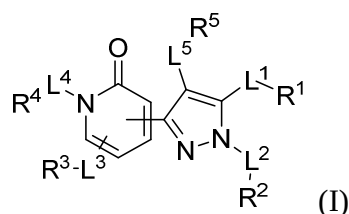


CLAIMS

1. A compound comprising a substituted or unsubstituted pyridone ring attached to a substituted or unsubstituted pyrazole ring with structure of Formula (I):



or pharmaceutically acceptable salt thereof;

wherein

L^1 is $-NR^6-$;

L^2 is $-C(=O)-$;

L^4 is a bond, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, $-S-$, $-SO-$, or $-SO_2-$;

L^3 and L^5 are independently a bond, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, or $-O-$;

R^1 is halogen, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkenyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted heterocycloalkenyl, substituted or unsubstituted aryl, substituted or unsubstituted fused ring aryl, or substituted or unsubstituted heteroaryl;

R^2 is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkenyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted heterocycloalkenyl, substituted or unsubstituted aryl, substituted or unsubstituted fused ring aryl, or substituted or unsubstituted heteroaryl;

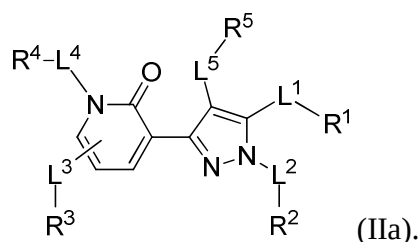
R^4 is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkenyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted heterocycloalkenyl,

substituted or unsubstituted aryl, substituted or unsubstituted fused ring aryl, or substituted or unsubstituted heteroaryl;

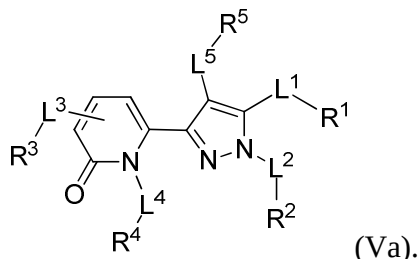
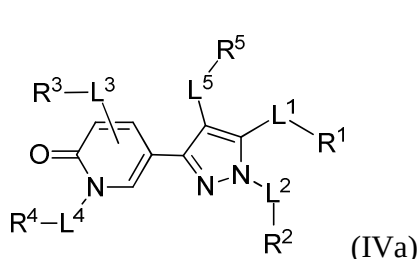
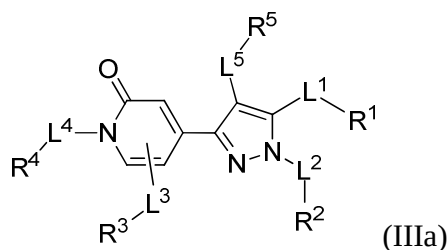
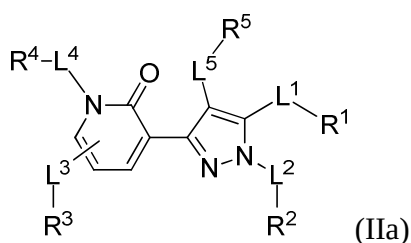
R^3 and R^5 are independently hydrogen, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; and

R^6 is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

provided that if the compound has a structure according to Formula (IIa), as follows, either L^3 is not a bond or R^3 is not hydrogen:



