

FIG. 1

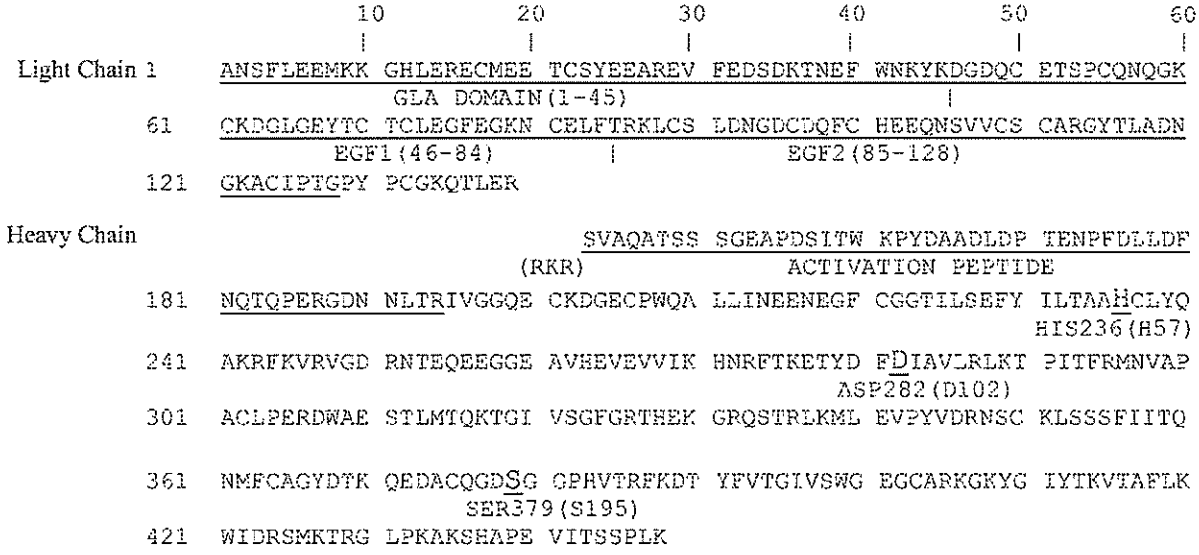


FIG. 2

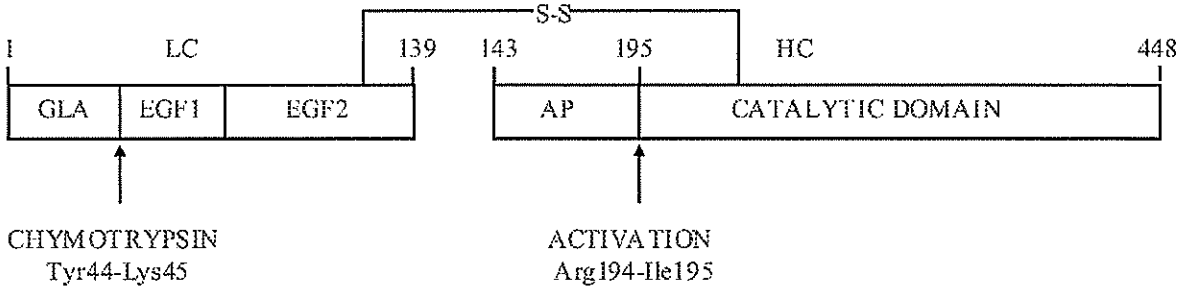


FIG. 3

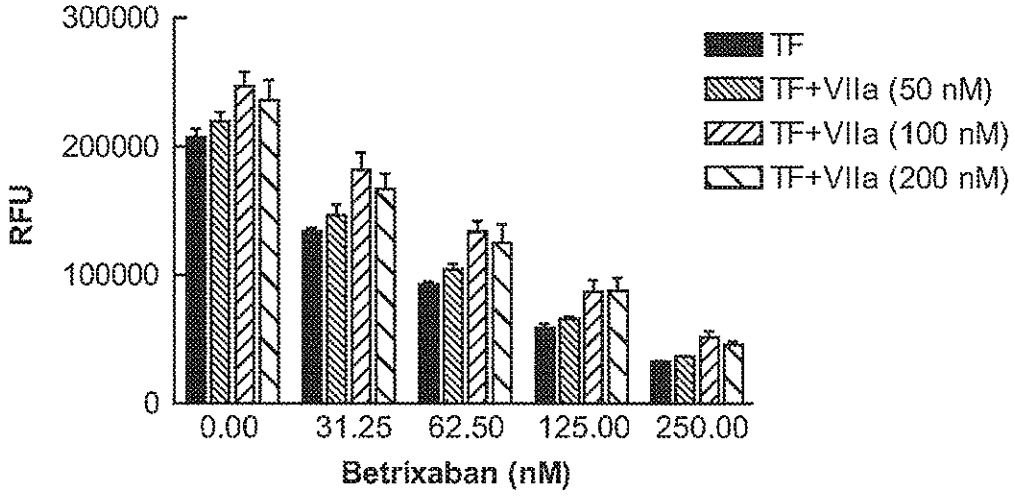

300000
200000
100000
0
RFU
0.00
31.25
62.50
125.00
250.00
Betrixaban (nM)
TF
TF+VIIa (50 nM)
TF+VIIa (100 nM)
TF+VIIa (200 nM)

