceptable salt thereof according to claim 1,

wherein the compound is selected from

N-[(4S,8S)-10-{5-[3-(cyclopropanecarbonyl)phenyl]-1,3,4-oxadiazol-2-yl}-4,7,8,9-tetrahydro-5H-4,8-epiminooxocino[5,4-d][1,3]thiazol-2-yl]-N’-methylurea,

(-)-N-{(4R^*,8R^*)-6-acetyl-10-[3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl]-4,5,6,7,8,9-hexahydro-4,8-epimino[1,3]thiazolo[5,4-d]azocin-2-yl}-N’-methylurea,

(-)-methyl(4R^*,8R^*)-10-[3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl]-2-[(methylcarbamoyl)amino]-4,7,8,9-tetrahydro-4,8-epimino[1,3]thiazolo[5,4-d]azocin-6(5H)-carboxylate,

N-{5-[3-(4,4-difluorocyclohexyl)-1,2,4-oxadiazol-5-yl]-4,5,6,7-tetrahydro[1,3]thiazolo[5,4-c]pyridin-2-yl}-N’-[(1R,2R)-2-hydroxycyclopentyl]urea,

N-{5-[3-(4,4-difluorocyclohexyl)-1,2,4-oxadiazol-5-yl]-4,5,6,7-tetrahydro[1,3]thiazolo[5,4-c]pyridin-2-yl}-N’-[(1r,4r)-4-hydroxycyclohexyl]urea,

N-{5-[3-(4,4-difluorocyclohexyl)-1,2,4-oxadiazol-5-yl]-4,5,6,7-tetrahydro[1,3]thiazolo[5,4-c]pyridin-2-yl}-N'-(3-methoxypropyl)urea,

N-{[(2S)-1,4-dioxan-2-yl]methyl}-N'-{(4S,8S)-10-[3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl]-4,7,8,9-tetrahydro-5H-4,8-epiminooxocino[5,4-d][1,3]thiazol-2-yl}urea,

N-[(2R)-1-hydroxypropan-2-yl]-N'-[(4S,8S)-10-(5-methoxy-1,3-benzoxazol-2-yl)-4,7,8,9-tetrahydro-5H-4,8-epiminooxocino[5,4-d][1,3]thiazol-2-yl]urea,

N-[(4S,8S)-10-(5-fluoro-1,3-benzoxazol-2-yl)-4,7,8,9-tetrahydro-5H-4,8-epiminooxocino[5,4-d][1,3]thiazol-2-yl]-N'-[(2R)-1-hydroxypropan-2-yl]urea,

N-[(4S,8S)-10-(5-ethoxy-1,3-benzoxazol-2-yl)-4,7,8,9-tetrahydro-5H-4,8-epiminooxocino[5,4-d][1,3]thiazol-2-yl]-N'-(2-hydroxy-2-methylpropyl)urea,

N-{(4S,8S)-10-[5-(dimethylamino)-1,3-benzoxazol-2-yl]-4,7,8,9-tetrahydro-5H-4,8-epiminooxocino[5,4-d][1,3]thiazol-2-yl}-N'-(2-hydroxy-2-methylpropyl)urea,

N-[(4S,8S)-10-(5,6-difluoro-1,3-benzoxazol-2-yl)-4,7,8,9-tetrahydro-5H-4,8-epiminooxocino[5,4-d][1,3]thiazol-2-yl]-N'-[(2R)-1-hydroxypropan-2-yl]urea,

N-{(4S,8S)-10-[5-(methanesulfonyl)-1,3-benzoxazol-2-yl]-4,7,8,9-tetrahydro-5H-4,8-epiminooxocino[5,4-d][1,3]thiazol-2-yl}-N'-(2-methylpropyl)urea,

N-(2-hydroxy-2-methylpropyl)-N'-[(4S,8S)-10-(5-methoxy-6-methyl-1,3-benzoxazol-2-yl)-4,7,8,9-tetrahydro-5H-4,8-epiminooxocino[5,4-d][1,3]thiazol-2-yl]urea,

N-[(4S,8S)-10-(5-methoxy-6-methyl-1,3-benzoxazol-2-yl)-4,7,8,9-tetrahydro-5H-4,8-epiminooxocino[5,4-d][1,3]thiazol-2-yl]-N'-[(3R)-oxolan-3-yl]urea,

N-(2-hydroxy-2-methylpropyl)-N'-[(4S,8S)-10-(5-methoxy-1,3-benzoxazol-2-yl)-4,7,8,9-tetrahydro-5H-4,8-epiminooxocino[5,4-d][1,3]thiazol-2-yl]urea,

N-[(4S,8S)-10-(5-methoxy-1,3-benzoxazol-2-yl)-4,7,8,9-tetrahydro-5H-4,8-epiminooxocino[5,4-d][1,3]thiazol-2-yl]-N'-[(3R)-oxolan-3-yl]urea,

