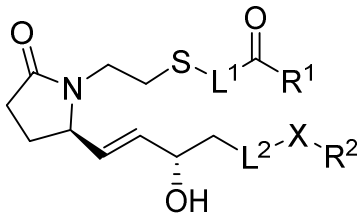
CLAIMS

1. A compound represented by general formula (I):



(I)

wherein

R^1 represents (1) an -OH group, (2) an $-NHCH_2CH_2SO_3H$ group, (3) an $-NHCH_2COOH$ group, or (4) an $-NHCH(COOH)CH_2CH_2COOH$ group;

L^1 represents (1) a thiazole ring or (2) C1-4 alkylene;

L^2 represents (1) C3-5 alkylene or (2) a benzene ring;

X represents (1) -CO-, (2) $-NR^X-$, or (3) a sulfur atom;

R^X represents (1) a hydrogen atom or (2) a C1-4 alkyl group;

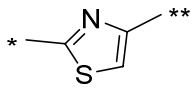
R^2 represents (1) a methyl group, (2) a benzene ring, (3) a 5- to 10-membered heterocyclic ring, (4) a $-COR^{2-1}$ group, (5) a -CO-(benzene ring) group, (6) a -CO-(5- to 10-membered heterocyclic ring) group, (7) an -NH-(benzene ring) group, or (8) an -OH group;

when R^2 represents a benzene ring, a 5- to 10-membered heterocyclic ring, a -CO-(benzene ring) group, a -CO-(5- to 10-membered heterocyclic ring) group, or an -NH-(benzene ring) group, the benzene ring or the 5- to 10-membered heterocyclic ring may be substituted with 1 to 5 R^{2-2}s;

R^{2-1} represents (1) a C1-4 alkyl group that may be substituted with a C1-4 alkoxy group or (2) an -NH-(C1-4 alkyl) group; and

R^{2-2} represents (1) a halogen atom, (2) a C1-4 alkyl group, (3) a C1-4 haloalkyl group, (4) a C1-4 alkoxy group, (5) a C1-4 haloalkoxy group, or (6) a benzene ring; or a pharmaceutically acceptable salt thereof.

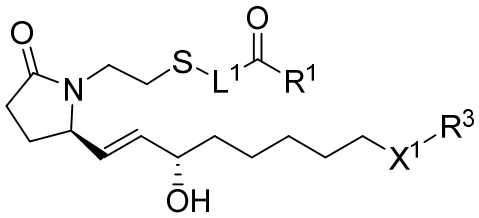
2. The compound according to claim 1 or a pharmaceutically acceptable salt thereof, wherein L^1 is a thiazole ring, and the thiazole ring is represented by:



wherein * represents a bonding site with a sulfur atom, and ** represents a bonding site with $-COR^1$.

3. The compound according to claim 1 or a pharmaceutically acceptable salt thereof, wherein the 5- to 10-membered heterocyclic ring in R^2 is a heterocyclic ring selected from the group consisting of (1) a pyridine ring, (2) a pyrazine ring, (3) a pyrimidine ring, (4) an imidazole ring, (5) a thiazole ring, (6) a triazole ring, (7) a tetrazole ring, (8) a furan ring, (9) a quinoline ring and (10) a pyrazole ring.

4. The compound according to claim 1 or a pharmaceutically acceptable salt thereof, which is represented by general formula (I-1):



(I-1)

wherein R^3 represents (1) a benzene ring, (2) a pyridine ring, (3) a pyrazine ring, (4) a pyrimidine ring, (5) an imidazole ring, (6) a thiazole ring, (7) a triazole ring, (8) a tetrazole ring, (9) a furan ring, (10) a quinoline ring, or (11) a pyrazole ring;

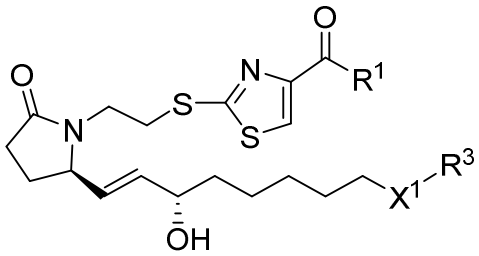
R^3 may be substituted with 1 to 5 $R^{3\text{-}1}$s;

$R^{3\text{-}1}$ represents (1) a halogen atom, (2) a C1-4 alkyl group, (3) a C1-4 haloalkyl group, (4) a C1-4 alkoxy group, (5) a C1-4 haloalkoxy group, or (6) a benzene ring;

X^1 represents (1) $-NR^X-$ or (2) a sulfur atom; and

the other symbols represent the same meaning as the symbols described in claim 1.

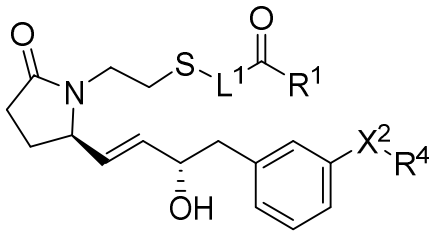
5. The compound according to claim 4 or a pharmaceutically acceptable salt thereof, which is represented by general formula (I-2):



(I-2)

wherein all symbols represent the same meaning as the symbols described in claim 4.