FIG. 4

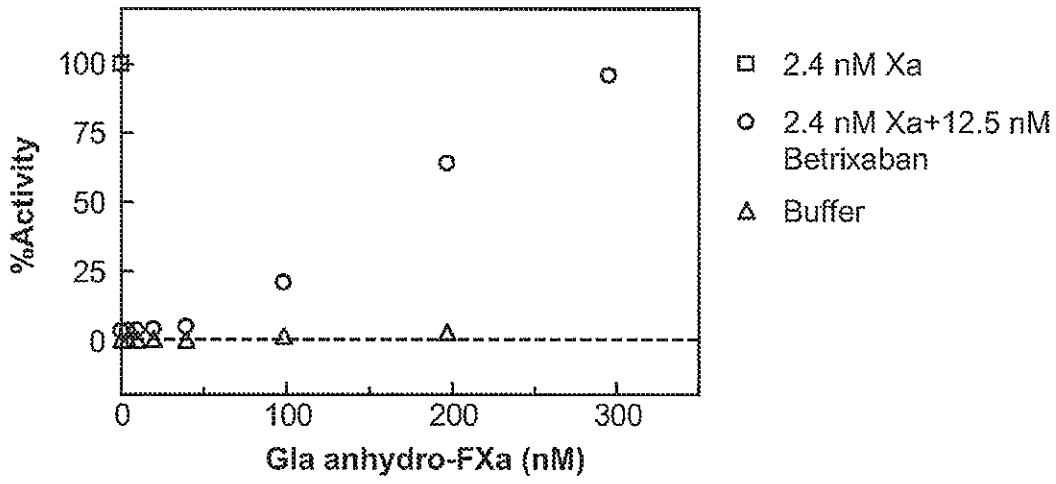

100
75
50
25
0
%Activity
0
100
200
300
Gla anhydro-FXa (nM)
2.4 nM Xa
2.4 nM Xa+12.5 nM Betrixaban
Buffer

FIG. 5

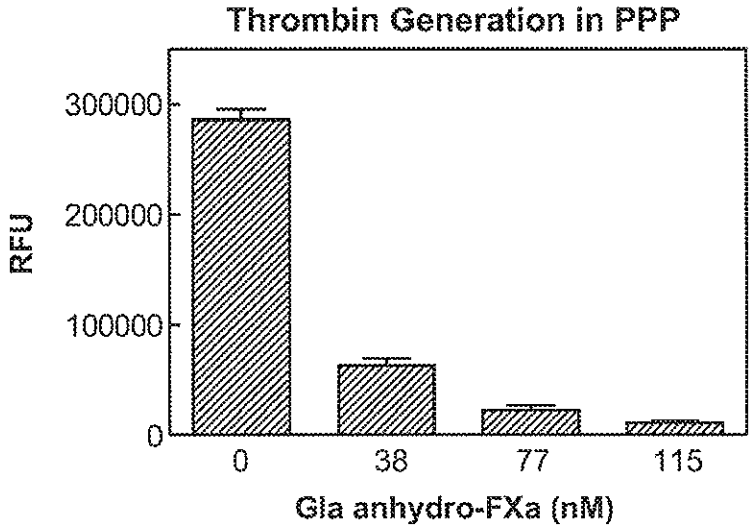

Thrombin Generation in PPP
RFU
300000
200000
100000
0
0
38
77
115
Gla anhydro-FXa (nM)

FIG. 6

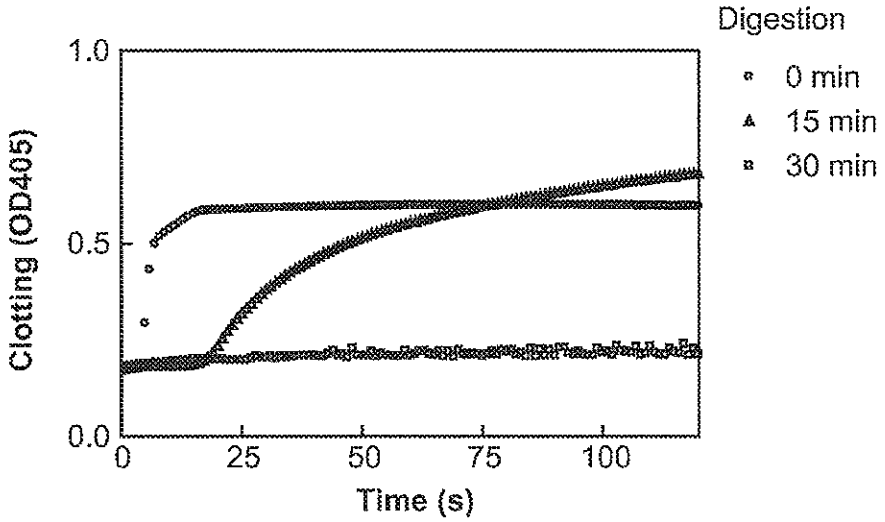

Digestion
0 min
15 min
30 min
Clotting (OD405)
1.0
0.5
0.0
0
25
50
75
100
Time (s)

