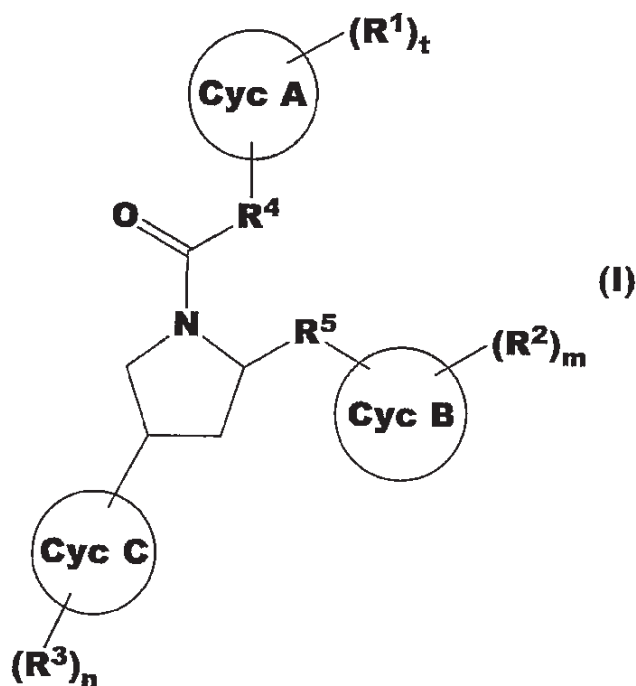


# CLAIMS

1. A compound represented by formula (I):



wherein Cyc A represents C3-C6 cycloalkyl, 5- to 6-membered heterocycloalkyl, C6-C10 aryl or 5- to 10-membered heteroaryl;

Cyc B represents C6-C10 aryl or 5- to 10-membered heteroaryl;

Cyc C represents 5- to 10-membered heterocycloalkyl,;

each  $R^1$  may be the same or different and represents (1)  $-C(=NH)NH_2$ , (2) 5- to 10-membered heteroaryl, (3) C6-C10 aryl or 5- to 10-membered heteroaryl substituted with 1 to 5 groups selected from halogen, C1-4 alkyl, C1-4 alkoxy, -C1-4 alkylene-C1-4 alkoxy, CN,  $-COOH$ ,  $-COO-C1-4$  alkyl,  $-CO-NH_2$ ,  $-OCONH_2$ ,  $-OCONH-C1-4$  alkyl,  $-CONH-C1-4$  alkyl,  $-NHCOO-C1-4$  alkyl and  $-NHCO-C1-4$  alkyl, (4) C6-C10 aryl, (5)  $-NH-C(=NH)NH_2$ , (6) C1-4 alkyl, (7) C2-4 alkenyl, (8) C2-4 alkynyl, (9)  $-C1-4$  alkylene- $NH_2$ , (10) C1-4 alkoxy, (11) CN, (12)  $-CO-C1-4$  alkyl, (13) halogen or (14)  $-R^{10}-C(=NR^{11})NR^{12}R^{13}$ ,

wherein  $R^{10}$  represents (1) a bond or (2) NH;

$R^{11}$ ,  $R^{12}$  and  $R^{13}$  each independently represents (1) hydrogen, (2) OH, (3) C1-4 alkyl, (4) C2-4 alkenyl, (5) C2-4 alkynyl, (6) C1-4 alkoxy, (7) -C1-4 alkylene-C1-4 alkoxy, (8) -CO-C1-4 alkyl, (9) -COO-C1-4 alkyl, (10) -OCO-C1-4 alkyl, (11) -CO- $R^{14}$ , (12) -COO- $R^{15}$  or (13) -OCO- $R^{16}$ , with the proviso that  $R^{11}$ ,  $R^{12}$  and  $R^{13}$  do not all simultaneously represent hydrogen;

wherein  $R^{14}$ ,  $R^{15}$  and  $R^{16}$  each independently represents C1-4 alkyl, C2-4 alkenyl or C2-4 alkynyl, which are substituted with 1 to 5 groups selected from C1-4 alkyl, C2-4 alkenyl, C2-4 alkynyl, halogen, trifluoromethyl, OH, -COO-C1-4 alkyl, COOH, oxo, C1-4 alkoxy, C6-C10 aryl, 5- to 10-membered heteroaryl and  $NR^{17}R^{18}$ ;

