The invention is also directed to an *in vitro* assay to determine the *in vivo* antithrombotic properties of a compound. The assay comprises the following steps:

a) introducing a test compound into an *in vitro* sample of whole blood or plasma comprising tissue factor (TF) and a detectably-labeled thrombin substrate to form a test sample;

b) determining the level of thrombin activity in the test sample by monitoring the cleavage of the detectably-labeled thrombin substrate in the test sample as a function of time;

c) determining the level of thrombin activity in a control sample by monitoring the cleavage of the detectably-labeled thrombin substrate in the control sample as a function of time, wherein the control sample comprises whole blood or plasma comprising tissue factor (TF) and a detectably-labeled thrombin substrate;

d) comparing the level of thrombin activity in the test sample and the control sample, wherein a lower level of thrombin activity in the test sample is an indication that the test compound has *in vivo* antithrombotic activity.

The blood and plasma may be anticoagulated or nonanticoagulated.

In certain embodiments of the invention, the detectably-labeled thrombin substrate is a Z-Gly-Gly-Arg-AMC.

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a) introducing a test compound into an *in vitro* sample of whole blood or plasma comprising tissue factor (TF) and a detectably-labeled thrombin substrate to form a test sample;

b) determining the level of thrombin activity in the test sample by monitoring the cleavage of the detectably-labeled thrombin substrate in the test sample as a function of time;

c) determining the level of thrombin activity in a control sample by monitoring the cleavage of the detectably-labeled thrombin substrate in the control sample as a function of time, wherein the control sample comprises whole blood or plasma comprising tissue factor (TF) and a detectably-labeled thrombin substrate;

d) comparing the level of thrombin activity in the test sample and the control sample, wherein a lower level of thrombin activity in the test sample is an indication that the test compound has *in vivo* antithrombotic activity.

The blood and plasma may be anticoagulated or nonanticoagulated.

In certain embodiments of the invention, the detectably-labeled thrombin substrate is a Z-Gly-Gly-Arg-AMC.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1A shows the correlation of thrombin generation with the international normalized ratio (INR) in anticoagulated patients treated with warfarin. Thrombin generation was measured at 10 minutes in plasma samples from patients receiving stable warfarin therapy (n = 137). Data from patients receiving warfarin therapy is presented as quintiles of the INR results. Error bars show standard errors.

FIG. 1B shows the correlation of thrombin generation with activated partial thromboplastin time (aPTT) in anticoagulated patients treated with enoxaparin. Plasma thrombin generation was measured in 16 enoxaparin-treated patients. Anti-fXa units were measured by COATEST LMW assay according to the manufacturer's instructions. Groups were compared by Student's t-test.

FIG. 1C shows the correlation of thrombin generation with aPTT in anticoagulated patients treated with unfractionated heparin (UFH). Plasma thrombin

The present invention also provides any one of the embodiments disclosed below and indicated with the numbers 1 to 33.

1. A method of inhibiting coagulation in a human patient in need thereof, comprising administering to the patient a coagulation inhibiting amount of a factor Xa inhibitor compound of the Formula I:

A-Q-D-E-G-J-X

I

wherein:

A is selected from:

(a) C_1-C_6-alkyl;

(b) C_3-C_8-cycloalkyl;

(c) -N(R^1,R^2), N(R^1,R^2)-C(=NR^3)-, N(R^1,R^2)-C(=NR^3)-N(R^4)-, R^1-C(=NR^3)-, R^1-C(=NR^3)-N(R^4)-;

(d) phenyl, which is independently substituted with 0-2 R substituents;

(e) naphthyl, which is independently substituted with 0-2 R substituents; and a monocyclic or fused bicyclic heterocyclic ring system having from 5 to 10 ring atoms, wherein 1-4 ring atoms of the ring system are selected from N, O and S, and wherein the ring system may be substituted with 0-2 R substituents;

R is selected from:

H, halo, -CN, -CO_2R^1, -C(=O)-N(R^1, R^2), -$(CH_2)_m$-CO_2R^1, -$(CH_2)_m$-C(=O)-N(R^1, R^2), -NO_2, -SO_2N(R^1, R^2), -SO_2R^1, -$(CH_2)_m$NR^1R^2, -$(CH_2)_m$-C(=NR^3)-R^1, -$(CH_2)_m$-C(=NR^3)-N(R^1,R^2), -$(CH_2)_m$-N(R^4)-C(=NR^3)-N(R^1,R^2), -$(CH_2)_m$NR^1-group appended to a 3 to 6 membered heterocyclic ring containing from 1-4 heteroatoms selected from N, O and S, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylene-C_{3-8}cycloalkyl, -CF_3, -OR^2, and a 5-6 membered heterocyclic system containing from 1-4 heteroatoms selected from N, O and S, wherein from 1-4 hydrogen atoms on the heterocyclic system may be independently replaced with a member selected from the group consisting of halo, -C_1-C_4-alkyl, -C_{1-4}alkyl-CN, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylene-C_{3-8}cycloalkyl and -NO_2;

m is an integer of 0-2;

R^1, R^2, R^3 and R^4 are independently selected from the group consisting of:

H, $-OR^5$, $-N(-R^5, -R^6)$, $-C_{1-4}$alkyl, $-C_{2-6}$alkenyl, $-C_{2-6}$alkynyl, $-C_{3-8}$cycloalkyl, $-C_{0-4}$alkylene-C_{3-8}cycloalkyl, $-C_{0-4}$alkylphenyl and $-C_{0-4}$alkylnaphthyl, wherein from 1-4 hydrogen atoms on the ring atoms of the phenyl and naphthyl moieties may be independently replaced with a member selected from the group consisting of halo, $-C_{1-4}$alkyl, $-C_{2-6}$alkenyl, $-C_{2-6}$alkynyl, $-C_{3-8}$cycloalkyl, $-C_{0-4}$alkylene-C_{3-8}cycloalkyl, -CN, and $-NO_2$; or R^1 and R^2, or R^2 and R^3 taken together can form a 3-8 membered cycloalkyl or a heterocyclic ring system, wherein the heterocyclic ring system may have from 3 to 10 ring atoms, with 1 to 2 rings being in the ring system and contain from 1-4 heteroatoms selected from N, O and S, wherein from 1-4 hydrogen atoms on the heterocyclic ring system may be independently replaced with a member selected from the group consisting of halo, C_1-C_4-alkyl, -CN, $-C_{2-6}$alkenyl, $-C_{2-6}$alkynyl, $-C_{3-8}$cycloalkyl, $-C_{0-4}$alkylene-C_{3-8}cycloalkyl and $-NO_2$;

R^5 and R^6 are independently selected from the group consisting of:

H, $-C_{1-4}$alkyl, $-C_{2-6}$alkenyl, $-C_{2-6}$alkynyl, $-C_{3-8}$cycloalkyl, $-C_{0-4}$alkylene-C_{3-8}cycloalkyl, $-C_{0-4}$alkylene-phenyl and $-C_{0-4}$alkylene-naphthyl, wherein from 1-4 hydrogen atoms on the ring atoms of the phenyl and naphthyl moieties may be independently replaced with a member selected from the group consisting of halo, $-C_{1-4}$alkyl, $-C_{2-6}$alkenyl, $-C_{2-6}$alkynyl, $-C_{3-8}$cycloalkyl, $-C_{0-4}$alkylene-C_{3-8}cycloalkyl, -CN, and $-NO_2$; or R^5 and R^6 taken together can form a 3-8 membered cycloalkyl or a heterocyclic ring system, wherein the heterocyclic ring system may have from 3 to 10 ring atoms, with 1 to 2 rings being in the ring system and contain from 1-4 heteroatoms selected from N, O and S, wherein from 1-4 hydrogen atoms on the heterocyclic ring system may be independently replaced with a member selected from the group consisting of halo, C_1-C_4-alkyl, -CN, $-C_{2-6}$alkenyl, $-C_{2-6}$alkynyl, $-C_{3-8}$cycloalkyl, $-C_{0-4}$alkylene-C_{3-8}cycloalkyl and $-NO_2$;

Q is a member selected from the group consisting of:

a direct link, $-CH_2-$, -C(=O)-, -O-, $-N(R^7)-$, $-N(R^7)CH_2-$, $-CH_2N(R^7)-$, $-C(=NR^7)-$, $-C(=O)-N(R^7)-$, $-N(R^7)-C(=O)-$, -S-, -SO-, $-SO_2-$, $-SO_2-N(R^7)-$ and $-N(R^7)-SO_2-$;

R^7 is selected from:

H, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylene-C_{3-8}cycloalkyl, -C_{0-4}alkylene-phenyl and -C_{0-4}alkylene-naphthyl, wherein from 1-4 hydrogen atoms on the ring atoms of the phenyl and naphthyl moieties may be independently replaced with a member selected from the group consisting of halo, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylene-C_{3-8}cycloalkyl, -CN, and -NO_2;

D is a direct link or is a member selected from the group consisting of:

(a) phenyl, which is independently substituted with 0-2 R^{1a} substituents;

(b) naphthyl, which is independently substituted with 0-2 R^{1a} substituents; and

(c) a monocyclic or fused bicyclic heterocyclic ring system having from 5 to 10 ring atoms, wherein 1-4 ring atoms of the ring system are selected from N, O and S, and wherein the ring system may be substituted from 0-2 R^{1a} substituents;

R^{1a} is selected from:

halo, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylene-C_{3-8}cycloalkyl, -CN, -NO_2, -$(CH_2)_nNR^{2a}R^{3a}$, -$(CH_2)_nCO_2R^{2a}$, -$(CH_2)_nCONR^{2a}R^{3a}$, -$SO_2NR^{2a}R^{3a}$, -SO_2R^{2a}, -CF_3, -OR^{2a}, and a 5-6 membered aromatic heterocyclic system containing from 1-4 heteroatoms selected from N, O and S, wherein from 1-4 hydrogen atoms on the aromatic heterocyclic system may be independently replaced with a member selected from the group consisting of halo, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylene-C_{3-8}cycloalkyl, -CN and -NO_2;

R^{2a} and R^{3a} are independently selected from the group consisting of:

H, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylene-C_{3-8}cycloalkyl, -C_{0-4}alkylene-phenyl and -C_{0-4}alkylene-naphthyl, wherein from 1-4 hydrogen atoms on the ring atoms of the phenyl and naphthyl moieties may be independently replaced with a member selected from the group consisting of halo, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylene-C_{3-8}cycloalkyl, -CN and -NO_2;

n is an integer of 0-2;

E is a direct link or a member selected from the group consisting of:

$-C_{1-2}$-alkylene-, -O-, -S-, -SO-, $-SO_2$-, $-C_{0-1}$-alkylene-C(=O), $-C_{0-1}$-alkylene-C(=O)-N($-R^8$)- C_{0-1}-alkylene-, $-C_{0-1}$-alkylene-N($-R^8$)-C(=O)-C_{0-1}-alkylene-, -N($-R^8$)-C(=O)-N($-R^8$)- and $-C_{0-1}$-alkylene-N($-R^8$)-;

R^8 is a member selected from the group consisting of:

H; $-C_{1-4}$-alkyl; $-C_{0-4}$-alkylene-aryl; $-C_{0-4}$-alkylene-heteroaryl; $-C_{1-4}$-alkylene-C(=O)-OH, $-C_{1-4}$-alkylene-C(=O)-O-C_{1-4}-alkyl, and $-C_{1-4}$-alkylene-C(=O)-N($-R^{2b}$, $-R^{3b}$);

R^{2b} and R^{3b} are each a member independently selected from the group consisting of:

H, $-C_{1-4}$-alkyl, $-C_{0-4}$-alkylene-aryl; $-C_{0-4}$-alkylene-heterocyclic group, and R^{2b} and R^{3b} together with the N atom to which they are attached can form a 5-8 membered heterocyclic ring containing 1-4 heteroatoms selected from N, O and S, wherein the heterocyclic ring may be substituted with 0-2 R^{1c} groups;

R^{1c} is a member selected from the group consisting of:

Halo; $-C_{1-4}$-alkyl; -CN; $-NO_2$; -C(=O)-N($-R^{2c}$, $-R^{3c}$); -C(=O)-OR^{2c}; $-(CH_2)_q$-N($-R^{2c}$, $-R^{3c}$); $-SO_2$-N($-R^{2c}$, $-R^{3c}$); $-SO_2R^{2c}$; $-CF_3$; and $-(CH_2)_q$-OR^{2c};