FIG. 7

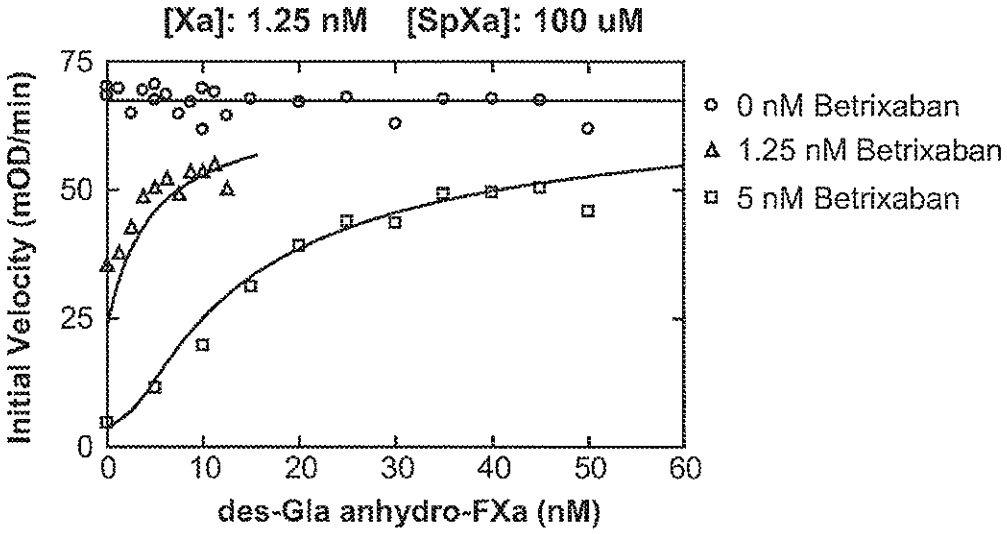

[Xa]: 1.25 nM [SpXa]: 100 uM
Initial Velocity (mOD/min)
75
50
25
0
0
10
20
30
40
50
60
des-Gla anhydro-FXa (nM)
0 nM Betrixaban
1.25 nM Betrixaban
5 nM Betrixaban

FIG. 8

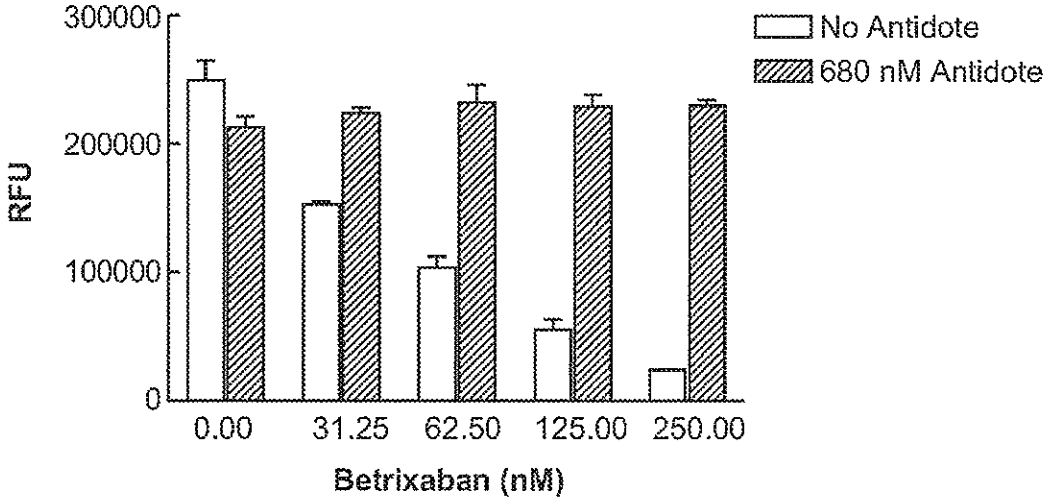

300000
200000
100000
0
RFU
0.00
31.25
62.50
125.00
250.00
Betrixaban (nM)
No Antidote
680 nM Antidote

FIG. 9

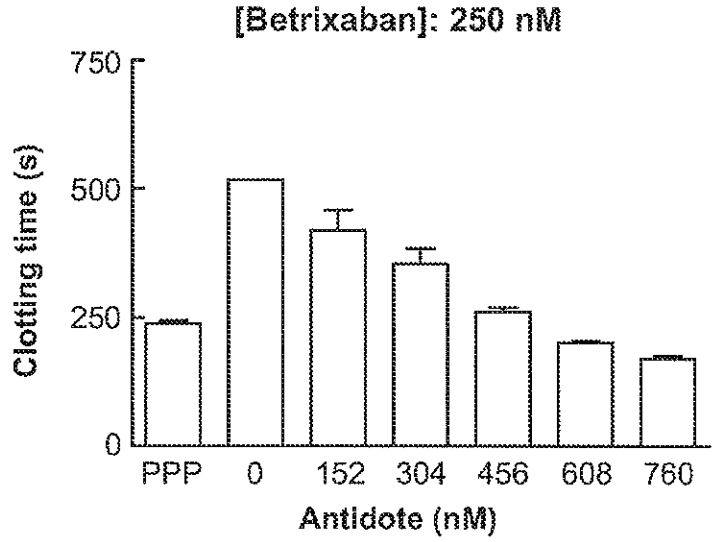

[Betrixaban]: 250 nM
Clotting time (s)
750
500
250
0
PPP
0
152
304
456
608
760
Antidote (nM)

FIG. 10

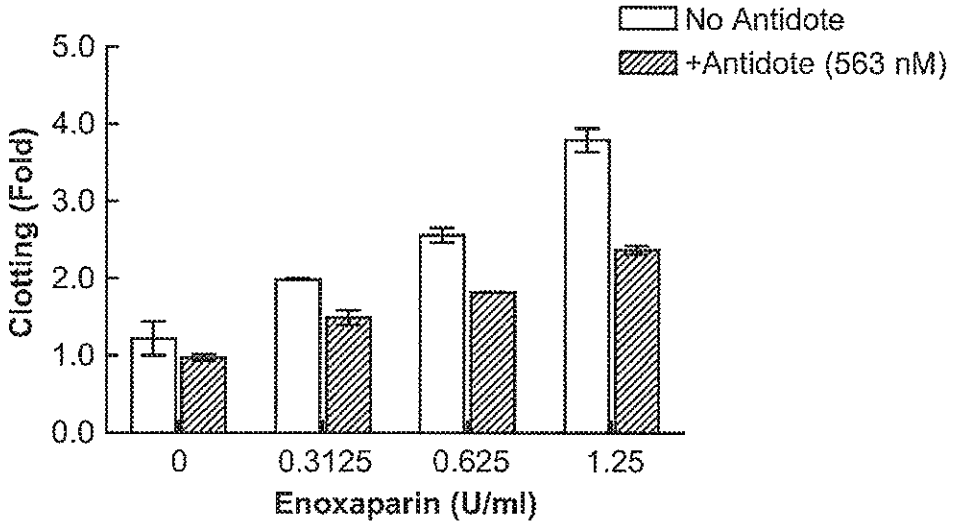

No Antidote
+Antidote (563 nM)
Clotting (Fold)
5.0
4.0
3.0
2.0
1.0
0.0
0
0.3125
0.625
1.25
Enoxaparin (U/ml)