N-[(4S,8S)-10-(5-methoxy-1,3-benzoxazol-2-yl)-4,7,8,9-tetrahydro-5H-4,8-epiminooxocino[5,4-d][1,3]thiazol-2-yl]-N'-methylurea,

N-methyl-N'-[(4S,8S)-10-(5-methyl-1,3-benzoxazol-2-yl)-4,7,8,9-tetrahydro-5H-4,8-epiminooxocino[5,4-d][1,3]thiazol-2-yl]urea,

N-(2-hydroxy-2-methylpropyl)-N'-[(4S,8S)-10-{5-[($^{2}H_{3}$)methyloxy]-1,3-benzoxazol-2-yl}-4,7,8,9-tetrahydro-5H-4,8-epiminooxocino[5,4-d][1,3]thiazol-2-yl]urea,

N-{(4S,8S)-10-[5-(4-fluorophenyl)-1,2-oxazol-3-yl]-4,7,8,9-tetrahydro-5H-4,8-epiminooxocino[5,4-d][1,3]thiazol-2-yl}-N'-[(1s,4s)-4-hydroxycyclohexyl]urea,

N-{(4S,8S)-10-[5-(6-methoxypyridin-2-yl)-1,2-oxazol-3-yl]-4,7,8,9-tetrahydro-5H-4,8-epiminooxocino[5,4-d][1,3]thiazol-2-yl}-N’-oxan-4-ylurea,

N-[(4S,8S)-10-{5-[6-(difluoromethoxy)pyridin-2-yl]-1,3-oxazol-2-yl}-4,7,8,9-tetrahydro-5H-4,8-epiminooxocino[5,4-d][1,3]thiazol-2-yl]-N’-[(2R)-1-hydroxypropan-2-yl]urea,

N-[(2R)-1-hydroxypropan-2-yl]-N’-{(4S,8S)-10-[5-(6-methoxypyridin-2-yl)-1,3-oxazol-2-yl]-4,7,8,9-tetrahydro-5H-4,8-epiminooxocino[5,4-d][1,3]thiazol-2-yl}urea,

N-{(4S,8S)-10-[5-(6-ethoxypyridin-2-yl)-1,3-oxazol-2-yl]-4,7,8,9-tetrahydro-5H-4,8-epiminooxocino[5,4-d][1,3]thiazol-2-yl}-N’-[(2R)-1-hydroxypropan-2-yl]urea,

N-[(2R)-1-hydroxypropan-2-yl]-N’-{5-[5-(methanesulfonyl)-1,3-benzoxazol-2-yl]-6,6-dimethyl-4,5,6,7-tetrahydro[1,3]thiazolo[5,4-c]pyridin-2-yl}urea,

N-(2-hydroxy-2-methylpropyl)-N’-{5-[5-(methanesulfonyl)-1,3-benzoxazol-2-yl]-6,6-dimethyl-4,5,6,7-tetrahydro[1,3]thiazolo[5,4-c]pyridin-2-yl}urea,

N-[(2R)-1-hydroxypropan-2-yl]-N’-[(4S,8S)-10-{5-[($^{2}H_{3}$)methyloxy]-1,3-benzoxazol-2-yl}-4,7,8,9-tetrahydro-5H-4,8-epiminooxocino[5,4-d][1,3]thiazol-2-yl]urea,

N-[(4S,8S)-10-{5-[($^{2}H_{3}$)methyloxy]-1,3-benzoxazol-2-yl}-4,7,8,9-tetrahydro-5H-4,8-epiminooxocino[5,4-d][1,3]thiazol-2-yl]-N’-[(3R)-oxolan-3-yl]urea,

N-[(1r,3S)-3-hydroxycyclobutyl]-N’-{(4S,8S)-10-[5-(6-methoxypyridin-2-yl)-1,3-oxazol-2-yl]-4,7,8,9-tetrahydro-5H-4,8-epiminooxocino[5,4-d][1,3]thiazol-2-yl}urea,

N-{(4S,8S)-10-[5-(6-ethoxypyridin-2-yl)-1,3-oxazol-2-yl]-4,7,8,9-tetrahydro-5H-4,8-epiminooxocino[5,4-d][1,3]thiazol-2-yl}-N’-(2-hydroxy-2-methylpropyl)urea,

N-{(4S,8S)-10-[5-(6-ethoxypyridin-2-yl)-1,3-oxazol-2-yl]-4,7,8,9-tetrahydro-5H-4,8-epiminooxocino[5,4-d][1,3]thiazol-2-yl}-N’-[(1r,3S)-3-hydroxycyclobutyl]urea, and

N-{(4S,8S)-10-[5-(6-methoxypyridin-2-yl)-1,3-oxazol-2-yl]-4,7,8,9-tetrahydro-5H-4,8-epiminooxocino[5,4-d][1,3]thiazol-2-yl}-N’-oxan-4-ylurea.