R^{2c} and R^{3c} are each independently a member selected from the group consisting of:

H; $-C_{1-4}$-alkyl; and $-C_{1-4}$-alkylene-aryl;

q is an integer of 0-2;

G is a member selected from the group consisting of:

(a) C_2-alkenyl or C_{3-8}-cycloalkenyl, wherein the alkenyl and cycloalkenyl attachment points are the alkenyl carbon atoms and wherein the $-C_2$-alkenyl or $-C_{3-8}$-cycloalkenyl are substituted with 0-4 R^{1d} groups;

(b) a phenyl group wherein the ring carbon atoms of the phenylene group are substituted with 0-4 R^{1d} groups;

(c) a 3-8 membered heterocyclic ring system containing 1-4 heteroatoms selected from N, O and S, wherein 0-2 ring atoms of the heterocyclic ring may be substituted with 0-4 R^{1d} groups; and,

(d) an 8-10 membered fused heterocyclic bicyclic ring system, containing 1-4 heteroatoms selected from N, O and S, wherein 0-2 ring atoms of the fused bicyclic ring system may be substituted with 0-4 R^{1d} groups;

R^{1d} is a member selected from the group consisting of:

H, halo; C_{1-6}-alkyl, aryl, -CN; $-NO_2$; $-(CH_2)_{0-6}-NR^{2d}R^{3d}$; $-SO_2NR^{2d}R^{3d}$; $-SO_2R^{2d}$; $-CF_3$; $-(CH_2)_{0-6}-OR^{2d}$; $-O-(CH_2)_{1-6}OR^{2d}$; $-O-(CH_2)_{1-6}-C(=O)-O-R^{2d}$; $-O-(CH_2)_{1-6}-C(=O)-N(R^{2d},R^{3d})$; $-N(R^{5a})-(CH_2)_{1-6}-OR^{2d}$; $-N(R^{5a})-(CH_2)_{1-6}-N(R^{2d},R^{3d})$; $-C(=O)-N(R^{2d},R^{3d})$; $-N(R^{5a})-(CH_2)_{1-6}-C(=O)-N(R^{2d},R^{3d})$; $-N(-(CH_2)_{1-6}-OR^{2d})_2$; $-N(R^{5a})-(CH_2)_{1-6}-OR^{2d}$; $-N(R^{5a})-C(=O)-R^{2d}$; $-N(R^{5a})-SO_2-R^{2d}$; $-(CH_2)_{0-6}-C(=O)-O-R^{2d}$; $-(CH_2)_{0-6}-C(=O)-N(R^{2d},R^{3d})$; $-(CH_2)_{0-6}-C(=NR^{2d})-N(R^{3d},R^{4d})$; $-(CH_2)_{0-6}-N(R^{5a})C(=NR^{2d})-N(R^{3d},R^{4d})$; a $-(CH_2)_{0-6}-N(R^{3d})C_{5-6}$ membered heterocyclic ring containing 1-4 heteroatoms selected from N, O and S, and a $-(CH_2)_{0-6}$-5-6 membered heterocyclic ring containing 1-4 heteroatoms selected from N, O and S;

R^{5a}, R^{2d}, R^{3d} and R^{4d} are each independently a member selected from the group consisting of:

H, C_{1-6}-alkyl, C_{1-6}-alkylaryl, -CN; $-NO_2$; carbocyclic aryl, -CN; $-NO_2$; or R^{2d} and R^{3d} taken together with the N atoms they are independently attached form a 5-7 membered heterocyclic ring; or R^{3d} and R^{4d} taken together with the N atom to which they are attached form a 5-8 membered heterocyclic ring containing 1-4 heteroatoms selected from N, O and S;

J is a direct link or is a member selected from the group consisting of:

$-N(-R^9)-C(=O)-$; $-C(=O)-N(-R^9)-$; -O-; -S-; -SO-; $-SO_2-$; $-CH_2-$; $-N(-R^9)-$; and $-N(-R^9)-SO_2-$;

R^9 is a member selected from the group consisting of:

H; $-C_{1-4}$-alkyl; $-C_{0-4}$-alkyl-carbocyclic aryl; $-(CH_2)_{0-4}$-5-6 membered heterocyclic ring containing 1-4 heteroatoms selected from N, O and S; $-(CH_2)_{1-6}-C(=O)-O-C_{1-4}$-alkyl; and $-(CH_2)_{1-6}-C(=O)-N(R^{6a},R^{6b})$;

R^{6a} and R^{6b} are each a member independently selected from the group consisting of:

H and $-C_{1-6}$-alkyl;

X is a member selected from the group consisting of:

(a) phenyl substituted with 0-3 R^{1e} groups;

(b) naphthyl substituted with 0-3 R^{1e} groups and

(c) a 6-membered aromatic heterocyclic ring system containing 1-3 N atoms and having 0-3 ring atoms substituted with 0-3 R^{1e} groups; and

(d) an 8-10 membered fused aromatic heterocyclic bicyclic ring system containing 1-4 heteroatoms selected from N, O and S and 0-3 ring atoms of the fused heterocyclic bicyclic ring system are substituted with 0-3 R^{1e} groups;

R^{1e} is a member independently selected from the group consisting of:

Halo; CF_3; $-C_{1-4}$-alkyl; carbocyclic aryl; $-C_{0-2}$-alkylene-CN; $-O-R^{2e}$; $-C_{0-2}$-alkylene-C(=O)-O-R^{2e}; $-C_{0-2}$- alkylene-C(=O)-N(R^{2e}, R^{3e}); $-C_{0-2}$-alkylene-NO_2; $-C_{0-2}$-alkylene-N(R^{2e}, R^{3e}); $-C_{0-2}$-alkylene-SO_2-N(R^{2e}, R^{3e}); $-C_{0-2}$-alkylene-SO_2-R^{2e}; trihaloalkyl; $-O-C_{0-2}$-alkylene-O-R^{2e}; $-C_{0-2}$-alkylene-O-R^{2e}; $-O-C_{1-4}$-alkylene-C(=O)-N(R^{2e}, R^{3e}); $-O-C_{1-4}$-alkylene-C(=O)-O-R^{2e}; $-C_{0-2}$-alkylene-N(R^{2e})-C(=O)-R^{3e}; $-C_{0-2}$-alkylene-N(-R^{2e})-SO_2-R^{3e}; $-CH_2$-N(R^{2e})-C(=O)-R^{3e} ;$-CH_2$-N(R^{2e})-SO_2-R^{3e}; $-(CH_2)_{0-6}$-N$R^{2e}R^{3e}$; -C(=O)-N(R^{2e},R^{3e}); $-N(-(CH_2)_{1-6}-OR^{2e})_2$; $-N(R^{10})-(CH_2)_{1-6}-OR^{2e}$; $-N(R^{10})$-C(=O)-R^{2e}; $-N(R^{10})-SO_2-R^{2e}$; -C(=N(R^{10}))-N(R^{2e},R^{3e}); and a $-(CH_2)_{0-6}$-5-6 membered heterocyclic ring containing 1-4 heteroatoms selected from N, O and S;

R^{10}, R^{2e} and R^{3e} are each independently a member selected from the group consisting of:

H; $-C_{1-4}$-alkyl; $-C_{0-2}$-alkylene-O-R^{1g}; $-C_{0-2}$-alkylene-N(-R^{1g}, -R^{2g});-C_{1-4}-alkylene-carbocyclic aryl; $-C_{1-4}$-alkylene-heterocyclic; and R^{10} and R^{2e}, or R^{2e} and R^{3e} together with the N atom to which they are attached can form 5-8 membered heterocyclic ring containing 1-4 heteroatoms selected from N, O and S which can be substituted with 0-2 R^{1g} groups;

R^{1g} and R^{2g} are independently a member selected from the group of:

H; halo; $-C_{1-4}$-alkyl, a carbocyclic aryl group ; a heterocyclic group; -CN; -C(=O)-N(R^{3g})R^{4g}; -C(=O)-OR^{3g}; $-NO_2$; $-(CH_2)_p-NR^{3g}R^{4g}$; $-SO_2NR^{3g}R^{4g}$; $-SO_2R^{3g}$; $-CF_3$; and $-(CH_2)_pOR^{3g}$;

p is an integer of 0-2; and

R^{3g} and R^{4g} are each independently selected from the group consisting of:

H; C_{1-4}-alkyl and $-C_{0-4}$-alkylene-carbocyclic aryl;

or a pharmaceutically acceptable salt thereof;

wherein the coagulation inhibiting amount of the factor Xa inhibitor compound is an aggregate daily dose from between about 0.01 and about 2.0 mg/kg.

2. The method of claim 1, wherein the coagulation inhibiting amount of the factor Xa inhibitor compound is an aggregate daily dose from between about 0.1 and about 1.5 mg/kg.

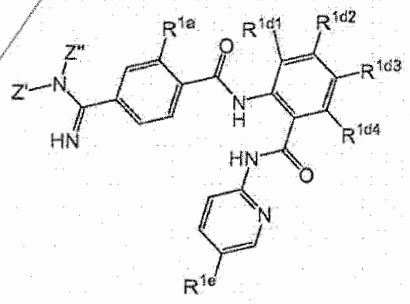
3. The method of claim 1, wherein the coagulation inhibiting amount of the factor Xa inhibitor compound is an aggregate daily dose from between about 0.4 and about 1.2 mg/kg.

4. The method of claim 1, wherein the pharmaceutically acceptable salt of the factor Xa inhibitor compound is a maleate salt.

5. The method of claim 1, wherein the factor Xa inhibitor compound is administered to the patient once daily.

6. The method of claim 1, wherein the factor Xa inhibitor compound is administered to the patient twice daily or three times daily.

7. The method of claim 1, wherein the factor Xa inhibitor compound is of formula IV:



IV

wherein:

Z' and Z'' are each independently a C_1-C_6 alkyl which is optionally substituted with a hydroxyl, carboxylic acid or carboxylic acid ester group;

R^{1a} is selected from the group consisting of:

H, -F, -Cl, and Br;

R^{1d2} and R^{1d4} are each H;

R^{1d1} and R^{1d3} are each independently a member selected from the group consisting of:

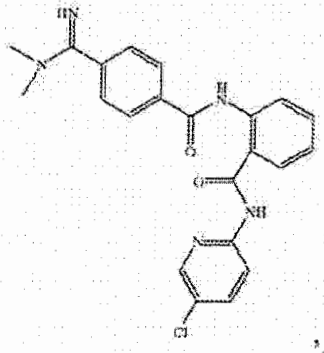
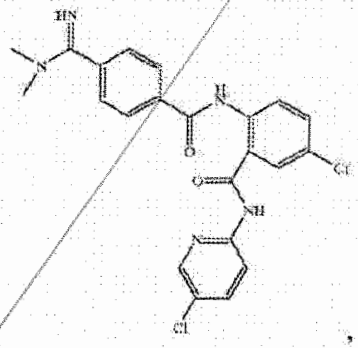
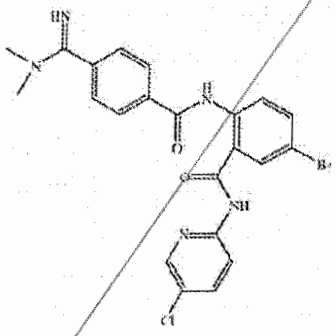
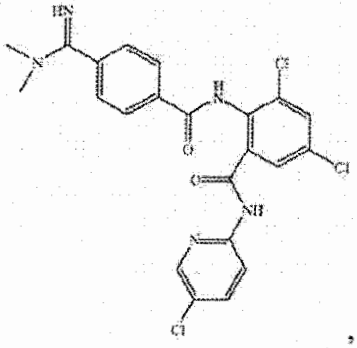
H, -Cl, -F, -Br, -OH and $-OCH_3$; and