FIG. 11

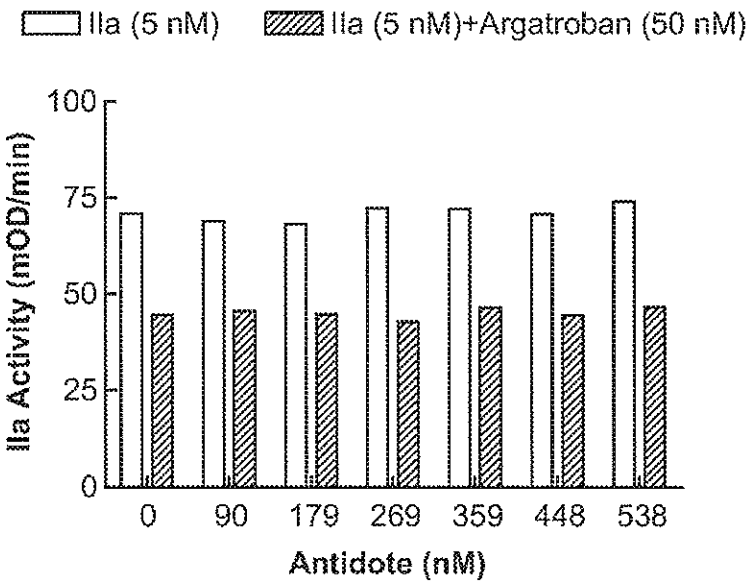

IIa (5 nM)
IIa (5 nM)+Argatroban (50 nM)
IIa Activity (mOD/min)
100
75
50
25
0
0
90
179
269
359
448
538
Antidote (nM)

FIG. 12

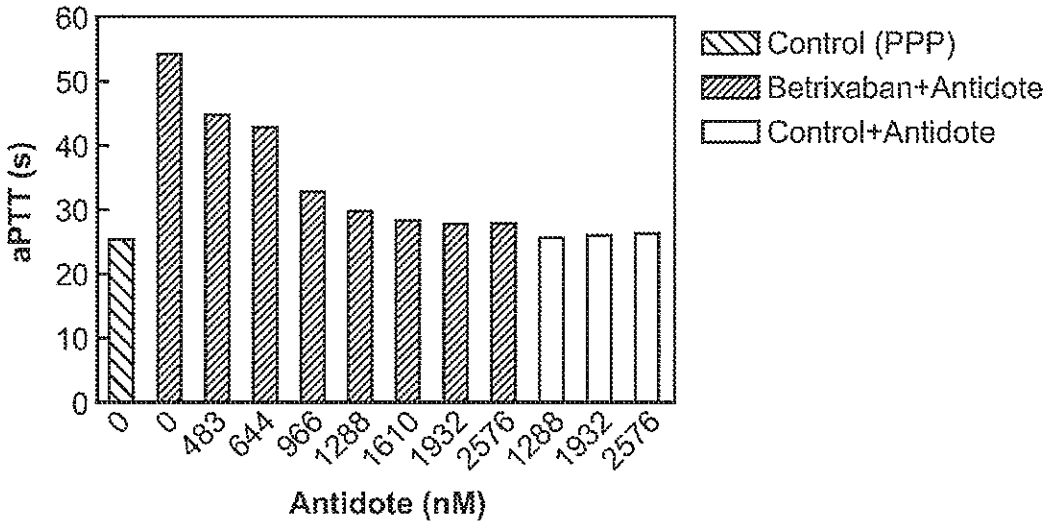

aPTT (s)
60
50
40
30
20
10
0
0
0
483
644
966
1288
1610
1932
2576
1288
1932
2576
Antidote (nM)
Control (PPP)
Betrixaban+Antidote
Control+Antidote

