Claims

[Claim 1]

An agent for improving left ventricular diastolic function, which comprises 4-[(2-{(2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-buten-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]butanoic acid, a salt thereof, a solvate thereof or a cyclodextrin clathrate thereof.

[Claim 2]

The agent according to claim 1, which is an agent for treating heart failure and/or relieving a symptom.

[Claim 3]

The agent according to claim 2, wherein the heart failure is acute heart failure or chronic heart failure.

[Claim 4]

The agent according to claim 2, wherein the heart failure is diastolic heart failure.

[Claim 5]

The agent according to claim 2, wherein the symptom is congestion, dyspnea, shortness of breath, malaise, decrease in urine volume, limb edema and/or hepatomegaly.

[Claim 6]

The agent according to claim 1, which further has an effect to improve left ventricular systolic function.

[Claim 7]

The agent according to claim 6, which is an agent for treating systolic heart failure and/or relieving a symptom.

[Claim 8]

The agent according to claim 7, wherein the symptom is congestion, dyspnea, shortness of breath, malaise, decrease in urine volume, limb edema and/or hepatomegaly.

[Claim 9]

An agent for improving the survival rate of heart failure, which comprises 4-[(2-{(2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-buten-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]butanoic acid, a salt thereof, a solvate thereof or a cyclodextrin clathrate thereof.

[Claim 10]

An agent for improving left ventricular distensibility, which comprises 4-[(2-{(2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-buten-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]butanoic acid, a salt thereof, a solvate thereof or a cyclodextrin clathrate thereof.

[Claim 11]

An agent for preventing myocardial fibrillization, which comprises 4-[(2-{(2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-buten-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]butanoic acid, a salt thereof, a solvate thereof or a cyclodextrin clathrate thereof.

[Claim 12]

A medicine for treating heart failure, which is produced by combining 4-[(2-{(2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-buten-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]butanoic acid, a salt thereof, a solvate thereof or a cyclodextrin clathrate thereof, with one or more compounds selected from an angiotensin-converting enzyme inhibitor, an angiotensin II receptor antagonist, a β-blocker, a digitalis preparation, a diuretic agent, a natriuretic peptide, a vasodilator, a phosphodiesterase III inhibitor and/or an aldosterone antagonist.

[Claim 13]

An agent for treating diastolic heart failure and/or relieving a symptom, which includes a drug having an effect to improve left ventricular systolic function and an effect to improve left ventricular diastolic function, wherein the agent improves left ventricular diastolic function more selectively in comparison with left ventricular systolic function.

[Claim 14]

The agent according to claim 13, wherein the agent is 4-[(2-{(2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-buten-1-yl]-5-oxo-1-

pyrrolidinyl}ethyl)thio]butanoic acid, a salt thereof, a solvate thereof or a cyclodextrin clathrate thereof.

[Claim 15]

An agent for selectively improving left ventricular diastolic function, which comprises 4-[(2-{(2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-buten-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]butanoic acid, a salt thereof, a solvate thereof or a cyclodextrin clathrate thereof as an active ingredient, and which selectively improves left ventricular diastolic function in comparison with left ventricular systolic function.

[Claim 16]

The agent according to claim 15, which is an agent for treating diastolic heart failure and/or relieving a symptom.

[Claim 17]

An agent for treating heart failure, which comprises 4-[(2-{(2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-buten-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]butanoic acid, a salt thereof, a solvate thereof or a cyclodextrin clathrate thereof as an active ingredient, and which changes Peak positive dP/dt and Peak negative dP/dt of a mammal having a pathological condition of heart failure, wherein the change ratio of the Peak negative dP/dt calculated from the values before and after the administration of the agent is larger than the change ratio of the Peak positive dP/dt.

[Claim 18]

The agent according to claim 17, which is an agent for treating diastolic heart failure and/or relieving a symptom.

[Claim 19]

An agent for preventing heart failure associated with hypertension from occurring, which comprises 4-[(2-{(2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-buten-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]butanoic acid, a salt thereof, a solvate thereof or a cyclodextrin clathrate thereof.

[Claim 20]

An agent for treating diastolic heart failure and/or relieving a symptom, which comprises 4-[(2-{(2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-

buten-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]butanoic acid, a salt thereof, a solvate thereof or a cyclodextrin clathrate thereof.

[Claim 21]

An agent for treating heart failure in which diastolic function is impaired, which comprises 4-[(2-{(2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-buten-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]butanoic acid, a salt thereof, a solvate thereof or a cyclodextrin clathrate thereof.

Claims

[Claim 1]

Use of 4-[(2-{(2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-buten-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]butanoic acid, a salt thereof, a solvate thereof or a cyclodextrin clathrate thereof for the manufacture of an agent for treating heart failure and/or relieving a symptom.

[Claim 2]

The use according to claim 1, wherein the heart failure is acute heart failure or chronic heart failure.

[Claim 3]

The use according to claim 1, wherein the heart failure is diastolic heart failure.

[Claim 4]

The use according to any one of claims 1 to 3, wherein the symptom is congestion, dyspnea, shortness of breath, malaise, decrease in urine volume, limb edema and/or hepatomegaly.