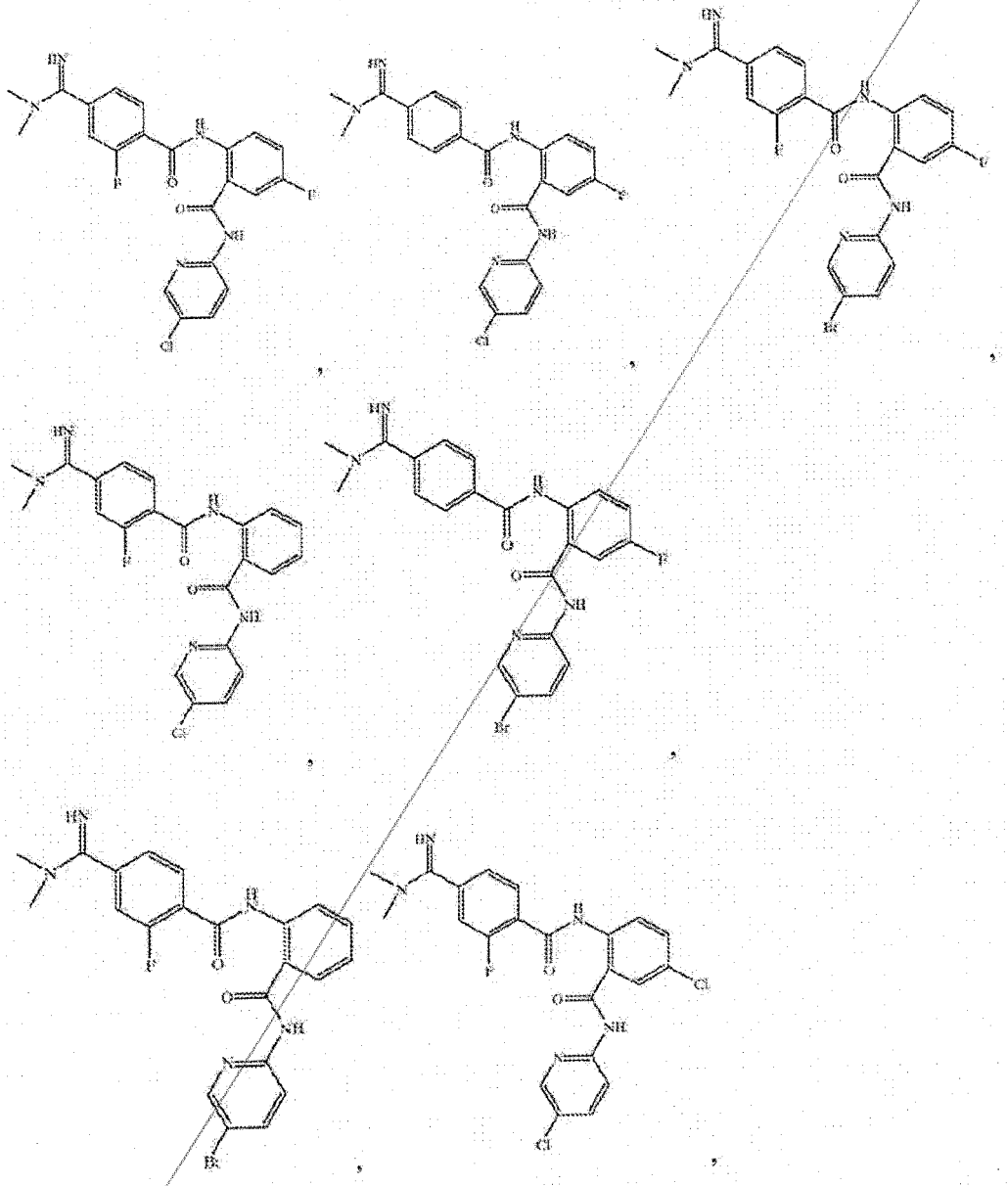
R^{1e} is a member selected from the group consisting of:

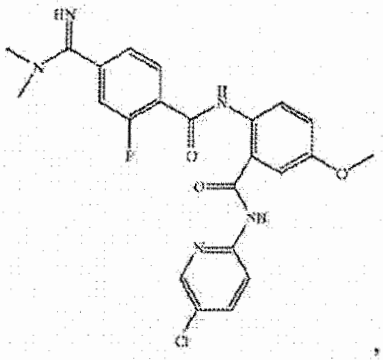
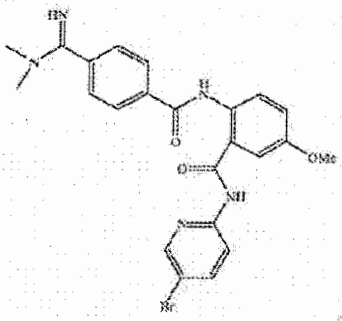
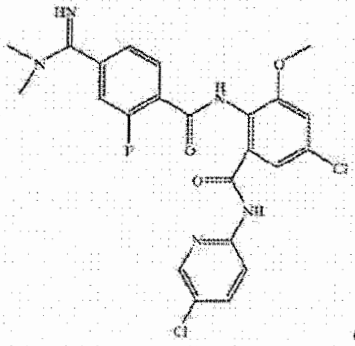
-F, -Cl, -Br, -OH, $-CH_3$, and $-OCH_3$,

or a pharmaceutically acceptable salt thereof.

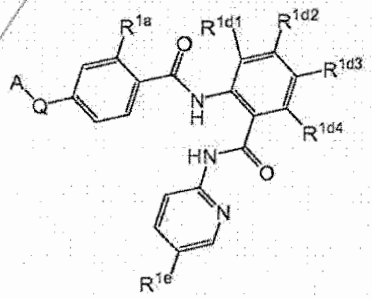
8. The method of claim 1, wherein the compound is selected from the group consisting of:


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or a pharmaceutically acceptable salt thereof.

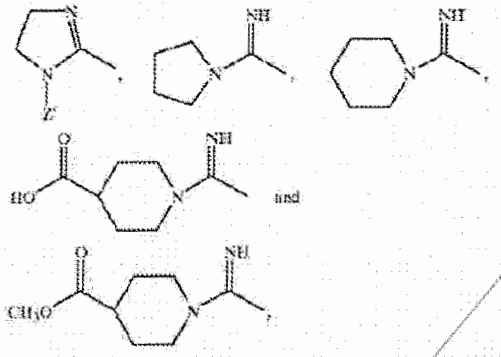
9. The method of claim 1, wherein the factor Xa inhibitor compound is of Formula V:



V

wherein:

A-Q is a member selected from the group consisting of:



where Z^3 is a C_{1-6} alkyl which is optionally substituted with a hydroxyl, carboxylic acid or carboxylic acid ester group;

R^{1a} is selected from the group consisting of:

H, -F, -Cl, and Br;

R^{1d2} and R^{1d4} are each H;

R^{1d1} and R^{1d3} are each independently a member selected from the group consisting of:

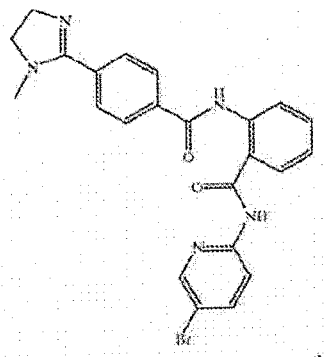
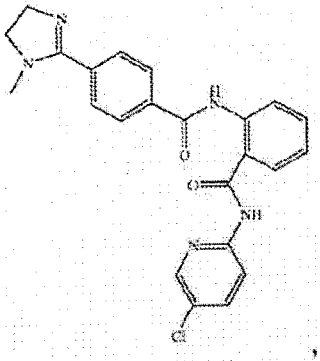
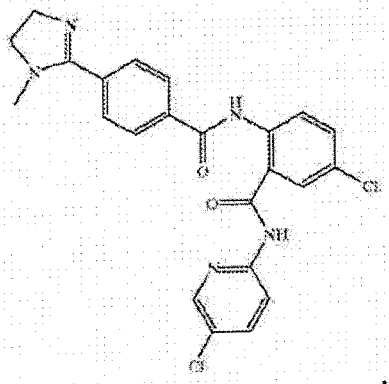
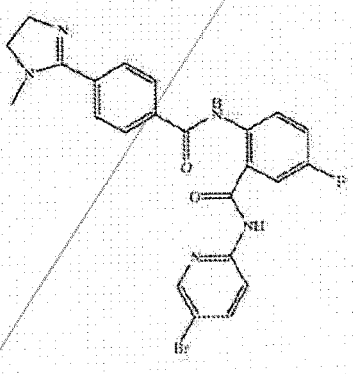
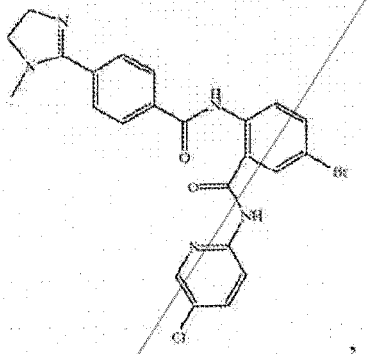
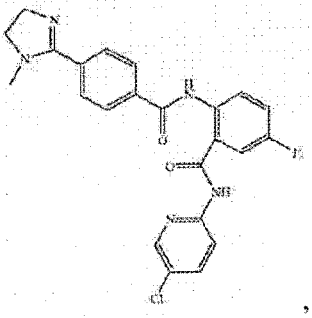
H, -Cl, -F, -Br, -OH and $-OCH_3$; and

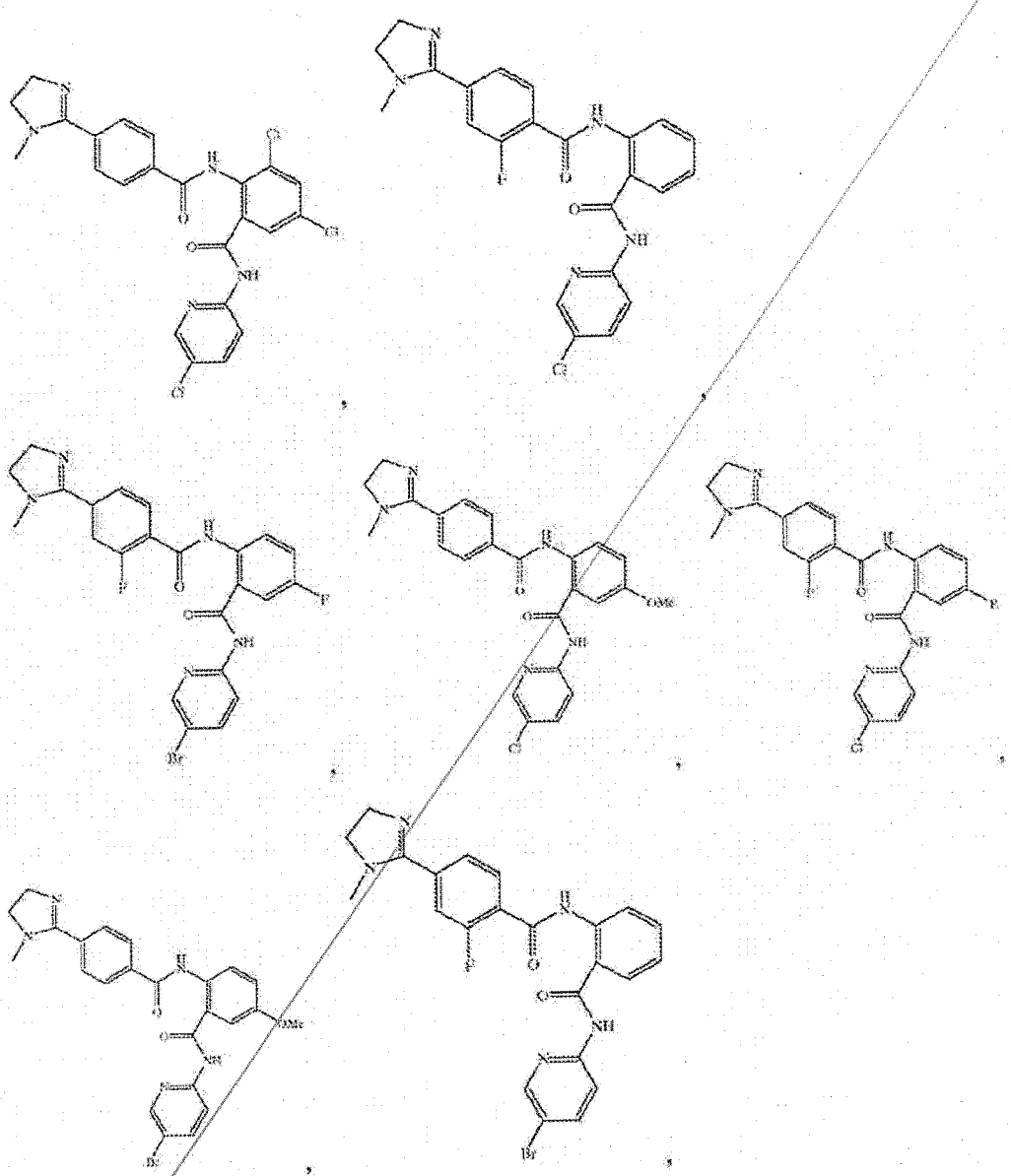
R^{1e} is a member selected from the group consisting of:

-F, -Cl, -Br, -OH, $-CH_3$, and $-OCH_3$,

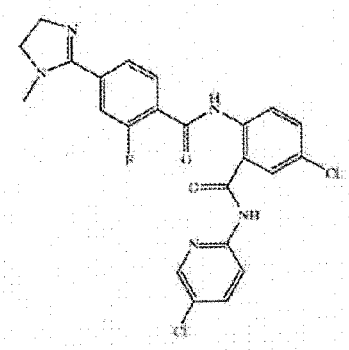
or a pharmaceutically acceptable salt thereof.