FIG. 13

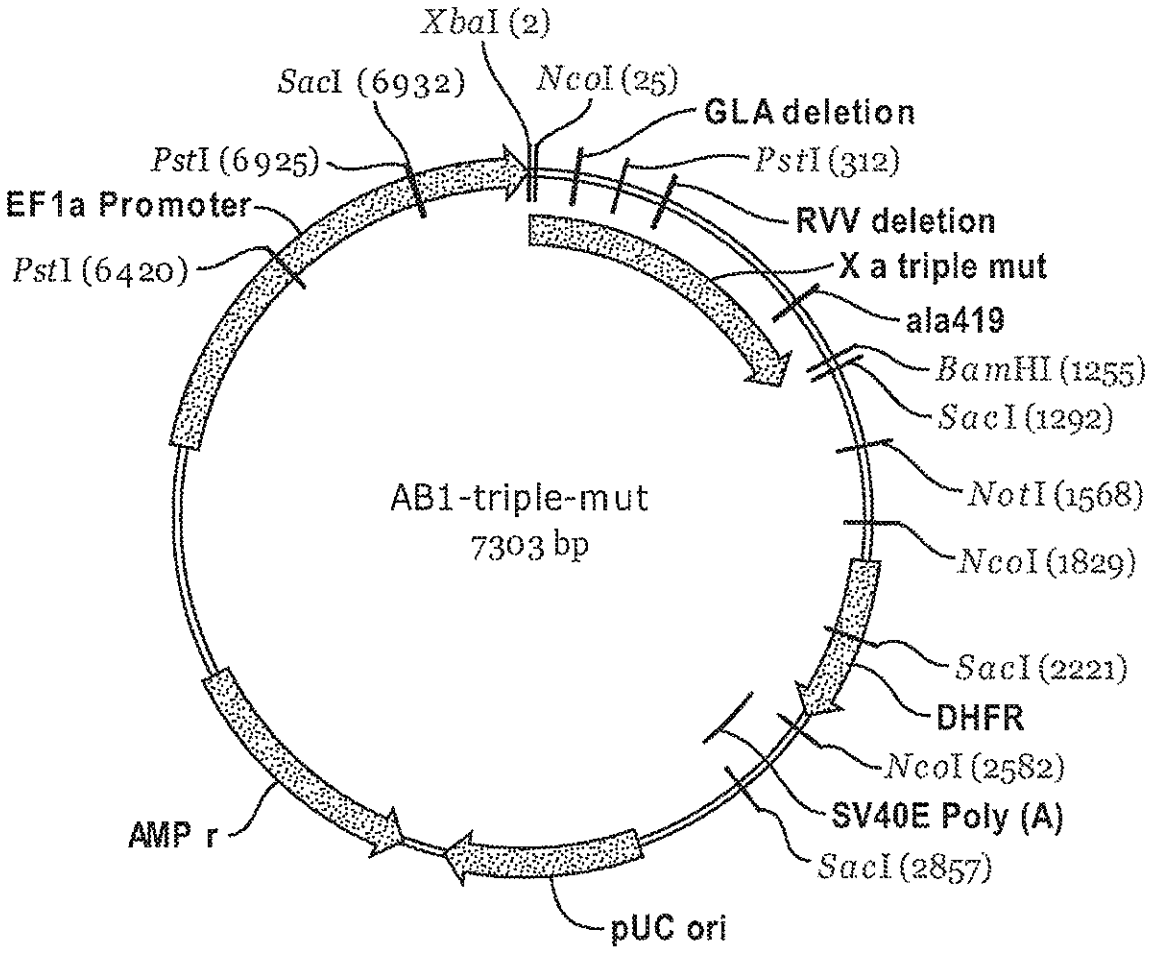

XbaI (2)
SacI (6932)
NcoI (25)
GLA deletion
PstI (6925)
PstI (312)
EF1a Promoter
RVV deletion
PstI (6420)
X a triple mut
ala419
BamHI (1255)
SacI (1292)
AB1-triple-mut
7303 bp
NotI (1568)
NcoI (1829)
SacI (2221)
DHFR
NcoI (2582)
SV40E Poly (A)
SacI (2857)
AMP r
pUC ori

FIG. 14

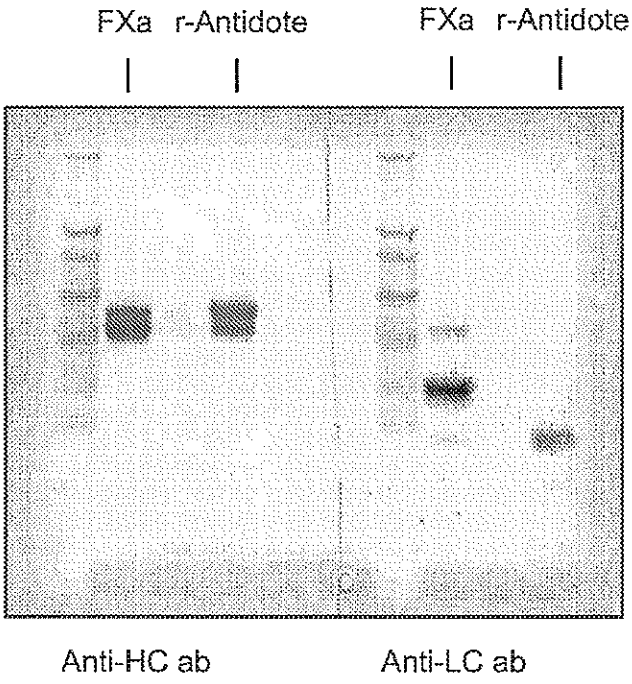

FXa
r-Antidote
FXa
r-Antidote
Anti-HC ab
Anti-LC ab

FIG. 15

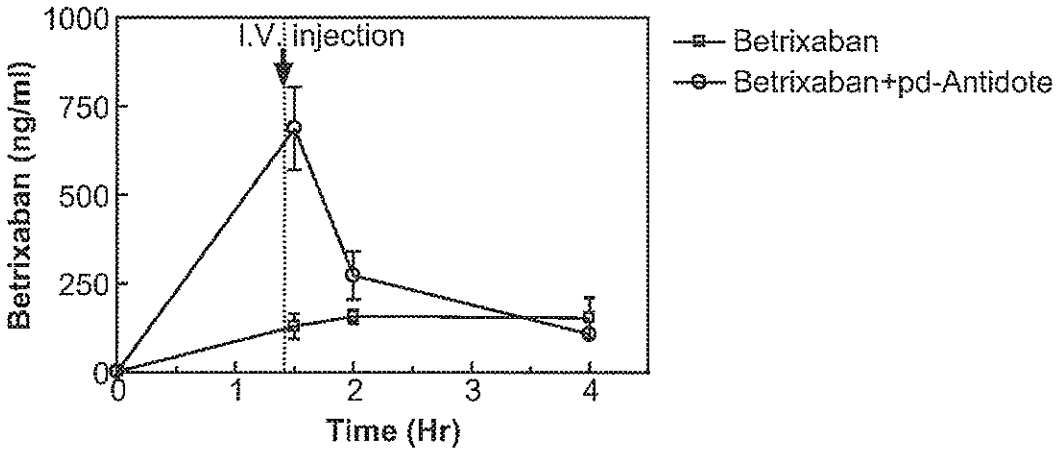

1000
750
500
250
0
Betrixaban (ng/ml)
I.V. injection
0
1
2
3
4
Time (Hr)
Betrixaban
Betrixaban+pd-Antidote