2. The compound according to claim 1, with structure of Formula (IIa), Formula (IIIa), Formula (IVa), or Formula (Va):



3. The compound according to claim 2, wherein R^2 is hydrogen.

4. The compound according to any of Formula (IIIa), Formula (IVa), or Formula (Va) as set forth in claim 2, wherein L^3 is a bond, and R^3 is hydrogen.
5. The compound according to claim 2, wherein L^4 is a bond and R^4 is hydrogen.
6. The compound according to claim 2, wherein L^5 is a bond, and R^5 is hydrogen.
7. The compound according to claim 2, wherein L^2 is $-C(O)-$, and R^2 is substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkenyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted heterocycloalkenyl, substituted or unsubstituted aryl, substituted or unsubstituted fused ring aryl, or substituted or unsubstituted heteroaryl.
8. The compound according to claim 7, wherein R^2 is substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl.
9. The compound according to claim 8, wherein R^2 is substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl selected from the group consisting of phenyl, 2-chlorophenyl, 2-methoxyphenyl, phenyl-3-carboxylic acid, phenyl-3-carboxamide, 3-(hydroxymethyl)phenyl, phenyl-4-carboxylic acid, phenyl-4-carboxamide, 4-(hydroxymethyl)phenyl, 2-thienyl, 3-thienyl, 2-furyl, 3-furyl, 1,3-thiazol-2-yl, 1,3-thiazol-4-yl, 1,3-thiazol-5-yl, 1,3-oxazol-2-yl, 1,3-oxazol-4-yl, and 1,3-oxazol-5-yl.
10. The compound according to claim 7, wherein R^2 is substituted or unsubstituted alkyl.
11. The compound according to claim 10, wherein R^2 is *tert*-butyl, 1,1-dimethyl-2-hydroxy-ethyl, 1,1-dimethyl-2-methoxy-ethyl, or 1,1-dimethyl-2-cyclopropoxy-ethyl.
12. The compound according to claim 2, wherein R^1 is substituted alkyl.
13. The compound according to claim 12, wherein R^1 is substituted alkyl, wherein said R^1 substituted alkyl has a substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl substituent group selected from the group consisting of phenyl, 4-fluorophenyl, 4-chlorophenyl, 2-thienyl, or 5-chloro-thien-2-yl, 1,3-thiazol-2-yl, 1,3-thiazol-4-yl, 2-chloro-1,3-thiazol-5-yl, and 5-chloro-1,3-thiazol-2-yl.

14. The compound according to claim 2, wherein L^4 is a bond or substituted or unsubstituted alkylene, and R^4 is substituted or unsubstituted aryl, substituted or unsubstituted fused ring aryl, or substituted or unsubstituted heteroaryl.

15. The compound according to claim 14, wherein R^4 is substituted or unsubstituted heteroaryl selected from the group consisting of substituted or unsubstituted pyridyl, substituted or unsubstituted pyridazinyl, substituted or unsubstituted pyrimidinyl, substituted or unsubstituted thienyl, and substituted or unsubstituted furyl.

16. The compound according to claim 2, wherein L^4 is substituted or unsubstituted alkylene, and R^4 is substituted or unsubstituted heterocycloalkyl.

17. The compound according to claim 16, wherein R^4 is substituted or unsubstituted heterocycloalkyl selected from the group consisting of substituted or unsubstituted morpholinyl, substituted or unsubstituted oxanyl, and substituted or unsubstituted oxetanyl.

18. The compound according to claim 2, wherein L^4 is a bond, and R^4 is substituted or unsubstituted alkyl or substituted or unsubstituted heteroalkyl.

19. The compound according to claim 2, wherein L^3 is bond, and R^3 is halogen, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl.

20. The compound according to claim 19, wherein R^3 is substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl selected from the group consisting of substituted or unsubstituted phenyl, substituted or unsubstituted pyridyl, substituted or unsubstituted pyridazinyl, substituted or unsubstituted pyrimidinyl, substituted or unsubstituted thienyl, and substituted or unsubstituted furyl.

21. The compound according to claim 19, wherein R^3 is substituted or unsubstituted alkyl or substituted or unsubstituted heteroalkyl selected from the group consisting of methyl and cyano.

22. The compound according to claim 1, wherein L^5 is bond, and R^5 is hydrogen, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl.