10. The compound of claim 9, wherein the compound is selected from the group consisting of:

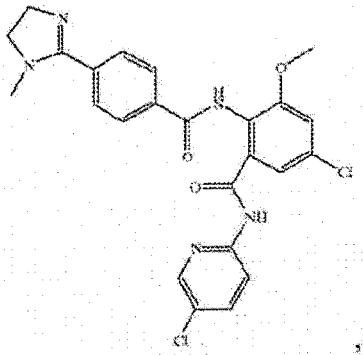

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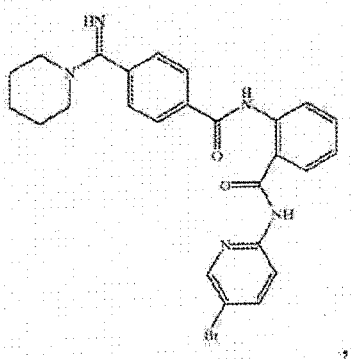
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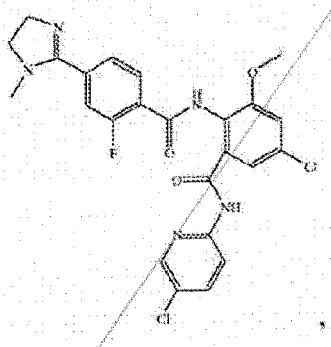
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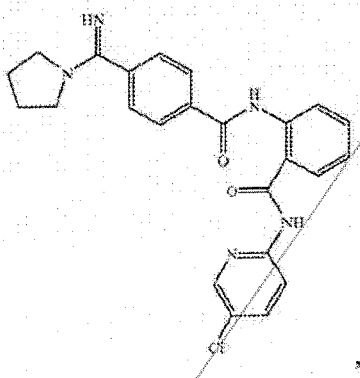
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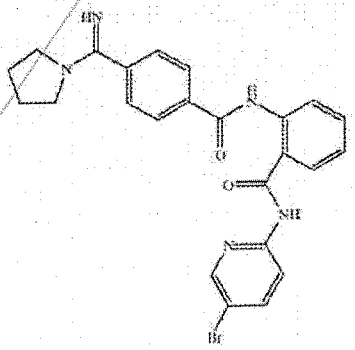
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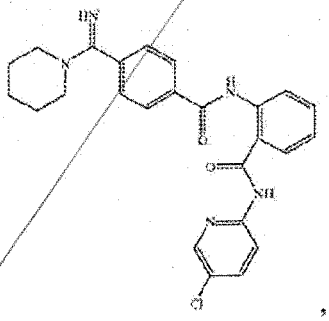
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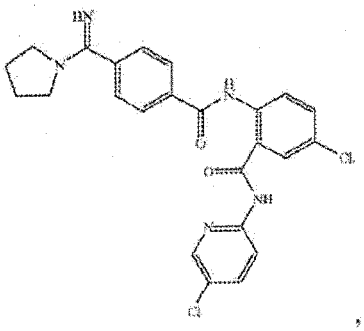
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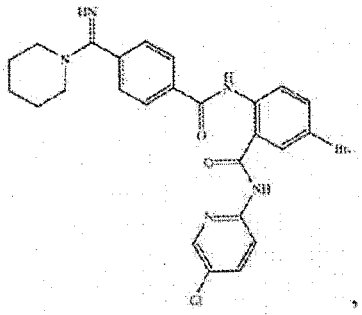
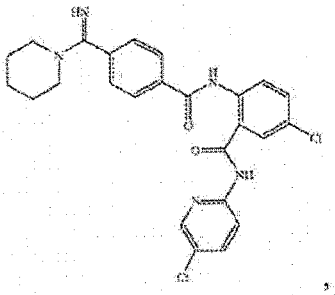
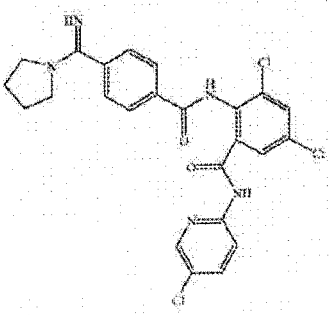
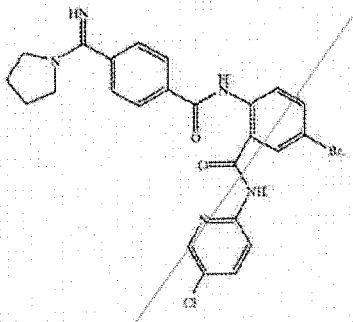
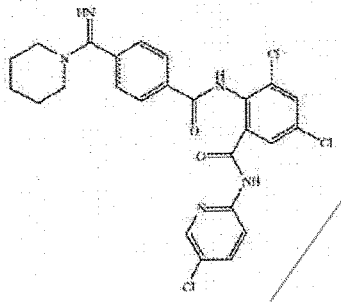
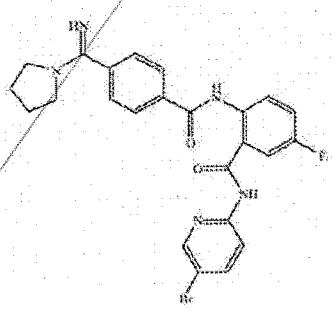
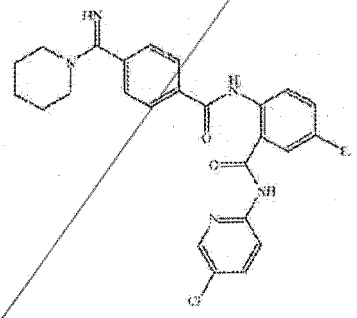
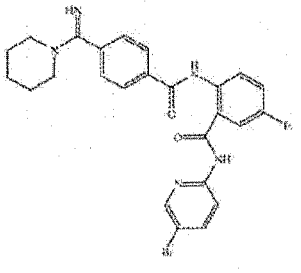


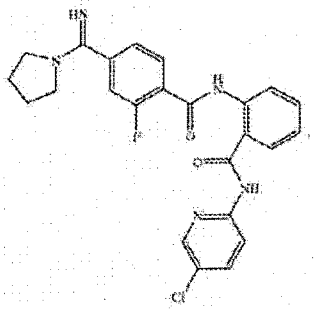
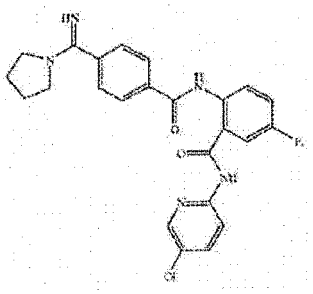
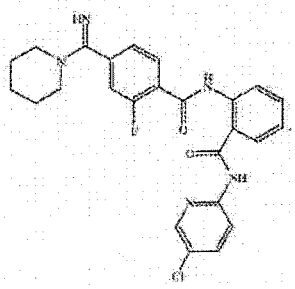
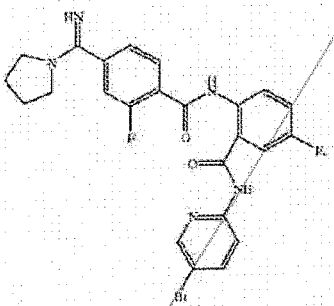
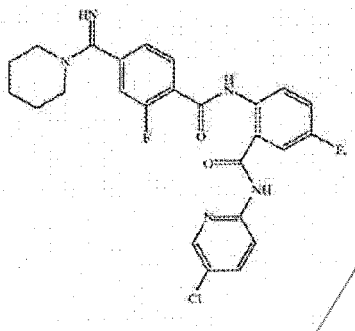
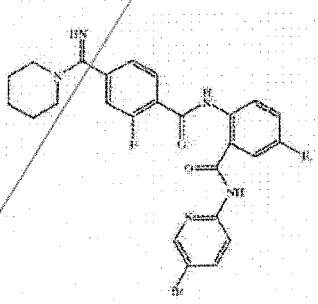
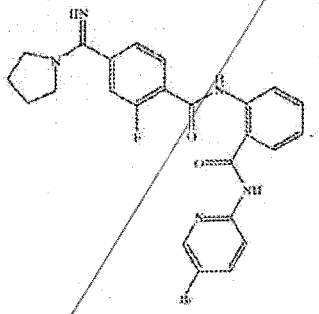
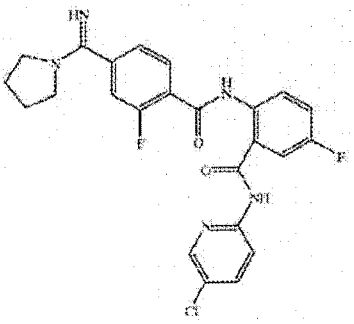
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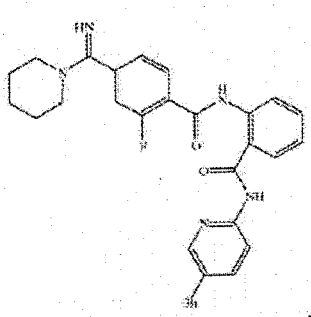


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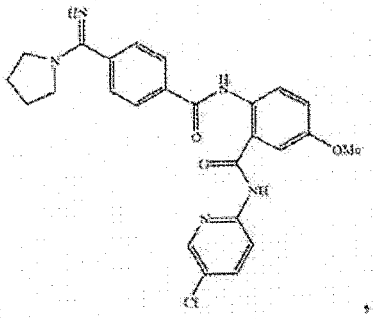
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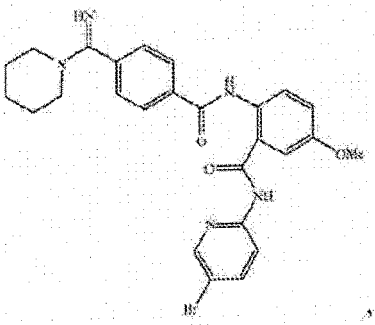

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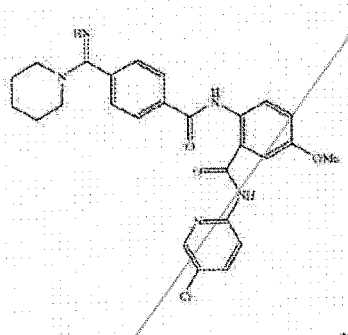
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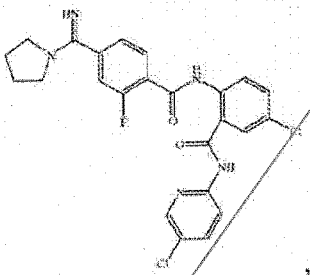
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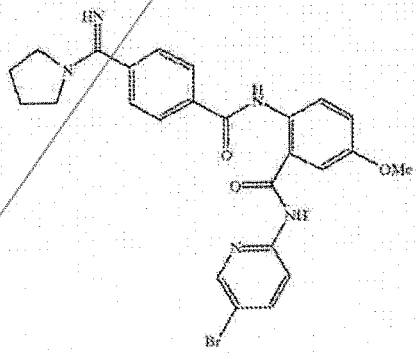
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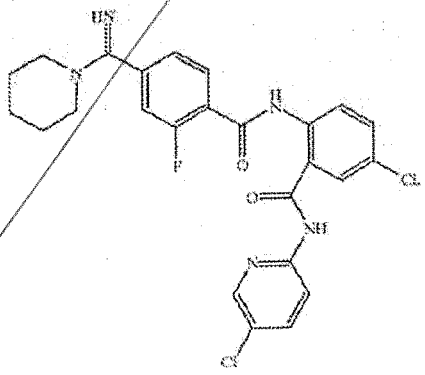
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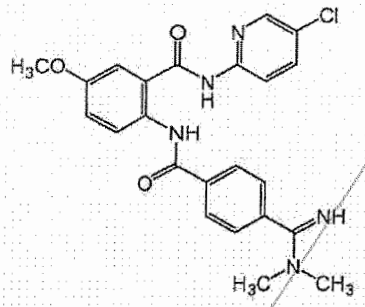


, and



or a pharmaceutically acceptable salt thereof.