FIG. 16

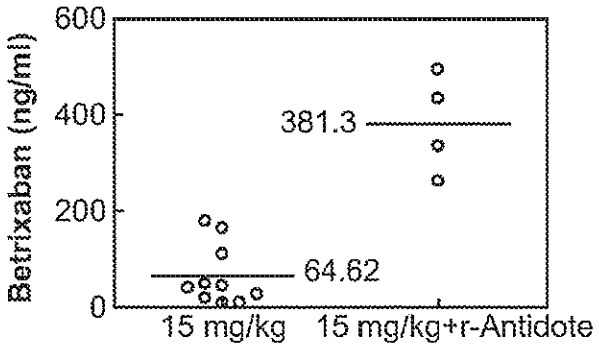


FIG. 17A

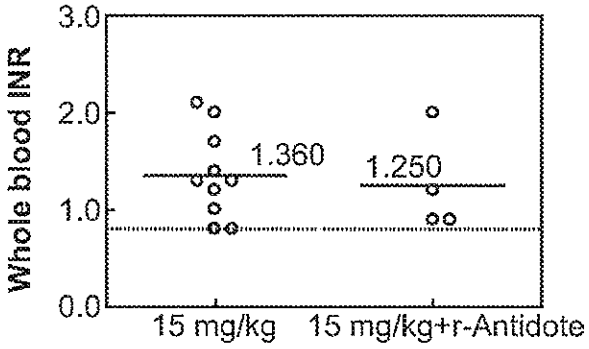


FIG. 17B

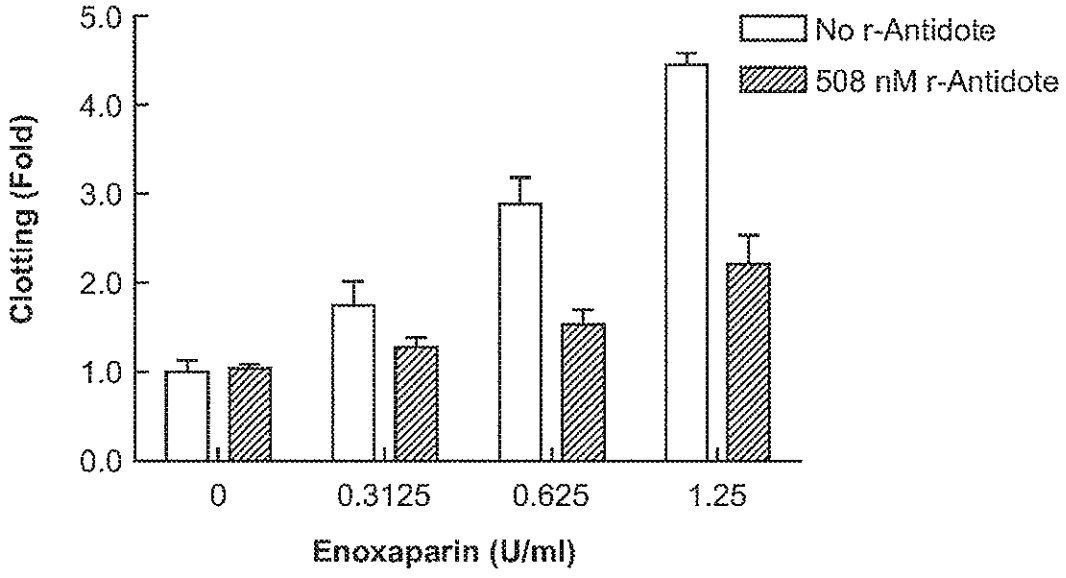


FIG. 18

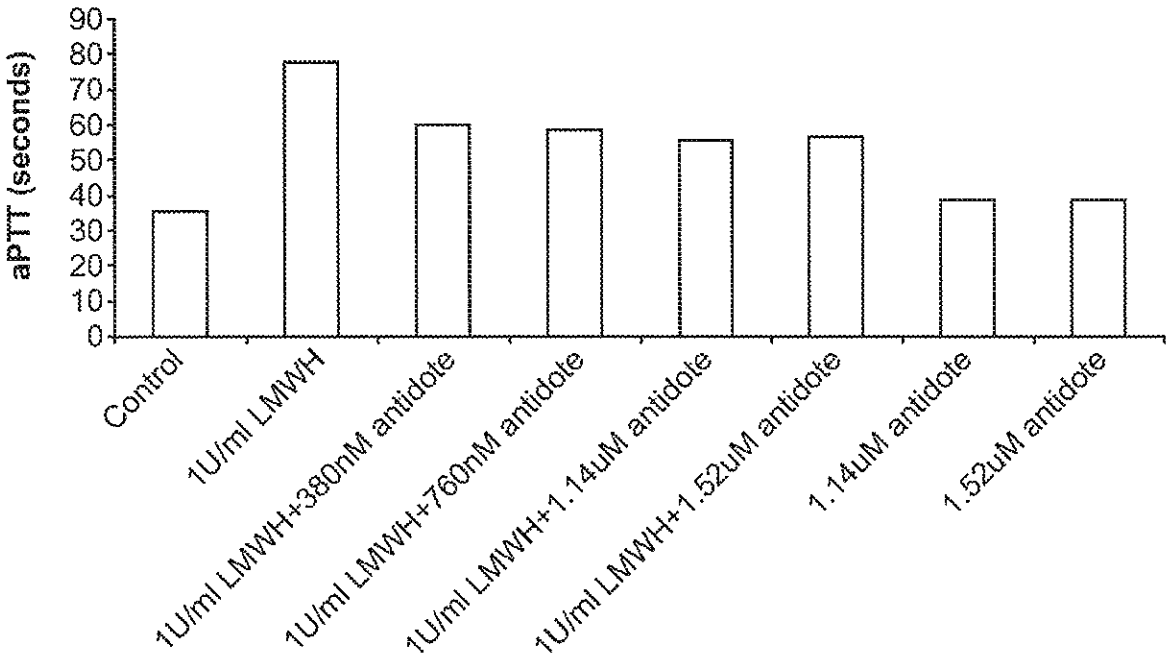

aPTT (seconds)
90
80
70
60
50
40
30
20
10
0
Control
1U/ml LMWH
1U/ml LMWH+380nM antidote
1U/ml LMWH+760nM antidote
1U/ml LMWH+1.14uM antidote