wherein  $R^{17}$  and  $R^{18}$  each independently represents (1) hydrogen, (2) C1-4 alkyl, (3) C2-4 alkenyl or (4) C2-4 alkynyl;

t represents an integer of 0 to 6;

each  $R^2$  may be the same or different and represents (1) -COOH, (2) -COO-C1-4 alkyl, (3) -COO-C1-4 alkylene-C1-4 alkoxy, (4) -NH<sub>2</sub>, (5) -NH-C1-4 alkyl, (6) -NH-C1-4 alkylene-C1-4 alkoxy, (7) -NHCO-C1-4 alkyl, (8) -NHCO-C1-4 alkylene-C1-4 alkoxy, (9) -NHCOO-C1-4 alkyl, (10) -NHCOO-C1-4 alkylene-C1-4 alkoxy, (11) -CONH<sub>2</sub>, (12) -CONH-C1-4 alkyl, (13) -CONH-C2-4 alkylene-C1-4 alkoxy, (14) halogen, (15) -SO<sub>2</sub>-C1-4 alkyl, (16) oxo, (17) C1-4 alkoxy, (18) -CO-C1-4 alkyl, (19) -CO-C1-4 alkylene-C1-4 alkoxy or (20) -COO-C1-4 alkyl substituted with 1 to 5 groups selected from C1-4 alkyl, C2-4 alkenyl, C2-4 alkynyl, halogen, trifluoromethyl, OH, -COO-C1-4 alkyl, COOH, oxo, C1-4 alkoxy, C6-C10 aryl, 5- to 10-membered heteroaryl and  $NR^{19}R^{20}$ ;

wherein  $R^{19}$  and  $R^{20}$  each independently represents (1) hydrogen, (2) C1-4 alkyl, (3) C2-4 alkenyl or (4) C2-4 alkynyl;

m represents an integer of 0 to 6;

each  $R^3$  may be the same or different and represents (1)  $-SO_2-R^6-R^7$ , (2) oxo, (3)  $-CO-C1-4$  alkyl, (4)  $-CO-NH_2$ , (5)  $-SO_2-NH_2$  or (6)  $-COO-C1-4$  alkyl;

n represents an integer of 0 to 6;

$R^6$  represents (1) a bond or (2)  $NH$ ;

$R^7$  represents (1)  $C1-4$  alkyl, (2) Cyc D or (3)  $C1-4$  alkyl or Cyc D substituted with 1 to 5  $R^8$ ;

wherein Cyc D represents  $C3-C8$  cycloalkyl, 5- to 10-membered heterocycloalkyl,  $C6-C10$  aryl or 5- to 10-membered heteroaryl;

each  $R^8$  may be the same or different and represents (1)  $-COOH$ , (2)  $-COO-C1-4$  alkyl, (3)  $-COO-C1-4$  alkylene- $C1-4$  alkoxy, (4)  $-NH_2$ , (5)  $-NH-C1-4$  alkyl, (6)  $-NHCO-C1-4$  alkyl, (8)  $-CONH_2$ , (12)  $-CONH-C1-4$  alkyl (13)  $OH$  or (14) halogen;

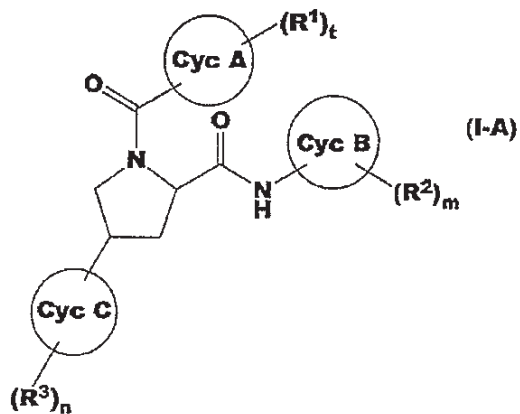
$R^4$  represents (1) a bond, (2)  $C1-4$  alkylene, (3)  $C2-4$  alkenylene or (4)  $C2-4$  alkynylene;