23. The compound according to claim 1, wherein the compound is selected from the group consisting of:

Compound 1, 3-(5-{[(5-chlorothiophen-2-yl)methyl]amino}-1-(2,2-dimethylpropanoyl)-1H-pyrazol-3-yl)-5-(morpholin-4-yl)-1,2-dihydropyridin-2-one;

Compound 2, 3-(5-{[(5-chlorothiophen-2-yl)methyl]amino}-1-(2,2-dimethylpropanoyl)-1H-pyrazol-3-yl)-5-phenyl-1,2-dihydropyridin-2-one;

Compound 3, 3-(5-{[(5-chlorothiophen-2-yl)methyl]amino}-1-(2-methoxybenzoyl)-1H-pyrazol-3-yl)-5-(pyridin-3-yl)-1,2-dihydropyridin-2-one;

Compound 4, 3-(5-{[(5-chlorothiophen-2-yl)methyl]amino}-1-(furan-3-carbonyl)-1H-pyrazol-3-yl)-5-methyl-1,2-dihydropyridin-2-one;

Compound 5, 3-bromo-5-(5-{[(5-chlorothiophen-2-yl)methyl]amino}-1-(2-methoxybenzoyl)-1H-pyrazol-3-yl)-1,2-dihydropyridin-2-one;

Compound 7, 3-bromo-6-(5-{[(5-chlorothiophen-2-yl)methyl]amino}-1-(furan-3-carbonyl)-1H-pyrazol-3-yl)-1,2-dihydropyridin-2-one;

Compound 8, 4-(5-{[(5-chlorothiophen-2-yl)methyl]amino}-1-(2,2-dimethylpropanoyl)-1H-pyrazol-3-yl)-1,2-dihydropyridin-2-one;

Compound 9, 4-(5-{[(5-chlorothiophen-2-yl)methyl]amino}-1-(2,2-dimethylpropanoyl)-1H-pyrazol-3-yl)-1-(2-methoxyethyl)-1,2-dihydropyridin-2-one;

Compound 10, 4-(5-{[(5-chlorothiophen-2-yl)methyl]amino}-1-(2,2-dimethylpropanoyl)-1H-pyrazol-3-yl)-1-(pyridin-2-ylmethyl)-1,2-dihydropyridin-2-one;

Compound 11, 4-(5-{[(5-chlorothiophen-2-yl)methyl]amino}-1-(2,2-dimethylpropanoyl)-1H-pyrazol-3-yl)-1-(pyridin-3-ylmethyl)-1,2-dihydropyridin-2-one;

Compound 12, 4-(5-{[(5-chlorothiophen-2-yl)methyl]amino}-1-(2,2-dimethylpropanoyl)-1H-pyrazol-3-yl)-1-[2-(morpholin-4-yl)-2-oxoethyl]-1,2-dihydropyridin-2-one;

Compound 13, 4-(5-{[(5-chlorothiophen-2-yl)methyl]amino}-1-(2,2-dimethylpropanoyl)-1H-pyrazol-3-yl)-6-(morpholin-4-yl)-1,2-dihydropyridin-2-one;

Compound 14, 4-(5-{[(5-chlorothiophen-2-yl)methyl]amino}-1-(2-methoxybenzoyl)-1H-pyrazol-3-yl)-6-ethenyl-1,2-dihydropyridin-2-one;

Compound 15, 4-(5-[[5-chlorothiophen-2-yl)methyl]amino}-1-(furan-2-carbonyl)-1H-pyrazol-3-yl)-6-(pyridin-3-yl)-1,2-dihydropyridin-2-one;

Compound 16, 4-(5-[[5-chlorothiophen-2-yl)methyl]amino}-1-(furan-3-carbonyl)-1H-pyrazol-3-yl)-1,2-dihydropyridin-2-one;

Compound 17, 4-(5-[[5-chlorothiophen-2-yl)methyl]amino}-1-(furan-3-carbonyl)-1H-pyrazol-3-yl)-1-(2-methoxyethyl)-1,2-dihydropyridin-2-one;

Compound 18, 4-(5-[[5-chlorothiophen-2-yl)methyl]amino}-1-(furan-3-carbonyl)-1H-pyrazol-3-yl)-1-(pyridin-2-ylmethyl)-1,2-dihydropyridin-2-one;