1U/ml LMWH+1.52uM antidote
1.14uM antidote
1.52uM antidote

FIG. 19

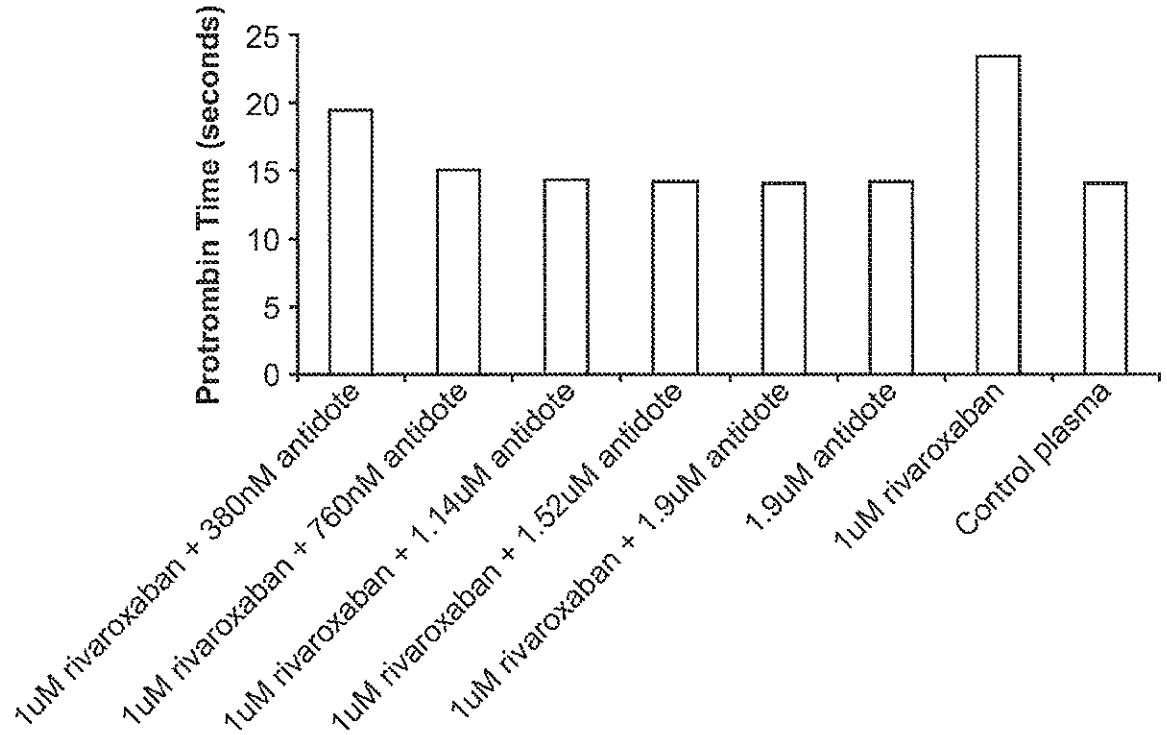

Protrombin Time (seconds)
25
20
15
10
5
0
1uM rivaroxaban + 380nM antidote
1uM rivaroxaban + 760nM antidote
1uM rivaroxaban + 1.14uM antidote
1uM rivaroxaban + 1.52uM antidote
1uM rivaroxaban + 1.9uM antidote
1.9uM antidote
1uM rivaroxaban
Control plasma