$R^5$  represents (1)  $-CONH-$ , (2) Cyc E or (3) Cyc E substituted with 1 to 5  $R^9$ ;

wherein Cyc E represents 5- to 10-membered heteroaryl; and

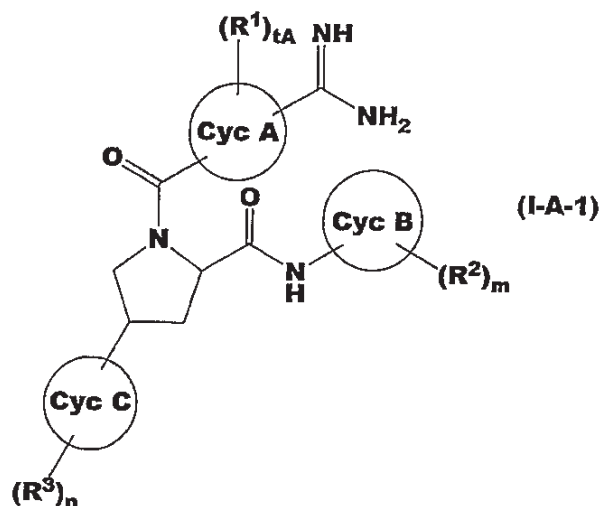
each  $R^9$  may be the same or different and represents  $C1-4$  alkyl or halogen; a salt thereof or a solvate thereof.

2. The compound according to claim 1, wherein the compound represented by formula (I) represents a compound represented by formula (I-A):



- 15 wherein all symbols have the same meanings as described in claim 1.

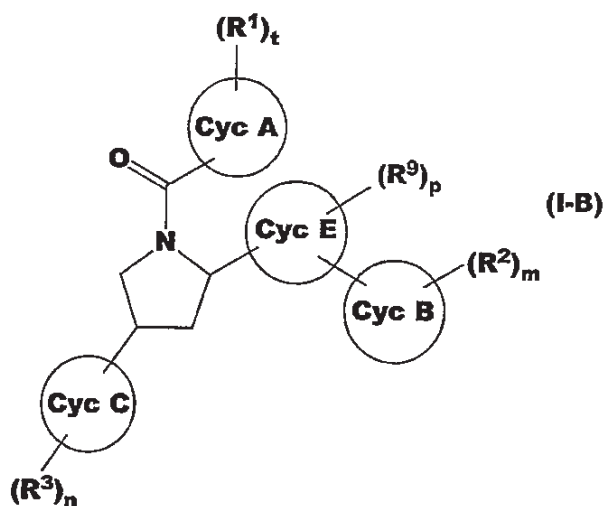
3. The compound according to claim 2, wherein the compound represented by formula (I-A) represents a compound represented by formula (I-A-1):



wherein  $t_A$  represents an integer of 0 to 5; and

the other symbols have the same meanings as described in claim 1.

- 5            4. The compound according to claim 1, wherein the compound represented by formula (I) represents a compound represented by formula (I-B):

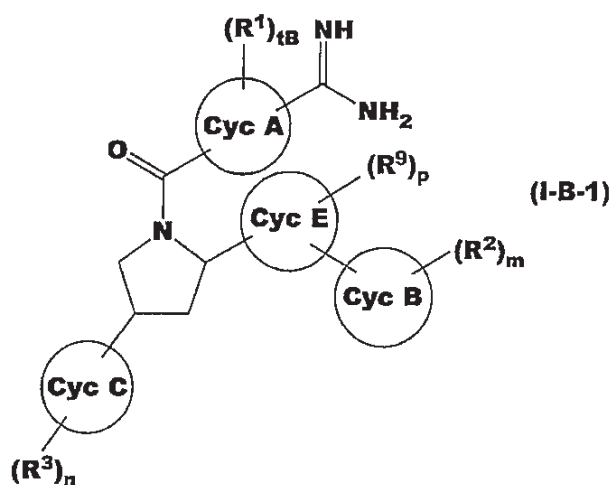


wherein  $p$  represents an integer of 0 to 5; and

the other symbols have the same meanings as described in claim 1.