11. A method of inhibiting coagulation in a human patient in need thereof, comprising administering to the patient a coagulation inhibiting amount of a factor Xa inhibitor compound of the Formula II :



or pharmaceutically acceptable salt thereof, wherein the coagulation inhibiting amount of the factor Xa inhibitor compound is an aggregate daily dose from between about 0.01 and about 2.0 mg/kg.

12. The method of claim 11, wherein the coagulation inhibiting amount of the factor Xa inhibitor compound is an aggregate daily dose from between about 0.1 and about 1.5 mg/kg.

13. The method of claim 12, wherein the coagulation inhibiting amount of the factor Xa inhibitor compound is an aggregate daily dose from between about 0.4 and about 1.2 mg/kg.

14. The method of claim 12, wherein the pharmaceutically acceptable salt of the factor Xa inhibitor compound is a maleate salt.

15. A unit dose formulation comprising a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a coagulation inhibiting amount of the factor Xa inhibitor compound of Formula I :

A-Q-D-E-G-J-X

I

wherein:

A is selected from:

(a) C_1-C_6-alkyl;

(b) C_3-C_8-cycloalkyl;

(c) -$N(R^1,R^2)$, $N(R^1,R^2)$-$C(=NR^3)$-, $N(R^1,R^2)$-$C(=NR^3)$-$N(R^4)$-, R^1-$C(=NR^3)$-, R^1-$C(=NR^3)$-$N(R^4)$-;

(d) phenyl, which is independently substituted with 0-2 R substituents;

(e) naphthyl, which is independently substituted with 0-2 R substituents; and a monocyclic or fused bicyclic heterocyclic ring system having from 5 to 10 ring atoms, wherein 1-4 ring atoms of the ring system are selected from N, O and S, and wherein the ring system may be substituted with 0-2 R substituents;

R is selected from:

H, halo, -CN, -CO_2R^1, -$C(=O)$-$N(R^1, R^2)$, -$(CH_2)_m$-CO_2R^1, -$(CH_2)_m$-$C(=O)$-$N(R^1, R^2)$, -NO_2, -$SO_2N(R^1, R^2)$, -SO_2R^1, -$(CH_2)_mNR^1R^2$, -$(CH_2)_m$-$C(=NR^3)$-R^1, -$(CH_2)_m$-$C(=NR^3)$-$N(R^1,R^2)$, -$(CH_2)_m$-$N(R^4)$-$C(=NR^3)$-$N(R^1,R^2)$, -$(CH_2)_mNR^1$- group appended to a 3 to 6 membered heterocyclic ring containing from 1-4 heteroatoms selected from N, O and S, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylene-C_{3-8}cycloalkyl, -CF_3, -OR^2, and a 5-6 membered heterocyclic system containing from 1-4 heteroatoms selected from N, O and S, wherein from 1-4 hydrogen atoms on the heterocyclic system may be independently replaced with a member selected from the group consisting of halo, -C_1-C_4-alkyl, -C_{1-4}alkyl-CN, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylene-C_{3-8}cycloalkyl and -NO_2;

m is an integer of 0-2;

R^1, R^2, R^3 and R^4 are independently selected from the group consisting of:

H, -OR^5, -$N(-R^5, -R^6)$, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylene-C_{3-8}cycloalkyl, -C_{0-4}alkylphenyl and -C_{0-4}alkylnaphthyl, wherein from 1-4 hydrogen atoms on the ring atoms of the phenyl and naphthyl moieties may be

independently replaced with a member selected from the group consisting of halo, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylene-C_{3-8}cycloalkyl, -CN, and -NO_2; or R^1 and R^2, or R^2 and R^3 taken together can form a 3-8 membered cycloalkyl or a heterocyclic ring system, wherein the heterocyclic ring system may have from 3 to 10 ring atoms, with 1 to 2 rings being in the ring system and contain from 1-4 heteroatoms selected from N, O and S, wherein from 1-4 hydrogen atoms on the heterocyclic ring system may be independently replaced with a member selected from the group consisting of halo, C_1-C_4-alkyl, -CN, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylene-C_{3-8}cycloalkyl and -NO_2;

R^5 and R^6 are independently selected from the group consisting of:

H, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylene-C_{3-8}cycloalkyl, -C_{0-4}alkylene-phenyl and -C_{0-4}alkylene-naphthyl, wherein from 1-4 hydrogen atoms on the ring atoms of the phenyl and naphthyl moieties may be independently replaced with a member selected from the group consisting of halo, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylene-C_{3-8}cycloalkyl, -CN, and -NO_2; or R^5 and R^6 taken together can form a 3-8 membered cycloalkyl or a heterocyclic ring system, wherein the heterocyclic ring system may have from 3 to 10 ring atoms, with 1 to 2 rings being in the ring system and contain from 1-4 heteroatoms selected from N, O and S, wherein from 1-4 hydrogen atoms on the heterocyclic ring system may be independently replaced with a member selected from the group consisting of halo, C_1-C_4-alkyl, -CN, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylene-C_{3-8}cycloalkyl and -NO_2;

Q is a member selected from the group consisting of:

a direct link, -CH_2-, -C(=O)-, -O-, -N(R^7)-, -N(R^7)CH_2-, -CH_2N(R^7)-, -C(=NR^7)-, -C(=O)-N(R^7)-, -N(R^7)-C(=O)-, -S-, -SO-, -SO_2-, -SO_2-N(R^7)- and –N(R^7)-SO_2-;

R^7 is selected from:

H, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylene-C_{3-8}cycloalkyl, -C_{0-4}alkylene-phenyl and -C_{0-4}alkylene-naphthyl, wherein from 1-4 hydrogen atoms on the ring atoms of the phenyl and naphthyl moieties may be independently replaced with a member selected from the group consisting of halo,

-C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylene-C_{3-8}cycloalkyl, -CN, and -NO_2;

D is a direct link or is a member selected from the group consisting of:

(a) phenyl, which is independently substituted with 0-2 R^{1a} substituents;

(b) naphthyl, which is independently substituted with 0-2 R^{1a} substituents; and

(c) a monocyclic or fused bicyclic heterocyclic ring system having from 5 to 10 ring atoms, wherein 1-4 ring atoms of the ring system are selected from N, O and S, and wherein the ring system may be substituted from 0-2 R^{1a} substituents;

R^{1a} is selected from:

halo, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylene-C_{3-8}cycloalkyl, -CN, -NO_2, -$(CH_2)_nNR^{2a}R^{3a}$, -$(CH_2)_nCO_2R^{2a}$, -$(CH_2)_nCONR^{2a}R^{3a}$, -$SO_2NR^{2a}R^{3a}$, -SO_2R^{2a}, -CF_3, -OR^{2a}, and a 5-6 membered aromatic heterocyclic system containing from 1-4 heteroatoms selected from N, O and S, wherein from 1-4 hydrogen atoms on the aromatic heterocyclic system may be independently replaced with a member selected from the group consisting of halo, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylene-C_{3-8}cycloalkyl, -CN and -NO_2;

R^{2a} and R^{3a} are independently selected from the group consisting of:

H, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylene-C_{3-8}cycloalkyl, -C_{0-4}alkylene-phenyl and -C_{0-4}alkylene-naphthyl, wherein from 1-4 hydrogen atoms on the ring atoms of the phenyl and naphthyl moieties may be independently replaced with a member selected from the group consisting of halo, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylene-C_{3-8}cycloalkyl, -CN and -NO_2;

n is an integer of 0-2;

E is a direct link or a member selected from the group consisting of:

-C_{1-2}-alkylene-, -O-, -S-, -SO-, -SO_2-, -C_{0-1}-alkylene-C(=O), -C_{0-1}-alkylene-C(=O)-N(-R^8)- C_{0-1}-alkylene-, -C_{0-1}-alkylene-N(-R^8)-C(=O)-C_{0-1}-alkylene-, -N(-R^8)-C(=O)-N(-R^8)- and -C_{0-1}-alkylene-N(-R^8)-;

R^8 is a member selected from the group consisting of:

H; -C_{1-4}-alkyl; -C_{0-4}-alkylene-aryl; -C_{0-4}-alkylene-heteroaryl; -C_{1-4}-alkylene-C(=O)-OH, -C_{1-4}-alkylene-C(=O)-O-C_{1-4}-alkyl, and -C_{1-4}-alkylene-C(=O)-N(-R^{2b}, -R^{3b});

R^{2b} and R^{3b} are each a member independently selected from the group consisting of:

H, -C_{1-4}-alkyl, -C_{0-4}-alkylene-aryl; -C_{0-4}-alkylene-heterocyclic group, and R^{2b} and R^{3b} together with the N atom to which they are attached can form a 5-8 membered heterocyclic ring containing 1-4 heteroatoms selected from N, O and S, wherein the heterocyclic ring may be substituted with 0-2 R^{1c} groups;

R^{1e} is a member selected from the group consisting of:

Halo; -C_{1-4}-alkyl; -CN; -NO_2; -C(=O)-N(-R^{2e}, -R^{3e}); -C(=O)-OR^{2e}; -$(CH_2)_q$-N(-R^{2e}, -R^{3e}); -SO_2-N(-R^{2e}, -R^{3e}); -SO_2R^{2e}; -CF_3; and -$(CH_2)_q$-OR^{2e};

R^{2e} and R^{3e} are each independently a member selected from the group consisting of:

H; -C_{1-4}-alkyl; and -C_{1-4}-alkylene-aryl;

q is an integer of 0-2;

G is a member selected from the group consisting of:

(a) C_2-alkenyl or C_{3-8}-cycloalkenyl, wherein the alkenyl and cycloalkenyl attachment points are the alkenyl carbon atoms and wherein the -C_2-alkenyl or -C_{3-8}-cycloalkenyl are substituted with 0-4 R^{1d} groups;

(b) a phenyl group wherein the ring carbon atoms of the phenylene group are substituted with 0-4 R^{1d} groups;

(c) a 3-8 membered heterocyclic ring system containing 1-4 heteroatoms selected from N, O and S, wherein 0-2 ring atoms of the heterocyclic ring may be substituted with 0-4 R^{1d} groups; and,

(d) an 8-10 membered fused heterocyclic bicyclic ring system, containing 1-4 heteroatoms selected from N, O and S, wherein 0-2 ring atoms of the fused bicyclic ring system may be substituted with 0-4 R^{1d} groups;

R^{1d} is a member selected from the group consisting of:

H, halo; C_{1-6}-alkyl, aryl, -CN; -NO_2; -$(CH_2)_{0-6}$-$NR^{2d}R^{3d}$; -$SO_2NR^{2d}R^{3d}$; -SO_2R^{2d}; -CF_3; -$(CH_2)_{0-6}$-OR^{2d}; -O-$(CH_2)_{1-6}$-OR^{2d}; -O-$(CH_2)_{1-6}$-C(=O)-O-R^{2d}; -O-$(CH_2)_{1-6}$-C(=O)-N(R^{2d},R^{3d}); -N(R^{5a})-$(CH_2)_{1-6}$-OR^{2d}; -N(R^{5a})-$(CH_2)_{1-6}$-N(R^{2d},R^{3d}); -C(=O)-N(R^{2d},R^{3d}); -N(R^{5a})-$(CH_2)_{1-6}$-C(=O)-N(R^{2d},R^{3d}); -N(-$(CH_2)_{1-6}$-OR^{2d})$_2$;