[Claim 8] A SIRT6 activator containing:

the compound or the pharmaceutically acceptable salt thereof according to any one of claims 1 to 7 as an active component.

[Claim 9] A pharmaceutical composition containing:

the compound or the pharmaceutically acceptable salt thereof according to any one of

claims 1 to 7 as an active component.

[Claim 10] The pharmaceutical composition according to claim 9, wherein the pharmaceutical composition is an oral preparation.

[Claim 11] The pharmaceutical composition according to claim 9, wherein the pharmaceutical composition is an external preparation.

[Claim 12] The compound or the pharmaceutically acceptable salt thereof according to any one of claims 1 to 7 for use in treating and/or preventing a peripheral inflammatory disease.

[Claim 13] The compound or the pharmaceutically acceptable salt thereof for use according to claim 12, wherein the peripheral inflammatory disease is any one 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, hepatic cirrhosis, peripheral neuritis, ankylosing spondylitis, acute eczema, subacute eczema, chronic eczema, contact dermatitis, solar dermatitis due to sunlight and/or ultraviolet rays, radiation dermatitis, atopic dermatitis, seborrheic dermatitis, psoriasis vulgaris, psoriasis arthropica, psoriatic erythroderma, pustular psoriasis, lichen planus, erythema, rosacea, urticaria, alopetia areata, pemphigus, erythroderma, acne vulgaris, decubitus, wounds, burns, conjunctivitis, keratitis, scleritis, acute/chronic otitis media, perennial allergic rhinitis, pollinosis, sinusitis, laryngitis, esophagitis, refractory stomatitis, glossitis, acute/chronic sialadenitis, angular stomatitis, cheilitis, Behcet's disease, multiple sclerosis, type I diabetes, type II diabetes, atherosclerosis, pancreatitis, chronic heart failure, vitiligo vulgaris, verruca vulgaris, diabetic ulcer, ulcus cruris, keloid, hypertrophic scar, seborrhoic keratosis, male pattern alopecia, female pattern alopecia, senile alopecia, acne scar, pigmentation disorder, solar keratosis, chronic hand eczema, chronic pruritus, generalized cutaneous pruritus, glaucoma, cataract, age-related

macular degeneration, idiopathic pulmonary fibrosis, acute glomerulonephritis, chronic glomerulonephritis, diabetic glomerulonephritis, hypertrophic cardiomyopathy, osteoporosis, neurogenic muscular dystrophy, myogenic muscular dystrophy, and high blood pressure.

[Claim 14] The compound or the pharmaceutically acceptable salt thereof for use according to claim 12,

wherein the peripheral inflammatory disease is any one selected from the group consisting of rheumatoid arthritis, systemic lupus erythematosus, scleroderma, bronchial asthma, acute hepatitis, autoimmune hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis, alcoholic hepatitis, non-alcoholic steatohepatitis, ankylosing spondylitis, contact dermatitis, solar dermatitis due to sunlight and/or ultraviolet rays, radiation dermatitis, atopic dermatitis, seborrheic dermatitis, psoriasis vulgaris, psoriasis arthropica, psoriatic erythroderma, pustular psoriasis, lichen planus, erythema, rosacea, urticaria, alopetia areata, pemphigus, erythroderma, acne vulgaris, decubitus, wounds, burns, sinusitis, laryngitis, esophagitis, refractory stomatitis, glossitis, acute/chronic sialadenitis, angular stomatitis, cheilitis, Behcet’s disease, vitiligo vulgaris, verruca vulgaris, diabetic ulcer, ulcus cruris, keloid, hypertrophic scar, seborrhoic keratosis, male pattern alopecia, female pattern alopecia, senile alopecia, acne scar, pigmentation disorder, solar keratosis, chronic hand eczema, chronic pruritus, generalized cutaneous pruritus, and idiopathic pulmonary fibrosis.

[Claim 15] The compound or the pharmaceutically acceptable salt thereof for use according to claim 12,

wherein the peripheral inflammatory disease is any one selected from the group consisting of rheumatoid arthritis, systemic lupus erythematosus, alcoholic hepatitis, non-alcoholic steatohepatitis, contact dermatitis, solar dermatitis due to sunlight and/or ultraviolet rays, radiation dermatitis, atopic dermatitis, seborrheic dermatitis, psoriasis vulgaris, psoriasis arthropica, psoriatic erythroderma, pustular psoriasis, lichen planus, erythema, rosacea, urticaria, alopetia areata, pemphigus, erythroderma, acne vulgaris, decubitus, wounds, burns, refractory stomatitis, glossitis, Behcet’s disease, vitiligo vulgaris, verruca vulgaris, diabetic ulcer, ulcus cruris, keloid, hypertrophic scar, seborrhoic keratosis, male pattern alopecia, female pattern alopecia, senile alopecia, acne scar, pigmentation disorder, solar keratosis, chronic hand eczema, chronic pruritus, generalized cutaneous pruritus, and idiopathic

pulmonary fibrosis.