FIG. 20

```
atggggcgcccactgcacctcgtcctgctcagtgcctccctggctggcctcctgctgctc
 M  G  R  P  L  H  L  V  L  L  S  A  S  L  A  G  L  L  L  L
ggggaaagtctgttcatccgcagggagcaggccaacaacatcctggcgagggtcacgagg
 G  E  S  L  F  I  R  R  E  Q  A  N  N  I  L  A  R  V  T  R
gccaattcctttctttttctggaataaatacaaagatggcgaccagtgtgagaccagtcct
 A  N  S  F  L  F  W  N  K  Y  K  D  G  D  Q  C  E  T  S  P
tgccagaaccagggcaaatgtaaagacggcctcggggaatacacctgcacctgtttagaa
 C  Q  N  Q  G  K  C  K  D  G  L  G  E  Y  T  C  T  C  L  E
ggattcgaaggcaaaaactgtgaattattcacacggaagctctgcagcctggacaacggg
 G  F  E  G  K  N  C  E  L  F  T  R  K  L  C  S  L  D  N  G
gactgtgaccagttctgccacgaggaacagaactctgtggtgtgctcctgcgcccgcggg
 D  C  D  Q  F  C  H  E  E  Q  N  S  V  V  C  S  C  A  R  G
tacaccctggctgacaacggcaaggcctgcattcccacagggccctaccccctgtgggaaa
 Y  T  L  A  D  N  G  K  A  C  I  P  T  G  P  Y  P  C  G  K
cagaccctggaacgcaggaagaggaggaagaggatcgtgggaggccaggaatgcaaggac
 Q  T  L  E  R  R  K  R  R  K  R  I  V  G  G  Q  E  C  K  D
ggggagtgtccctggcaggccctgctcatcaatgaggaaaacgagggtttctgtggtgga
 G  E  C  P  W  Q  A  L  L  I  N  E  E  N  E  G  F  C  G  G
accattctgagcgagttctacatcctaacggcagcccactgtctctaccaagccaagaga
 T  I  L  S  E  F  Y  I  L  T  A  A  H  C  L  Y  Q  A  K  R
ttcaaggtgagggtagggacggaacacggagcaggaggagggcggtgaggcggtgcac
 F  K  V  R  V  G  D  R  N  T  E  Q  E  E  G  G  E  A  V  H
gaggtggaggtggtcatcaagcacaaccggttcacaaaggagacctatgacttcgacatc
 E  V  E  V  V  I  K  H  N  R  F  T  K  E  T  Y  D  F  D  I
gccgtgctccggctcaagacccccatcaccttccgcatgaacgtggcgcctgcctgcctc
 A  V  L  R  L  K  T  P  I  T  F  R  M  N  V  A  P  A  C  L
cccgagcgtgactgggccgagtccacgctgatgacgcagaagacggggattgtgagcggc
 P  E  R  D  W  A  E  S  T  L  M  T  Q  K  T  G  I  V  S  G
ttcgggcgcacccacgagaagggccggcagtccaccaggctcaagatgctggaggtgccc
 F  C  R  T  H  E  K  G  R  Q  S  T  R  L  K  M  L  E  V  P
tacgtggaccgcaacagctgcaagctgtccagcagcttcatcatcacccagaacatgttc
 Y  V  D  R  N  S  C  K  L  S  S  S  F  I  I  T  Q  N  M  F
tgtgccggctacgacaccaagcaggaggatgcctgccaggggacgcaggggcccgcac
 C  A  G  Y  D  T  K  Q  E  D  A  C  Q  G  D  A  G  G  P  H
gtcacccgcttcaaggacacctacttcgtgacaggcatcgtcagctggggagagggctgt
 V  T  R  F  K  D  T  Y  F  V  T  G  I  V  S  W  G  E  G  C
gcccgtaaggggaagtacgggatctacaccaaggtcaccgccttcctcaagtggatcgac
 A  R  K  G  K  Y  G  I  Y  T  K  V  T  A  F  L  K  W  I  D
aggtccatgaaaaccagggcttgcccaaggccaagagccatgccccggaggtcataacg
 R  S  M  K  T  R  G  L  P  K  A  K  S  H  A  P  E  V  I  T
tcctctccattaaagtga
 S  S  P  L  K  -
```

FIG. 21

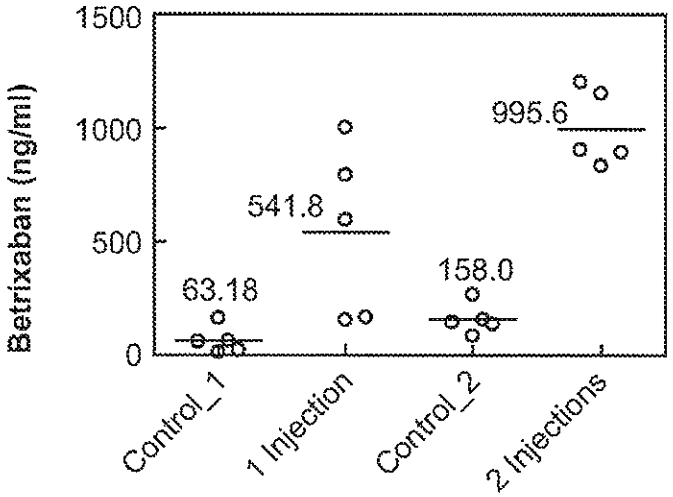


FIG. 22A

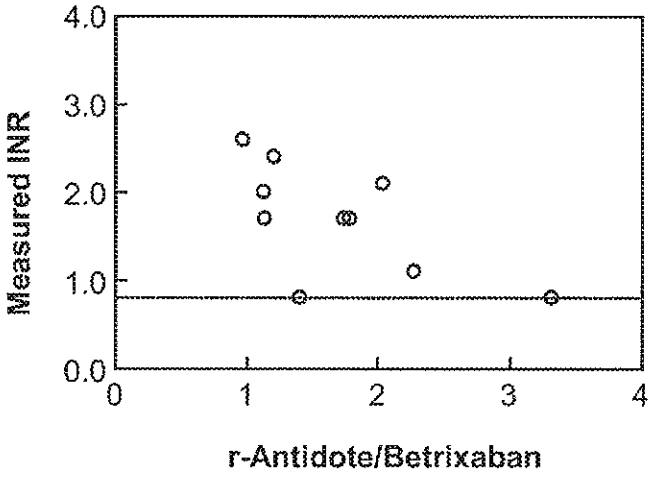


FIG. 22B