$-N(R^{5a})-(CH_2)_{1-6}-OR^{2d}$; $-N(R^{5a})-C(=O)-R^{2d}$; $-N(R^{5a})-SO_2-R^{2d}$; $-(CH_2)_{0-6}-C(=O)-O-R^{2d}$; $-(CH_2)_{0-6}-C(=O)-N(R^{2d},R^{3d})$; $-(CH_2)_{0-6}-C(=NR^{2d})-N(R^{3d},R^{4d})$; $-(CH_2)_{0-6}-N(R^{5a})C(=NR^{2d})-N(R^{3d},R^{4d})$; a $-(CH_2)_{0-6}-N(R^{3d})C_{5-6}$ membered heterocyclic ring containing 1-4 heteroatoms selected from N, O and S, and a $-(CH_2)_{0-6}$-5-6 membered heterocyclic ring containing 1-4 heteroatoms selected from N, O and S;

R^{5a}, R^{2d}, R^{3d} and R^{4d} are each independently a member selected from the group consisting of:

H, C_{1-6}-alkyl, C_{1-6}-alkylaryl, -CN; $-NO_2$; carbocyclic aryl, -CN; $-NO_2$; or R^{2d} and R^{3d} taken together with the N atoms they are independently attached form a 5-7 membered heterocyclic ring; or R^{3d} and R^{4d} taken together with the N atom to which they are attached form a 5-8 membered heterocyclic ring containing 1-4 heteroatoms selected from N, O and S;

J is a direct link or is a member selected from the group consisting of:

$-N(-R^9)-C(=O)-$; $-C(=O)-N(-R^9)-$; -O-; -S-; -SO-; $-SO_2-$; $-CH_2-$; $-N(-R^9)-$; and $-N(-R^9)-SO_2-$;

R^9 is a member selected from the group consisting of:

H; $-C_{1-4}$-alkyl; $-C_{0-4}$-alkyl-carbocyclic aryl; $-(CH_2)_{0-4}$-5-6 membered heterocyclic ring containing 1-4 heteroatoms selected from N, O and S; $-(CH_2)_{1-6}-C(=O)-O-C_{1-4}$-alkyl; and $-(CH_2)_{1-6}-C(=O)-N(R^{6a},R^{6b})$;

R^{6a} and R^{6b} are each a member independently selected from the group consisting of:

H and $-C_{1-6}$-alkyl;

X is a member selected from the group consisting of:

(a) phenyl substituted with 0-3 R^{1e} groups;

(b) naphthyl substituted with 0-3 R^{1e} groups and

(c) a 6-membered aromatic heterocyclic ring system containing 1-3 N atoms and having 0-3 ring atoms substituted with 0-3 R^{1e} groups; and

(d) an 8-10 membered fused aromatic heterocyclic bicyclic ring system containing 1-4 heteroatoms selected from N, O and S and 0-3 ring atoms of the fused heterocyclic bicyclic ring system are substituted with 0-3 R^{1e} groups;

R^{1e} is a member independently selected from the group consisting of:

Halo; CF_3; $-C_{1-4}$-alkyl; carbocyclic aryl; $-C_{0-2}$-alkylene-CN; $-O-R^{2e}$; $-C_{0-2}$-alkylene-$C(=O)-O-R^{2e}$; $-C_{0-2}$- alkylene-$C(=O)-N(R^{2e}, R^{3e})$; $-C_{0-2}$-alkylene-NO_2; $-C_{0-2}$-alkylene-$N(R^{2e}, R^{3e})$; $-C_{0-2}$-alkylene-$SO_2-N(R^{2e}, R^{3e})$; $-C_{0-2}$-alkylene-SO_2-R^{2e}; trihaloalkyl; $-O-C_{0-2}$-alkylene-$O-R^{2e}$; $-C_{0-2}$-alkylene-$O-R^{2e}$; $-O-C_{1-4}$-alkylene-$C(=O)-N(R^{2e}, R^{3e})$; $-O-C_{1-4}$-alkylene-$C(=O)-O-R^{2e}$; $-C_{0-2}$-alkylene-$N(R^{2e})-C(=O)-R^{3e}$; $-C_{0-2}$-alkylene-$N(-R^{2e})-SO_2-R^{3e}$; $-CH_2-N(R^{2e})-C(=O)-R^{3e}$;$-CH_2-N(R^{2e})-SO_2-R^{3e}$; $-(CH_2)_{0-6}-NR^{2e}R^{3e}$; $-C(=O)-N(R^{2e},R^{3e})$; $-N(-(CH_2)_{1-6}-OR^{2e})_2$; $-N(R^{10})-(CH_2)_{1-6}-OR^{2e}$; $-N(R^{10})-C(=O)-R^{2e}$; $-N(R^{10})-SO_2-R^{2e}$; $-C(=N(R^{10}))-N(R^{2e},R^{3e})$; and a $-(CH_2)_{0-6}$-5-6 membered heterocyclic ring containing 1-4 heteroatoms selected from N, O and S;

R^{10}, R^{2e} and R^{3e} are each independently a member selected from the group consisting of:

H; $-C_{1-4}$-alkyl; $-C_{0-2}$-alkylene-$O-R^{1g}$; $-C_{0-2}$-alkylene-$N(-R^{1g}, -R^{2g})$;$-C_{1-4}$-alkylene-carbocyclic aryl; $-C_{1-4}$-alkylene-heterocyclic; and R^{10} and R^{2e}, or R^{2e} and R^{3e} together with the N atom to which they are attached can form 5-8 membered heterocyclic ring containing 1-4 heteroatoms selected from N, O and S which can be substituted with 0-2 R^{1g} groups;

R^{1g} and R^{2g} are independently a member selected from the group of:

H; halo; $-C_{1-4}$-alkyl, a carbocyclic aryl group ; a heterocyclic group; -CN; $-C(=O)-N(R^{3g})R^{4g}$; $-C(=O)-OR^{3g}$; $-NO_2$; $-(CH_2)_p-NR^{3g}R^{4g}$; $-SO_2NR^{3g}R^{4g}$; $-SO_2R^{3g}$; $-CF_3$; and $-(CH_2)_pOR^{3g}$;

p is an integer of 0-2; and

R^{3g} and R^{4g} are each independently selected from the group consisting of:

H; C_{1-4}-alkyl and $-C_{0-4}$-alkylene-carbocyclic aryl;

or a pharmaceutically acceptable salt thereof;

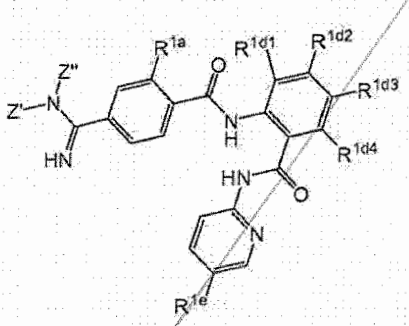
wherein the coagulation inhibiting amount of the factor Xa inhibitor compound is an aggregate daily dose from between about 0.01 and about 2.0 mg/kg.

16. The unit dose formulation of claim 15, wherein the coagulation inhibiting amount of the factor Xa inhibitor compound is an aggregate daily dose between about 0.1 and about 1.5 mg/kg.

17. The unit dose formulation of claim 15, wherein the coagulation inhibiting amount of the factor Xa inhibitor compound is an aggregate daily dose between about 0.4 and about 1.2 mg/kg.

18. The unit dose formulation of claim 15, wherein the pharmaceutically acceptable salt of the factor Xa inhibitor compound is a maleate salt.

19. The unit dose formulation of claim 15, wherein the factor Xa inhibitor compound is of formula IV:



IV

wherein:

Z' and Z'' are each independently a C_1-C_6 alkyl which is optionally substituted with a hydroxyl, carboxylic acid or carboxylic acid ester group;

R^{1a} is selected from the group consisting of:

H, -F, -Cl, and Br;

R^{1d2} and R^{1d4} are each H;

R^{1d1} and R^{1d3} are each independently a member selected from the group consisting of:

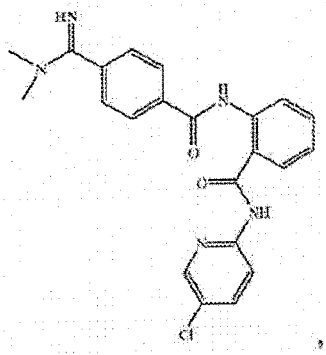
H, -Cl, -F, -Br, -OH and $-OCH_3$; and

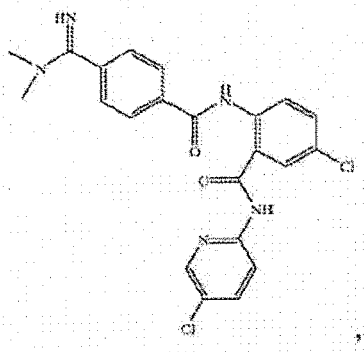
R^{1e} is a member selected from the group consisting of:

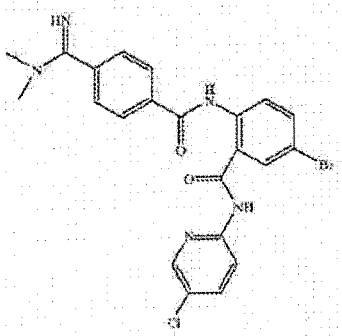
-F, -Cl, -Br, -OH, $-CH_3$, and $-OCH_3$,

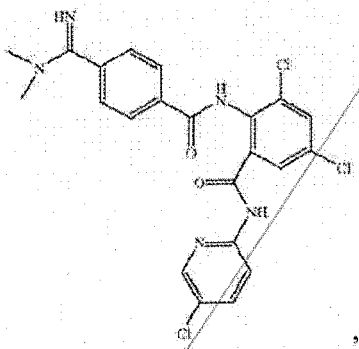
or a pharmaceutically acceptable salt thereof.

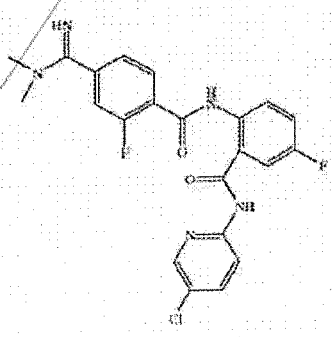
20. The unit dose formulation of claim 19, wherein the compound is selected from the group consisting of:

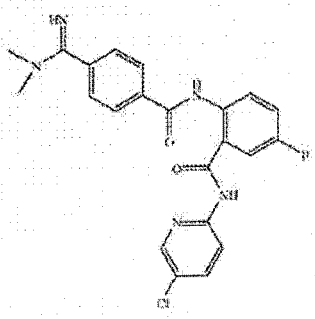


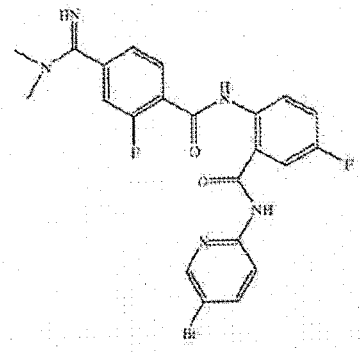


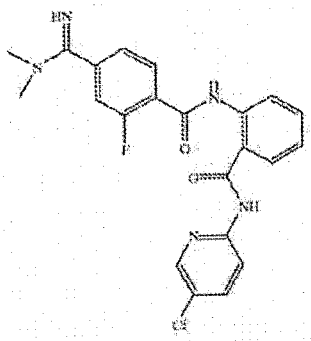


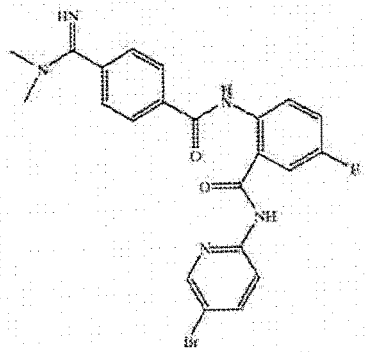


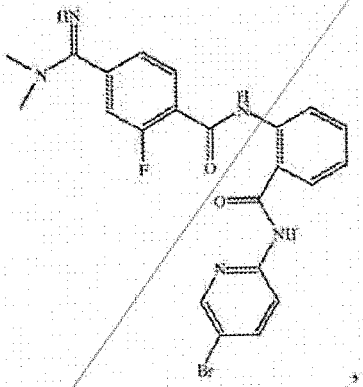


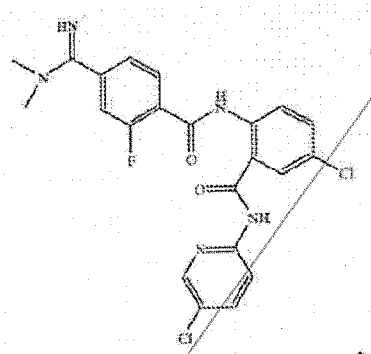


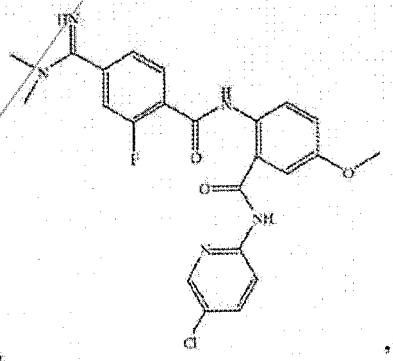


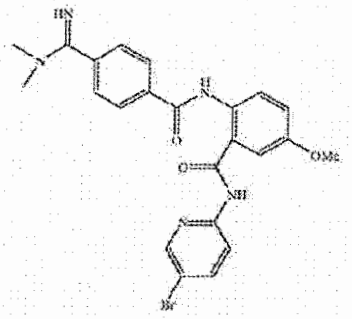


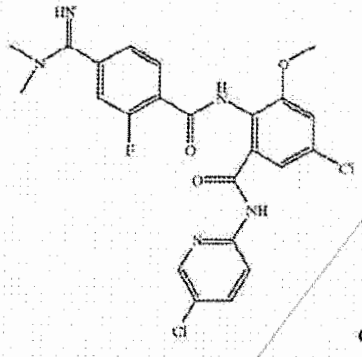






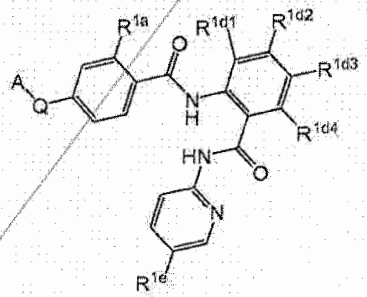






, and or a pharmaceutically acceptable salt thereof.