Compound 19, 4-(5-[[5-chlorothiophen-2-yl)methyl]amino}-1-(furan-3-carbonyl)-1H-pyrazol-3-yl)-1-(pyridin-3-ylmethyl)-1,2-dihydropyridin-2-one;

Compound 20, 4-(5-[[5-chlorothiophen-2-yl)methyl]amino}-1-(furan-3-carbonyl)-1H-pyrazol-3-yl)-1-[2-(morpholin-4-yl)-2-oxoethyl]-1,2-dihydropyridin-2-one;

Compound 21, 4-(5-[[5-chlorothiophen-2-yl)methyl]amino}-1-(furan-3-carbonyl)-1H-pyrazol-3-yl)-1-[2-(morpholin-4-yl)ethyl]-1,2-dihydropyridin-2-one;

Compound 22, 4-(5-[[5-chlorothiophen-2-yl)methyl]amino}-1-(thiophene-3-carbonyl)-1H-pyrazol-3-yl)-1,2-dihydropyridin-2-one;

Compound 23, 4-(5-[[5-chlorothiophen-2-yl)methyl]amino}-1-(thiophene-3-carbonyl)-1H-pyrazol-3-yl)-1-(2-methoxyethyl)-1,2-dihydropyridin-2-one;

Compound 24, 4-(5-[[5-chlorothiophen-2-yl)methyl]amino}-1-(thiophene-3-carbonyl)-1H-pyrazol-3-yl)-1-(pyridin-2-ylmethyl)-1,2-dihydropyridin-2-one;

Compound 25, 4-(5-[[5-chlorothiophen-2-yl)methyl]amino}-1-(thiophene-3-carbonyl)-1H-pyrazol-3-yl)-1-(pyridin-3-ylmethyl)-1,2-dihydropyridin-2-one;

Compound 26, 4-(5-[[5-chlorothiophen-2-yl)methyl]amino}-1-(thiophene-3-carbonyl)-1H-pyrazol-3-yl)-1-[2-(morpholin-4-yl)-2-oxoethyl]-1,2-dihydropyridin-2-one;

Compound 27, 4-(5-[[5-chlorothiophen-2-yl)methyl]amino}-1-(thiophene-3-carbonyl)-1H-pyrazol-3-yl)-1-[2-(morpholin-4-yl)ethyl]-1,2-dihydropyridin-2-one;

Compound 28, 4-(5-[[5-chlorothiophen-2-yl)methyl]amino}-1-(thiophene-3-carbonyl)-1H-pyrazol-3-yl)-6-phenyl-1,2-dihydropyridin-2-one;

Compound 31, 5-(5-[[[(5-chlorothiophen-2-yl)methyl]amino]-1-(2,2-dimethylpropanoyl)-1H-pyrazol-3-yl]-1,2-dihydropyridin-2-one;

Compound 32, 5-(5-[[[(5-chlorothiophen-2-yl)methyl]amino]-1-(2,2-dimethylpropanoyl)-1H-pyrazol-3-yl]-1-[2-(morpholin-4-yl)-2-oxoethyl]-1,2-dihydropyridin-2-one;

Compound 33, 5-(5-[[[(5-chlorothiophen-2-yl)methyl]amino]-1-(2,2-dimethylpropanoyl)-1H-pyrazol-3-yl]-3-(pyridin-3-yl)-1,2-dihydropyridin-2-one;

Compound 34, 5-(5-[[[(5-chlorothiophen-2-yl)methyl]amino]-1-(2,2-dimethylpropanoyl)-1H-pyrazol-3-yl]-3-methyl-1,2-dihydropyridin-2-one;

Compound 35, 5-(5-[[[(5-chlorothiophen-2-yl)methyl]amino]-1-(2,2-dimethylpropanoyl)-1H-pyrazol-3-yl]-3-phenyl-1,2-dihydropyridin-2-one;

Compound 36, 5-(5-[[[(5-chlorothiophen-2-yl)methyl]amino]-1-(2-methoxybenzoyl)-1H-pyrazol-3-yl]-6-oxo-1,6-dihydropyridine-3-carbonitrile;