10

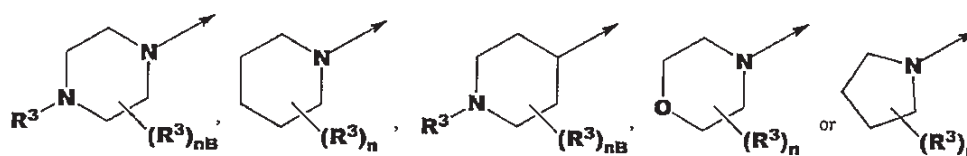
5. The compound according to claim 4, wherein the compound represented by formula (I-B) represents a compound represented by formula (I-B-1):



wherein  $tB$  represents an integer of 0 to 5; and

the other symbols have the same meanings as described in claim 1.

- 5            6. The compound according to claim 4 or 5, wherein Cyc E represents imidazolyl.
7. The compound according to any one of the preceding claims, wherein Cyc A represents C3-C6 cycloalkyl, C6-C10 aryl or 5- to 6-membered heterocycloalkyl.
- 10           8. The compound according to claim 7, wherein Cyc A represents cyclohexyl, phenyl, piperidinyl or piperazinyl.
9. The compound according to any one of the preceding claims, wherein Cyc B represents C6-C10 aryl or 5- to 6-membered heteroaryl.
- 15           10. The compound according to claim 9, wherein Cyc B represents phenyl or pyridyl.
11. The compound according to any one of the preceding claims, wherein
- 20           Cyc C represents pyrrolidinyl, piperidinyl, piperazinyl or morpholinyl.
12. The compound according to any one of claims 1 to 11, wherein -Cyc C -  $(R^3)_n$  represents



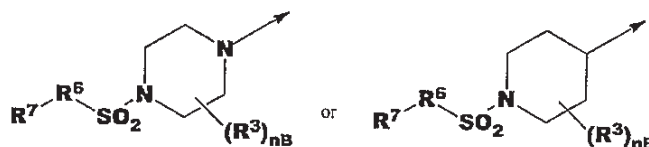
wherein nB represents an integer of 0 to 5;

the arrow represents a binding position; and

the other symbols have the same meanings as described in claim 1.

5

13. The compound according to claim 12, wherein -Cyc C -(R³)<sub>n</sub> represents



wherein the arrow represents a binding position; and

the other symbols have the same meanings as described in claim 1.

10

14. The compound according to any one of claims 1 to 5, wherein the compound is selected from the group consisting of

- (1) 4-[(2S,4S)-1-[(1-carbamimidoyl-4-piperidiny]carbonyl]-4-[4-(methylsulfonyl)-1-piperazinyl]-2-pyrrolidinyl]carbonyl]amino]benzoic acid,
- (2) 4-[(2S,4S)-1-(4-carbamimidoylbenzoyl)-4-[4-(methylsulfonyl)-1-piperazinyl]-2-pyrrolidinyl]carbonyl]amino]benzoic acid,
- (3) 4-[(2S,4S)-1-[(2E)-3-[5-chloro-2-(1H-tetrazol-1-yl)]phenyl]-2-propenoyl]-4-(4-morpholinyl)-2-pyrrolidinyl]carbonyl]amino]benzoic acid,
- (4) (2S,4S)-1-[(2E)-3-[5-chloro-2-(1H-tetrazol-1-yl)]phenyl]-2-propenoyl]-N-phenyl-4-[4-(phenylsulfonyl)-1-piperazinyl]-2-pyrrolidinecarboxamide,
- (5) (2S,4S)-N-(1H-benzotriazol-6-yl)-1-[(2E)-3-[5-chloro-2-(1H-tetrazol-1-yl)]phenyl]-2-propenoyl]-4-(4-morpholinyl)-2-pyrrolidinecarboxamide,
- (6) 4-[(2S,4S)-1-[(trans-4-(aminomethyl)cyclohexyl]carbonyl]-4-[4-(cyclopropylsulfonyl)-1-piperazinyl]-2-pyrrolidinyl]carbonyl]amino]benzoic acid,
- (7) (2S,4S)-1-[(2E)-3-[5-chloro-2-(1H-tetrazol-1-yl)]phenyl]-2-propenoyl]-4-[(3S)-3-methyl-4-sulfamoyl-1-piperazinyl]-N-phenyl-2-pyrrolidinecarboxamide,
- (8) methyl [4-(2-[(2S,4R)-1-[(1-carbamimidoyl-4-piperidiny]carbonyl]-4-[1-(methylsulfonyl)-4-piperidiny]-2-pyrrolidinyl]-1H-imidazol-5-yl)]phenyl]carbamate,