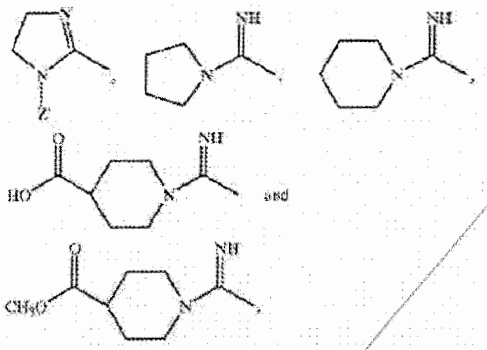
21. The unit dose formulation of claim 15, wherein the factor Xa inhibitor compound is of formula V:



V

wherein:

A-Q is a member selected from the group consisting of:



where Z' is a C_{1-6} alkyl which is optionally substituted with a hydroxyl, carboxylic acid or carboxylic acid ester group;

R^{1a} is selected from the group consisting of:

H, -F, -Cl, and Br;

R^{1d2} and R^{1d4} are each H;

R^{1d1} and R^{1d3} are each independently a member selected from the group consisting of:

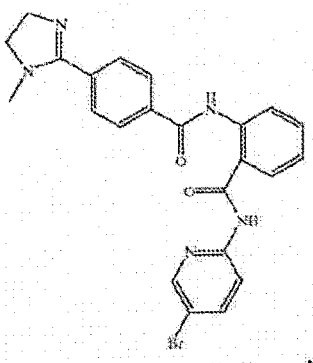
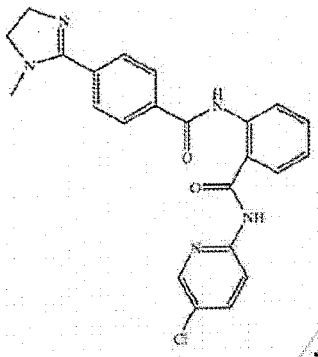
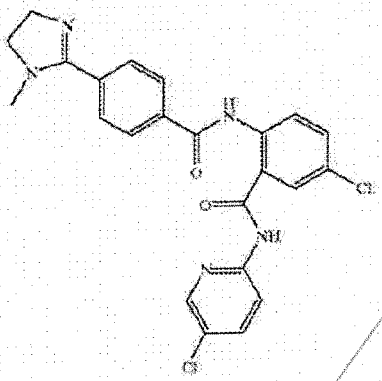
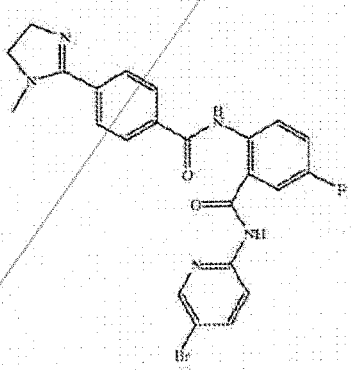
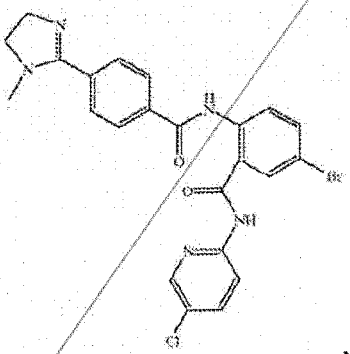
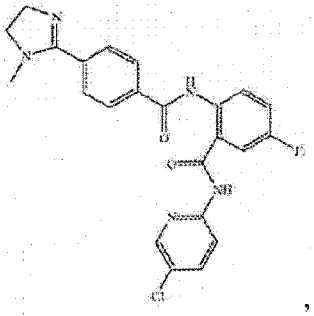
H, -Cl, -F, -Br, -OH and $-OCH_3$; and

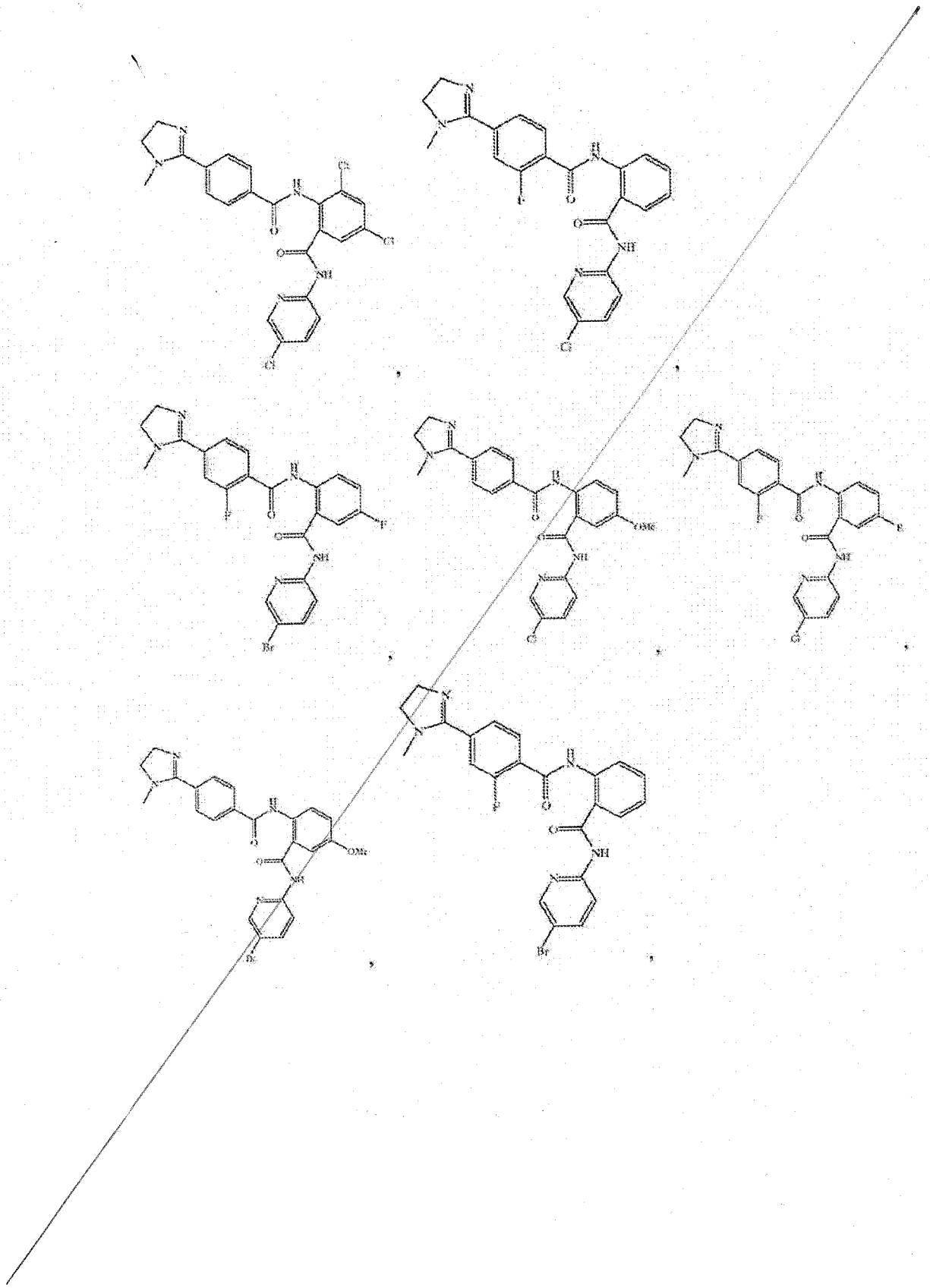
R^{1e} is a member selected from the group consisting of:

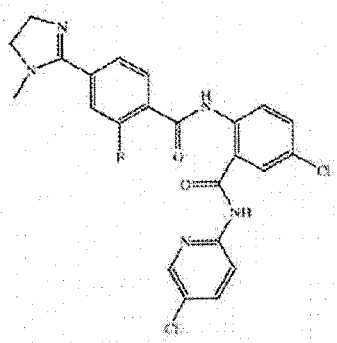
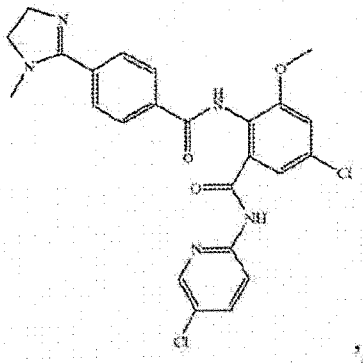
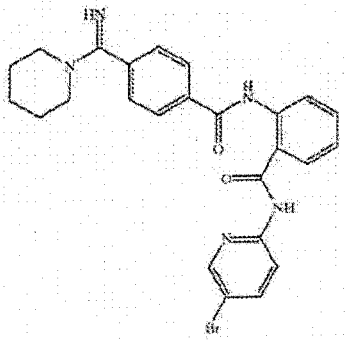
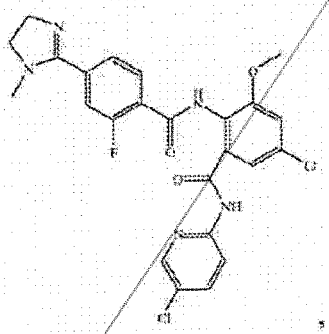
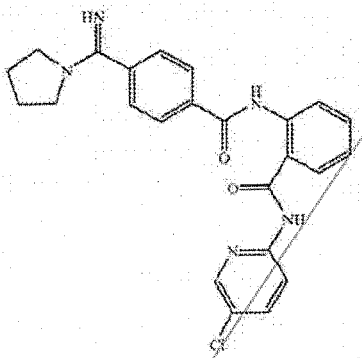
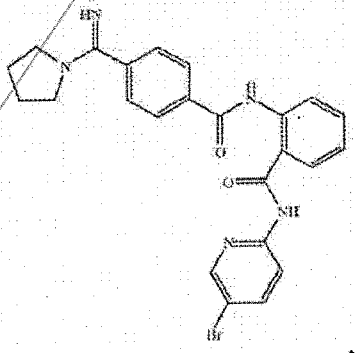
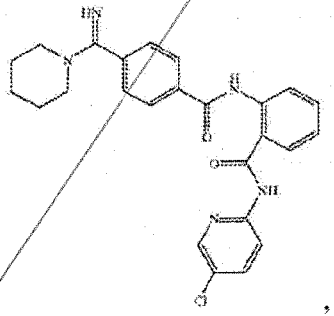
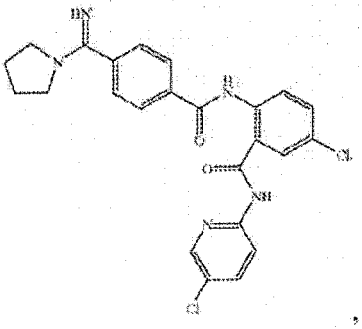
-F, -Cl, -Br, -OH, $-CH_3$, and $-OCH_3$,

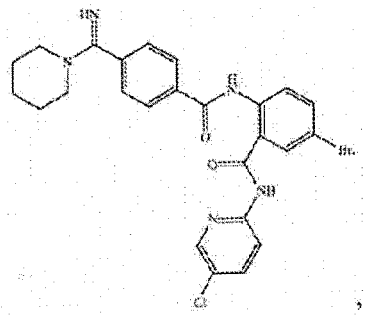
or a pharmaceutically acceptable salt thereof.