Compound 37, 5-(5-[[[(5-chlorothiophen-2-yl)methyl]amino]-1-(thiophene-3-carbonyl)-1H-pyrazol-3-yl]-1,2-dihydropyridin-2-one;

Compound 39, 5-bromo-3-(5-[[[(5-chlorothiophen-2-yl)methyl]amino]-1-(2,2-dimethylpropanoyl)-1H-pyrazol-3-yl]-1,2-dihydropyridin-2-one;

Compound 40, 5-bromo-3-(5-[[[(5-chlorothiophen-2-yl)methyl]amino]-1-(2,2-dimethylpropanoyl)-1H-pyrazol-3-yl]-1-[2-(morpholin-4-yl)-2-oxoethyl]-1,2-dihydropyridin-2-one;

Compound 41, 5-bromo-3-(5-[[[(5-chlorothiophen-2-yl)methyl]amino]-1-(thiophene-3-carbonyl)-1H-pyrazol-3-yl]-1,2-dihydropyridin-2-one;

Compound 43, 6-(5-[[[(5-chlorothiophen-2-yl)methyl]amino]-1-(2,2-dimethylpropanoyl)-1H-pyrazol-3-yl]-1,2-dihydropyridin-2-one;

Compound 44, 6-(5-[[[(5-chlorothiophen-2-yl)methyl]amino]-1-(2,2-dimethylpropanoyl)-1H-pyrazol-3-yl]-1-(pyridin-2-ylmethyl)-1,2-dihydropyridin-2-one;

Compound 45, 6-(5-[[[(5-chlorothiophen-2-yl)methyl]amino]-1-(2,2-dimethylpropanoyl)-1H-pyrazol-3-yl]-1-[2-(morpholin-4-yl)-2-oxoethyl]-1,2-dihydropyridin-2-one;

Compound 46, 6-(5-[[[(5-chlorothiophen-2-yl)methyl]amino]-1-(2,2-dimethylpropanoyl)-1H-pyrazol-3-yl]-3-ethenyl-1,2-dihydropyridin-2-one; and

Compound 48, 6-bromo-4-(5-[[[(5-chlorothiophen-2-yl)methyl]amino]-1-(2,2-dimethylpropanoyl)-1H-pyrazol-3-yl]-1,2-dihydropyridin-2-one.

24. A pharmaceutical composition comprising a compound according to claim 1, and a pharmaceutically acceptable excipient.

25. Use of a compound according to any of claims 1 to 23 or a pharmaceutical composition according to claim 24, in the manufacture of a medicament for the treatment of a disease or disorder, wherein said disease or disorder is selected from the group consisting of: a thrombotic disorder selected from the group consisting of acute coronary syndrome, thromboembolism, and thrombosis; a disease or disorder involving a blood clot thrombus; a fibrinolytic disease; fibrosis; multiple sclerosis; neuropathic pain; Type I diabetes mellitus; chronic liver injury; ischemia reperfusion injury; a type of cancer selected from the group consisting of cervical-, testicular-, and non-small-cell lung adenocarcinoma, limited small lung cancer, glioma, malignant breast cancer, micrometastasis, lung metastasis, and prostatic cancer; an inflammatory condition selected from the group consisting of sepsis, inflammatory bowel disease, systemic inflammatory response syndrome, hereditary angioedema, and rheumatoid arthritis; a dermatological condition selected from the group consisting of atopic dermatitis, psoriasis, and Netherton Syndrome; and an ophthalmic disease selected from the group consisting of diabetic macular edema, age-related macular degeneration, and diabetic retinopathy.

26. The use according to claim 25, wherein said disease or disorder is at least one of a thrombotic disorder selected from the group consisting of acute coronary syndrome, thromboembolism, and thrombosis, or a disease or disorder involving a blood clot thrombus.

27. The use according to claim 26, wherein said thrombotic disorder comprises at least one of acute coronary syndrome, thromboembolism, and thrombosis.