25

20

15

- (9) methyl [4-(2-((2S,4R)-1-(4-carbamimidoylbenzoyl)-4-[1-(methylsulfonyl)-4-piperidinyl]-2-pyrrolidinyl)-1H-imidazol-5-yl)phenyl]carbamate,
- (10) methyl [4-(2-((2S,4R)-1-(4-carbamimidamidobenzoyl)-4-[1-(methylsulfonyl)-4-piperidinyl]-2-pyrrolidinyl)-4-chloro-1H-imidazol-5-yl)phenyl]carbamate,
- (11) methyl [4-(2-((2S,4R)-1-({trans-4-[(1S)-1-aminoethyl]cyclohexyl} carbonyl)-4-[1-(methylsulfonyl)-4-piperidinyl]-2-pyrrolidinyl)-4-chloro-1H-imidazol-5-yl)phenyl]carbamate,
- (12) methyl [4-(2-((2S,4R)-1-[(4-carbamimidoyl-1-piperazinyl)carbonyl]-4-[1-(methylsulfonyl)-4-piperidinyl]-2-pyrrolidinyl)-4-chloro-1H-imidazol-5-yl)phenyl]carbamate,
- (13) 4-[(2S,4R)-1-[(3-chloro-4-fluoro-1-methyl-1H-indol-5-yl)carbonyl]-4-[1-(methylsulfonyl)-4-piperidinyl]-2-pyrrolidinyl] carbonyl]amino]benzoic acid,
- (14) methyl [4-(4-chloro-2-((2S,4R)-1-((2E)-3-[5-chloro-2-(1H-tetrazol-1-yl)phenyl]-2-propenoyl)-4-[1-(methylsulfonyl)-4-piperidinyl]-2-pyrrolidinyl)-1H-imidazol-5-yl)phenyl]carbamate,
- (15) methyl [4-(2-((2S,4R)-1-([4-(aminomethyl)cyclohexyl]carbonyl)-4-[1-(methylsulfonyl)-4-piperidinyl]-2-pyrrolidinyl)-4-chloro-1H-imidazol-5-yl)phenyl]carbamate,
- (16) methyl [4-(2-((2S,4S)-1-[(1-carbamimidoyl-4-piperidinyl)carbonyl]-4-[4-(methylsulfonyl)-1-piperazinyl]-2-pyrrolidinyl)-1H-imidazol-5-yl)phenyl]carbamate,
- (17) methyl [4-(2-((2S,4R)-1-[(1-carbamimidoyl-4-piperidinyl)carbonyl]-4-[1-(methylsulfonyl)-4-piperidinyl]-2-pyrrolidinyl)-4-chloro-1H-imidazol-5-yl)phenyl]carbamate,
- (18) methyl [4-(2-((2S,4R)-1-(4-carbamimidoylbenzoyl)-4-[1-(methylsulfonyl)-4-piperidinyl]-2-pyrrolidinyl)-4-chloro-1H-imidazol-5-yl)phenyl]carbamate,
- (19) methyl [4-(2-((2S,4S)-1-(4-carbamimidoylbenzoyl)-4-[4-(methylsulfonyl)-1-piperazinyl]-2-pyrrolidinyl)-1H-imidazol-5-yl)phenyl]carbamate,
- (20) methyl [4-(2-((2S,4S)-1-[(1-carbamimidoyl-4-piperidinyl)carbonyl]-4-[4-(methylsulfonyl)-1-piperazinyl]-2-pyrrolidinyl)-4-chloro-1H-imidazol-5-yl)phenyl]carbamate and

(21) 4-[(2S,4R)-1-(4-carbanimidoylbenzoyl)-4-[1-(methylsulfonyl)-4-piperidinyl]-2-pyrrolidinyl]carbonylamino]benzoic acid.