[Claim 16] Use of the compound or the pharmaceutically acceptable salt thereof according to any one of claims 1 to 7, for the manufacture of a pharmaceutical composition used for treating and/or preventing a peripheral inflammatory disease.

[Claim 17] The use according to claim 16,

wherein the peripheral inflammatory disease is any one 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, hepatic cirrhosis, peripheral neuritis, ankylosing spondylitis, acute eczema, subacute eczema, chronic eczema, contact dermatitis, solar dermatitis due to sunlight and/or ultraviolet rays, radiation dermatitis, atopic dermatitis, seborrheic dermatitis, psoriasis vulgaris, psoriasis arthropica, psoriatic erythroderma, pustular psoriasis, lichen planus, erythema, rosacea, urticaria, alopetia areata, pemphigus, erythroderma, acne vulgaris, decubitus, wounds, burns, conjunctivitis, keratitis, scleritis, acute/chronic otitis media, perennial allergic rhinitis, pollinosis, sinusitis, laryngitis, esophagitis, refractory stomatitis, glossitis, acute/chronic sialadenitis, angular stomatitis, cheilitis, Behcet's disease, multiple sclerosis, type I diabetes, type II diabetes, atherosclerosis, pancreatitis, chronic heart failure, vitiligo vulgaris, verruca vulgaris, diabetic ulcer, ulcus cruris, keloid, hypertrophic scar, seborrhoic keratosis, male pattern alopecia, female pattern alopecia, senile alopecia, acne scar, pigmentation disorder, solar keratosis, chronic hand eczema, chronic pruritus, generalized cutaneous pruritus, glaucoma, cataract, age-related macular degeneration, idiopathic pulmonary fibrosis, acute glomerulonephritis, chronic glomerulonephritis, diabetic glomerulonephritis, hypertrophic cardiomyopathy, osteoporosis, neurogenic muscular dystrophy, myogenic muscular dystrophy, and high blood pressure.

[Claim 18] The use according to claim 16,

wherein the peripheral inflammatory disease is any one selected from the group consisting of rheumatoid arthritis, systemic lupus erythematosus, scleroderma, bronchial

asthma, acute hepatitis, autoimmune hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis, alcoholic hepatitis, non-alcoholic steatohepatitis, ankylosing spondylitis, contact dermatitis, solar dermatitis due to sunlight and/or ultraviolet rays, radiation dermatitis, atopic dermatitis, seborrheic dermatitis, psoriasis vulgaris, psoriasis arthropica, psoriatic erythroderma, pustular psoriasis, lichen planus, erythema, rosacea, urticaria, alopetia areata, pemphigus, erythroderma, acne vulgaris, decubitus, wounds, burns, sinusitis, laryngitis, esophagitis, refractory stomatitis, glossitis, acute/chronic sialadenitis, angular stomatitis, cheilitis, Behcet's disease, vitiligo vulgaris, verruca vulgaris, diabetic ulcer, ulcus cruris, keloid, hypertrophic scar, seborrhoic keratosis, male pattern alopecia, female pattern alopecia, senile alopecia, acne scar, pigmentation disorder, solar keratosis, chronic hand eczema, chronic pruritus, generalized cutaneous pruritus, and idiopathic pulmonary fibrosis.

[Claim 19] The use according to claim 16,

wherein the peripheral inflammatory disease is any one selected from the group consisting of rheumatoid arthritis, systemic lupus erythematosus, alcoholic hepatitis, non-alcoholic steatohepatitis, contact dermatitis, solar dermatitis due to sunlight and/or ultraviolet rays, radiation dermatitis, atopic dermatitis, seborrheic dermatitis, psoriasis vulgaris, psoriasis arthropica, psoriatic erythroderma, pustular psoriasis, lichen planus, erythema, rosacea, urticaria, alopetia areata, pemphigus, erythroderma, acne vulgaris, decubitus, wounds, burns, refractory stomatitis, glossitis, Behcet's disease, vitiligo vulgaris, verruca vulgaris, diabetic ulcer, ulcus cruris, keloid, hypertrophic scar, seborrhoic keratosis, male pattern alopecia, female pattern alopecia, senile alopecia, acne scar, pigmentation disorder, solar keratosis, chronic hand eczema, chronic pruritus, generalized cutaneous pruritus, and idiopathic pulmonary fibrosis.