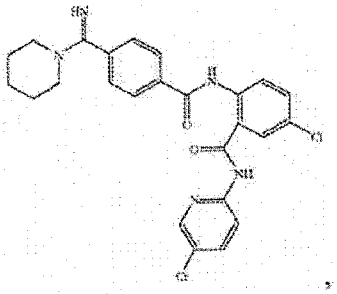
22. The unit dose formulation of claim 21, wherein the compound is selected from the group consisting of:

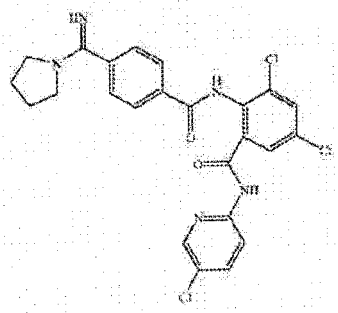

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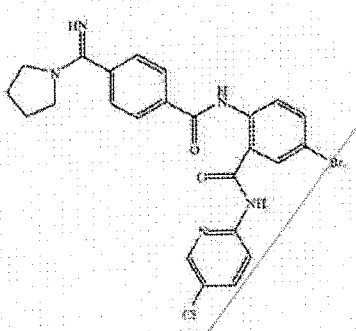


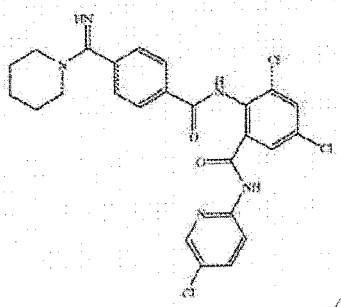

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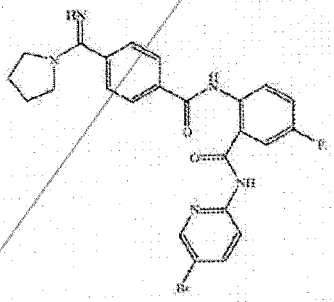


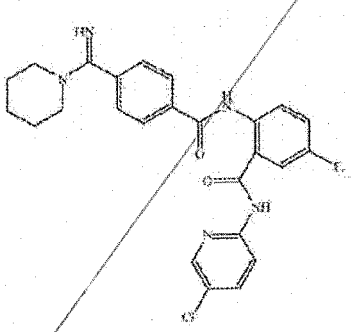


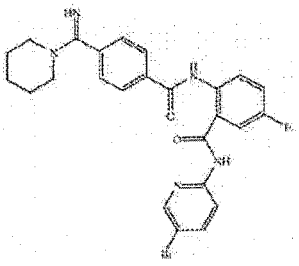




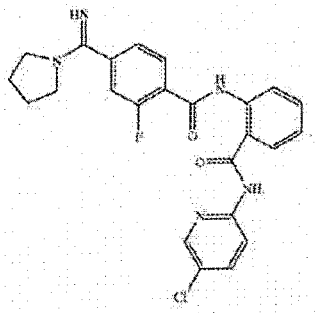
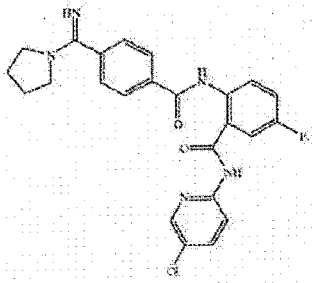
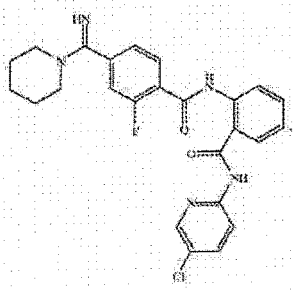
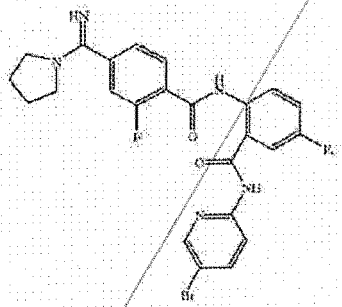
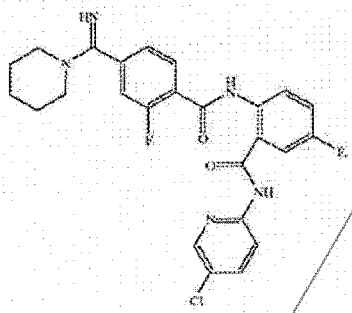
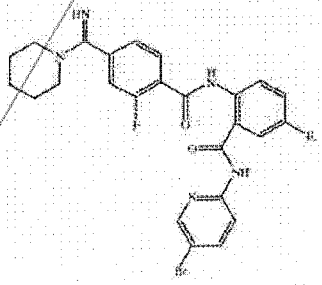
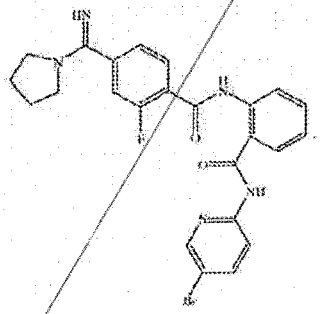
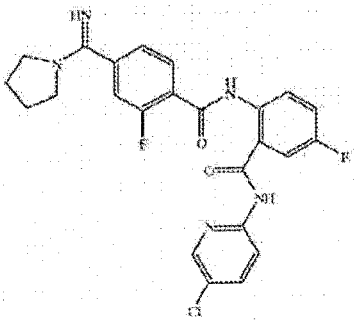




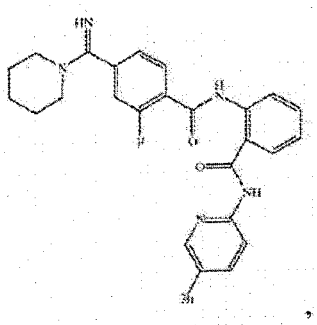
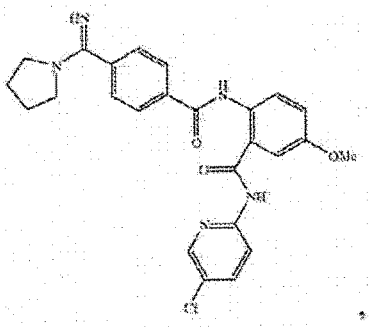
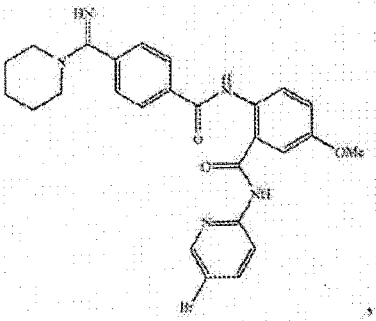
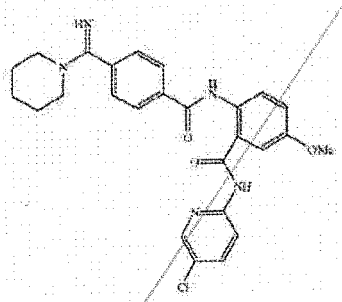
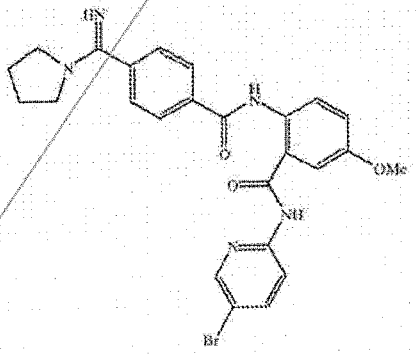
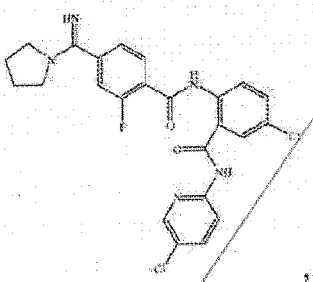
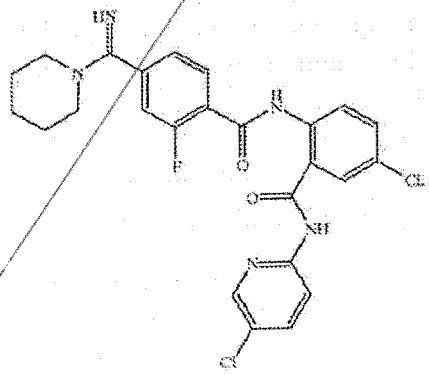




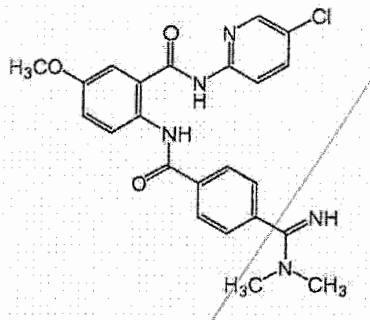
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or a pharmaceutically acceptable salt thereof.

23. A unit dose formulation comprising a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a coagulation inhibiting amount of the factor Xa inhibitor compound II :



II

or pharmaceutically acceptable salt thereof, wherein the coagulation inhibiting amount of the factor Xa inhibitor compound is an aggregate daily dose of from between about 0.01 and about 2.0 mg/kg.

24. The unit dose formulation of claim 23, wherein the coagulation inhibiting amount of the factor Xa inhibitor compound is an aggregate daily dose of from between about 0.1 and about 1.5 mg/kg.

25. The method of claim 10, wherein the pharmaceutically acceptable salt of the factor Xa inhibitor compound is a maleate salt.

26. An *in vitro* assay to determine whether a compound has *in vivo* antithrombotic activity comprising:

a) introducing a test compound into an *in vitro* sample of whole blood or plasma comprising tissue factor (TF) and a detectably-labeled thrombin substrate to form a test sample;

b) determining the level of thrombin activity in the test sample by monitoring the cleavage of the detectably-labeled thrombin substrate in the test sample as a function of time;

c) determining the level of thrombin activity in a control sample by monitoring the cleavage of the detectably-labeled thrombin substrate in the control sample as a function of time, wherein the control sample comprises whole blood or plasma comprising tissue factor (TF) and a detectably-labeled thrombin substrate;

d) comparing the level of thrombin activity in the test sample and the control sample, wherein a lower level of thrombin activity in the test sample is an indication that the test compound has *in vivo* antithrombotic activity.

27. The assay of claim 26, wherein the test sample and the control sample comprise whole blood.

28. The assay of claim 27, wherein the whole blood is anticoagulated.

29. The assay of claim 27, wherein the whole blood is nonanticoagulated.

30. The assay of claim 26, wherein the test sample and the control sample comprise plasma.

31. The assay of claim 30, wherein the plasma is anticoagulated.

32. The assay of claim 30, wherein the plasma is nonanticoagulated.

33. The assay of claim 26, wherein detectably-labeled thrombin substrate is a Z-Gly-Gly-Arg-AMC.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1A shows the correlation of thrombin generation with the international normalized ratio (INR) in anticoagulated patients treated with warfarin. Thrombin generation was measured at 10 minutes in plasma samples from patients receiving stable warfarin therapy (n = 137). Data from patients receiving warfarin therapy is presented as quintiles of the INR results. Error bars show standard errors.

FIG. 1B shows the correlation of thrombin generation with activated partial thromboplastin time (aPTT) in anticoagulated patients treated with enoxaparin. Plasma thrombin generation was measured in 16 enoxaparin-treated patients. Anti-fXa units were measured by COATEST LMW assay according to the manufacturer's instructions. Groups were compared by Student's t-test.

FIG. 1C shows the correlation of thrombin generation with aPTT in anticoagulated patients treated with unfractionated heparin (UFH). Plasma thrombin