15 15. A pharmaceutical composition which comprises the compound according to any one of claims 1 to 14, a salt thereof, or a solvate thereof.

10 16. The pharmaceutical composition according to claim 15, which is a factor XIa inhibitor.

17. The pharmaceutical composition according to claim 16, which is an agent for the treatment or prevention of a thromboembolic disease.

15 18. The compound according to any one of claims 1 to 14 for use in treating or preventing a thromboembolic disease.

20 19. The compound for use according to claim 18, wherein the thromboembolic disease is selected from the group consisting of arterial cardiovascular thromboembolic disorders, venous cardiovascular thromboembolic disorders, arterial cerebrovascular thromboembolic disorders, venous cerebrovascular thromboembolic disorders and thromboembolic disorders in the chambers of the heart or in the peripheral circulation.

25 20. The compound for use according to claim 19, wherein the thromboembolic disease is selected from disseminated intravascular coagulopathy (DIC), sepsis, angina, unstable angina, an acute coronary syndrome, coronary artery disease, myocardial infarction, atrial fibrillation, ischemic sudden death, transient ischemic attack, stroke, acute stroke, atherothrombosis, atherosclerosis, peripheral occlusive arterial disease, venous thrombosis, deep vein thrombosis, thrombophlebitis, 30 arterial embolism, coronary arterial thrombosis, cerebral thrombosis, cerebral arterial thrombosis, cerebral embolism, cardiogenic embolism, kidney embolism, portal vein thrombosis, pulmonary embolism, pulmonary infarction, liver embolism, mesenteric artery and/or vein embolism, occlusion of retinal vein and/or artery, systemic embolism,

antiphospholipid antibody syndrome, thrombosis resulting from coronary artery bypass graft surgery and thrombosis resulting from medical implants, devices, or procedures in which blood is exposed to an artificial surface that promotes thrombosis.

5           21. Use of a compound according to any one of claims 1 to 14, in the manufacture of a medicament for use in treating or preventing a thromboembolic disease.

10           22. The use according to claim 21 wherein the thromboembolic disease is selected from the group consisting of arterial cardiovascular thromboembolic disorders, venous cardiovascular thromboembolic disorders, arterial cerebrovascular thromboembolic disorders, venous cerebrovascular thromboembolic disorders and thromboembolic disorders in the chambers of the heart or in the peripheral circulation.

15           23. The use according to claim 22 wherein the thromboembolic disease is selected from disseminated intravascular coagulopathy (DIC), sepsis, angina, unstable angina, an acute coronary syndrome, coronary artery disease, myocardial infarction, atrial fibrillation, ischemic sudden death, transient ischemic attack, stroke, acute stroke, atherothrombosis, atherosclerosis, peripheral occlusive arterial disease, venous  
20 thrombosis, deep vein thrombosis, thrombophlebitis, arterial embolism, coronary arterial thrombosis, cerebral thrombosis, cerebral arterial thrombosis, cerebral embolism, cardiogenic embolism, kidney embolism, portal vein thrombosis, pulmonary embolism, pulmonary infarction, liver embolism, mesenteric artery and/or vein embolism, occlusion of retinal vein and/or artery, systemic embolism, antiphospholipid  
25 antibody syndrome, thrombosis resulting from coronary artery bypass graft surgery and thrombosis resulting from medical implants, devices, or procedures in which blood is exposed to an artificial surface that promotes thrombosis.

30           24. 4-[(2S,4S)-1-(4-carbamimidoylbenzoyl)-4-[4-(methylsulfonyl)-1-piperazinyl]-2-pyrrolidinyl]carbonyl)amino]benzoic acid or a salt thereof.