[Claim 5]

Use of 4-[(2-{(2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-buten-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]butanoic acid, a salt thereof, a solvate thereof or a cyclodextrin clathrate thereof for the manufacture of an agent for treating heart failure, which changes Peak positive dP/dt and Peak negative dP/dt of a mammal having a pathological condition of heart failure, wherein the change ratio of the Peak negative dP/dt calculated from the values before and after the administration of the agent is larger than the change ratio of the Peak positive dP/dt.

[Claim 6]

The use according to claim 5, which is a compound for treating diastolic heart failure and/or relieving a symptom.

[Claim 7]

Use of 4-[(2-{(2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-buten-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]butanoic acid, a salt thereof, a solvate

thereof or a cyclodextrin clathrate thereof for the manufacture of an agent for improving the survival rate of heart failure.

[Claim 8]

Use of 4-[(2-{(2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-buten-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]butanoic acid, a salt thereof, a solvate thereof or a cyclodextrin clathrate thereof for the manufacture of an agent for improving cardiac output.

[Claim 9]

A medicine for treating heart failure, which is produced by combining 4-[(2-{(2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-buten-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]butanoic acid, a salt thereof, a solvate thereof or a cyclodextrin clathrate thereof, with one or more compounds selected from an angiotensin-converting enzyme inhibitor, an angiotensin II receptor antagonist, a β-blocker, a digitalis preparation, a diuretic agent, a natriuretic peptide, a vasodilator, a phosphodiesterase III inhibitor and/or an aldosterone antagonist.

[Claim 10]

Use of 4-[(2-{(2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-buten-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]butanoic acid, a salt thereof, a solvate thereof or a cyclodextrin clathrate thereof for the manufacture of an agent for treating heart failure in which diastolic function is impaired.

[Claim 11]

Use of 4-[(2-{(2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-buten-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]butanoic acid, a salt thereof, a solvate thereof or a cyclodextrin clathrate thereof for the manufacture of an agent for reducing the dose of an existing agent for treating heart failure.

[Claim 12]

Use of 4-[(2-{(2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-buten-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]butanoic acid, a salt thereof, a solvate thereof or a cyclodextrin clathrate thereof for the manufacture of an agent for reducing the side effect of an existing agent for treating heart failure.

[Claim 13]

The use according to claim 11 or 12, wherein the existing agent is one or more compounds selected from an angiotensin-converting enzyme inhibitor, an angiotensin II receptor antagonist, a β-blocker, a digitalis preparation, a diuretic agent, a natriuretic peptide, a vasodilator, a phosphodiesterase III inhibitor and/or an aldosterone antagonist.

[Claim 14]

Use of 4-[(2-{(2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-buten-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]butanoic acid, a salt thereof, a solvate thereof or a cyclodextrin clathrate thereof for the manufacture of an agent for preventing heart failure associated with hypertension from occurring.

[Claim 15]

Use of 4-[(2-{(2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-buten-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]butanoic acid, a salt thereof, a solvate thereof or a cyclodextrin clathrate thereof for the manufacture of an agent for improving left ventricular diastolic function.

[Claim 16]

The use according to claim 15, which is use for treating heart failure and/or relieving a symptom.

[Claim 17]

The use according to claim 16, wherein the heart failure is acute heart failure or chronic heart failure.

[Claim 18]

The use according to claim 16, wherein the heart failure is diastolic heart failure.

[Claim 19]

The use according to claim 16, wherein the symptom is congestion, dyspnea, shortness of breath, malaise, decrease in urine volume, limb edema and/or hepatomegaly.

[Claim 20]

The use according to claim 15, which is use for further improving left ventricular systolic function.

[Claim 21]

The use according to claim 20, which is use for treating systolic heart failure and/or relieving a symptom.

[Claim 22]

The use according to claim 21, wherein the symptom is congestion, dyspnea, shortness of breath, malaise, decrease in urine volume, limb edema and/or hepatomegaly.

[Claim 23]

Use of 4-[(2-{(2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-buten-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]butanoic acid, a salt thereof, a solvate thereof or a cyclodextrin clathrate thereof for the manufacture of an agent for improving left ventricular distensibility.

[Claim 24]

Use of 4-[(2-{(2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-buten-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]butanoic acid, a salt thereof, a solvate thereof or a cyclodextrin clathrate thereof for the manufacture of an agent for preventing myocardial fibrillization.

[Claim 25]

Use of 4-[(2-{(2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-buten-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]butanoic acid, a salt thereof, a solvate thereof or a cyclodextrin clathrate thereof for the manufacture of an agent for selectively improving left ventricular diastolic function, which selectively improves left ventricular diastolic function in comparison with left ventricular systolic function.

[Claim 26]

The use according to claim 25, which is use for treating diastolic heart failure and/or relieving a symptom.

[Claim 27]

Use of 4-[(2-{(2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-buten-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]butanoic acid, a salt thereof, a solvate thereof or a cyclodextrin clathrate thereof for the manufacture of an agent treating and/or improving diastolic functional failure.

[Claim 28]

Use of 4-[(2-{(2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-buten-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]butanoic acid, a salt thereof, a solvate thereof or a cyclodextrin clathrate thereof for the manufacture of an agent treating and/or improving diastolic functional disorder.

[Claim 29]

Use of 4-[(2-{(2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-buten-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]butanoic acid, a salt thereof, a solvate thereof or a cyclodextrin clathrate thereof for the manufacture of an agent treating diastolic heart failure and/or relieving a symptom.