6. The compound according to claim 1 or a pharmaceutically acceptable salt thereof, which is represented by general formula (I-4):



(I-4)

wherein R^4 represents (1) a $-COR^{4-1}$ group, (2) a -CO-(benzene ring) group, (3) a -CO-(pyridine ring) group, (4) a -CO-(pyrazine ring) group, (5) a -CO-(furan ring) group, (6) an -NH-(benzene ring) group, or (7) an -OH group;

when R^4 represents a -CO-(benzene ring) group, a -CO-(pyridine ring) group, a -CO-(pyrazine ring) group, a -CO-(furan ring) group, or an -NH-(benzene ring) group, the benzene ring, the pyridine ring, the pyrazine ring, or the furan ring may be substituted with 1 to 5 R^{4-2}s;

R^{4-1} represents (1) a C1-4 alkyl group that may be substituted with a C1-4 alkoxy group or (2) an -NH-(C1-4 alkyl) group;

R^{4-2} represents (1) a halogen atom, (2) a C1-4 alkyl group, (3) a C1-4 haloalkyl group, (4) a C1-4 alkoxy group, (5) a C1-4 haloalkoxy group, or (6) a benzene ring;

X^2 represents (1) -CO- or (2) $-NR^X-$; and

the other symbols represent the same meaning as the symbols described in claim 1.

7. The compound according to claim 1, wherein the compound represented by general formula (I) is a compound selected from the group consisting of:

(1) 2-[(2-{(2R)-2-[(1E,3S)-3-hydroxy-8-(2-pyridinylthio)-1-octen-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]-1,3-thiazole-4-carboxylic acid;

(2) 2-[(2-{(2R)-2-[(1E,3S)-3-hydroxy-8-(2-pyrazinylthio)-1-octen-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]-1,3-thiazole-4-carboxylic acid;

(3) 2-({2-[(2R)-2-{(1E,3S)-3-hydroxy-8-[methyl(phenyl)amino]-1-octen-1-yl}-5-oxo-1-pyrrolidinyl]ethyl}thio)-1,3-thiazole-4-carboxylic acid;

(4) 2-({2-[(2R)-2-{(1E,3S)-3-hydroxy-8-[(3-methoxy-2-pyrazinyl)thio]-1-octen-1-yl}-5-oxo-1-pyrrolidinyl]ethyl}thio)-1,3-thiazole-4-carboxylic acid;

(5) 2-[(2-{(2R)-2-[(1E,3S)-3-hydroxy-9-(2-pyridinylthio)-1-nonen-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]-1,3-thiazole-4-carboxylic acid;

(6) 4-({2-[(2R)-2-{(1E,3S)-4-[3-(benzoylamino)phenyl]-3-hydroxy-1-buten-1-yl}-5-oxo-1-pyrrolidinyl]ethyl}thio)butanoic acid;

(7) 2-[({2-[(2-{(2R)-2-[(1E,3S)-3-hydroxy-8-(2-pyridinylthio)-1-octen-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]-1,3-thiazol-4-yl}carbonyl)amino]ethanesulfonic acid;

(8) 2-({[2-({2-[(2R)-2-{(1E,3S)-3-hydroxy-8-[(3-methoxy-2-pyrazinyl)thio]-1-octen-1-yl}-5-oxo-1-pyrrolidinyl]ethyl}thio)-1,3-thiazol-4-yl]carbonyl}amino)ethanesulfonic acid;

and

(9) 2-{[4-({2-[(2R)-2-{(1E,3S)-4-[3-(benzoylamino)phenyl]-3-hydroxy-1-buten-1-yl}-5-oxo-1-pyrrolidinyl]ethyl}thio)butanoyl]amino}ethanesulfonic acid; or a pharmaceutically acceptable salt thereof.

8. A compound 2-[(2-{(2R)-2-[(1E,3S)-3-hydroxy-8-(2-pyridinylthio)-1-octen-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]-1,3-thiazole-4-carboxylic acid, or a pharmaceutically acceptable salt thereof.

9. A compound 2-[({2-[(2-{(2R)-2-[(1E,3S)-3-hydroxy-8-(2-pyridinylthio)-1-octen-1-yl]-5-oxo-1-pyrrolidinyl}ethyl)thio]-1,3-thiazol-4-yl}carbonyl)amino]ethanesulfonic acid, or a pharmaceutically acceptable salt thereof.

10. A pharmaceutical composition comprising the compound according to any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof, as an active ingredient, and further comprising a pharmaceutically acceptable carrier.

11. The pharmaceutical composition according to claim 10, which is an EP4 agonist.

12. The compound according to any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition according to claim 10 or 11, for use in therapy.

13. Use of the compound according to any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition according to claim 10 or 11, in the manufacture of a medicament for the therapeutic and/or preventive treatment of a disease related to an EP4 receptor.

14. The use according to claim 13, wherein the disease related to an EP4 receptor is immune disease, asthma, neuronal cell death, arthritis, lung injury, pulmonary fibrosis, pulmonary emphysema, bronchitis, chronic obstructive pulmonary disease, liver injury, acute hepatitis, nephritis, renal failure, hypertension, myocardial ischemia, systemic inflammatory response syndrome, sepsis, hemophagocytic syndrome, macrophage activation syndrome, Still’s disease, Kawasaki disease, burn injury, systemic granuloma, inflammatory bowel disease, hypercytokinemia during dialysis, multiple organ failure, and/or shock.

15. The use according to claim 13, wherein the disease related to an EP4 receptor is inflammatory bowel disease, and the inflammatory bowel disease is ulcerative colitis or Crohn’s disease.