28. The use according to claim 26, wherein said compound acts by inhibiting thrombin, or at least one of plasma kallikrein and tissue kallikrein.

29. The use according to claim 26, wherein said kallikrein-related disorder is one or more selected from the group consisting of a fibrinolytic disease; a type of cancer selected from the group consisting of cervical-, testicular-, and non-small-cell lung adenocarcinoma; an inflammatory condition selected from the group consisting of sepsis, inflammatory bowel disease, systemic inflammatory response syndrome, hereditary angioedema, and rheumatoid arthritis; a dermatological condition selected from the group consisting of atopic dermatitis, psoriasis, and Netherton Syndrome; an ophthalmic disease selected from the group consisting of diabetic macular edema, age-related macular degeneration, and diabetic retinopathy; or wherein said disease or disorder is selected from the group consisting of fibrosis, multiple sclerosis, a type of cancer selected from the group consisting of limited small lung cancer, glioma, malignant breast cancer, micrometastasis, lung metastasis, and prostatic cancer, and Type I diabetes mellitus.

30. The use according to claim 27, wherein said thromboembolism comprises at least one of venous thromboembolism, arterial thromboembolism, and cardiogenic thromboembolism.

31. The use according to claim 30, wherein said venous thromboembolism comprises at least one of deep vein thrombosis and pulmonary embolism, or wherein said venous thromboembolism is associated with at least one of formation of a thrombus within a vein that is associated with one or more acquired or inherited risk factors and embolism of peripheral veins caused by a detached thrombus.

32. The use according to claim 27, wherein said thrombotic disorder involves dysfunctional coagulation or disseminated intravascular coagulation, or wherein said thrombotic disorder involves a blood clot thrombus and further involves at least one of stroke and one or more transient ischemic attacks (TIA), or wherein said thrombotic disorder involves a blood clot thrombus and further involves pulmonary hypertension.

33. The use according to claim 32, wherein the subject is undergoing percutaneous coronary intervention (PCI), or wherein said thrombotic disorder involving a blood clot thrombus further involves stroke and wherein the subject has non-valvular atrial fibrillation.

34. The use according to claim 32, wherein said pulmonary hypertension is associated with at least one or more lung diseases selected from the group consisting of idiopathic pulmonary fibrosis, non-idiopathic pulmonary fibrosis, and hypoxia.

35. The use according to claim 30, wherein said cardiogenic thromboembolism is due to formation of a thrombus in the heart associated with at least one of cardiac arrhythmia, a heart valve defect, prosthetic heart valves or heart disease, and embolism of peripheral arteries caused by a detached thrombus, or wherein said cardiogenic thromboembolism is due to non-valvular atrial fibrillation.

36. The use according to claim 35, wherein said detached thrombus is in the brain (ischemic stroke), or wherein said detached thrombus causes a transient ischemic attack (TIA).

37. The use according to claim 27, wherein said thrombosis is arterial thrombosis.

38. The use according to claim 25, wherein the subject has had at least one myocardial infarction; or wherein the subject has at least one of unstable angina pectoris, thrombosis, and heparin-induced thrombocytopenia; or wherein the subject has non-valvular atrial fibrillation.

39. The use according to claim 29, wherein said kallikrein-related disorder is an ophthalmic disease selected from the group consisting of diabetic macular edema, age-related macular degeneration, and diabetic retinopathy, and wherein said compound or pharmaceutical composition is administered orally, in the form of an ophthalmic composition applied topically to the eye, or in the form of an ophthalmic composition via intravitreal injection.

40. The use according to claim 39, wherein said ophthalmic composition is in the form of eye drops, and/or wherein said compound acts by reducing retinal vascular permeability.

41. The use according to claim 25 wherein said disease or disorder is an inflammatory condition selected from the group consisting of sepsis, inflammatory bowel disease, systemic inflammatory response syndrome, hereditary angioedema, and rheumatoid arthritis, and wherein said compound is administered orally.

42. The use according to claim 25, wherein said compound inhibits blood coagulation.