

FIG. 1

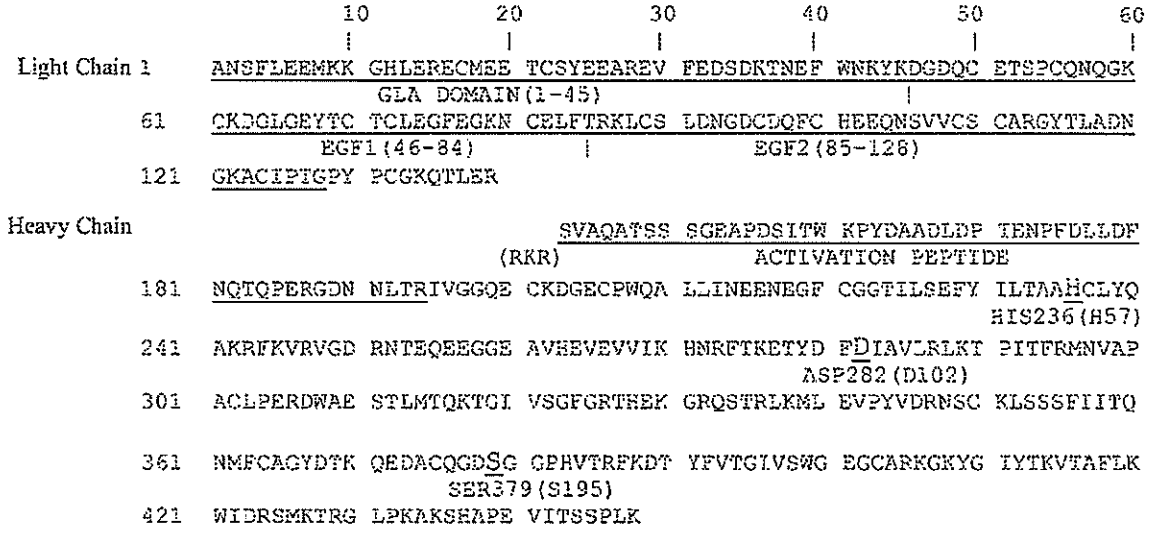


FIG. 2

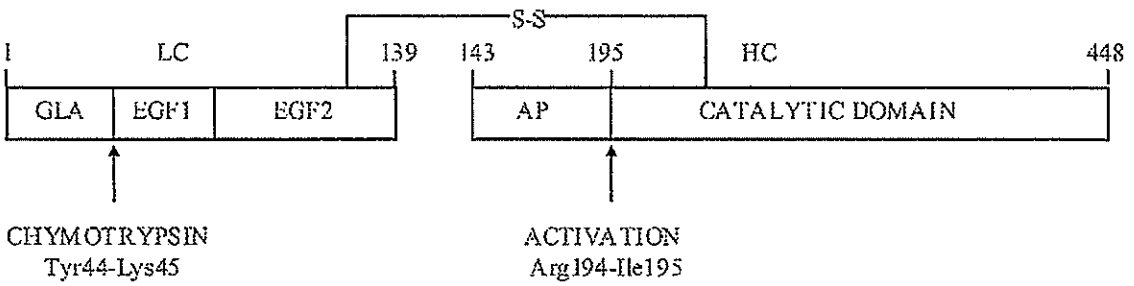


FIG. 3

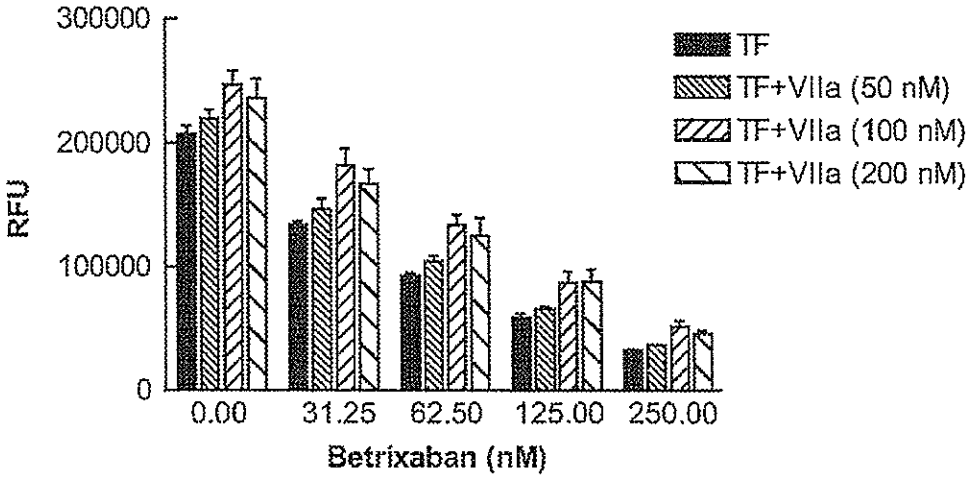

300000
200000
100000
0
RFU
0.00
31.25
62.50
125.00
250.00
Betrixaban (nM)
TF
TF+VIIa (50 nM)
TF+VIIa (100 nM)
TF+VIIa (200 nM)

FIG. 4

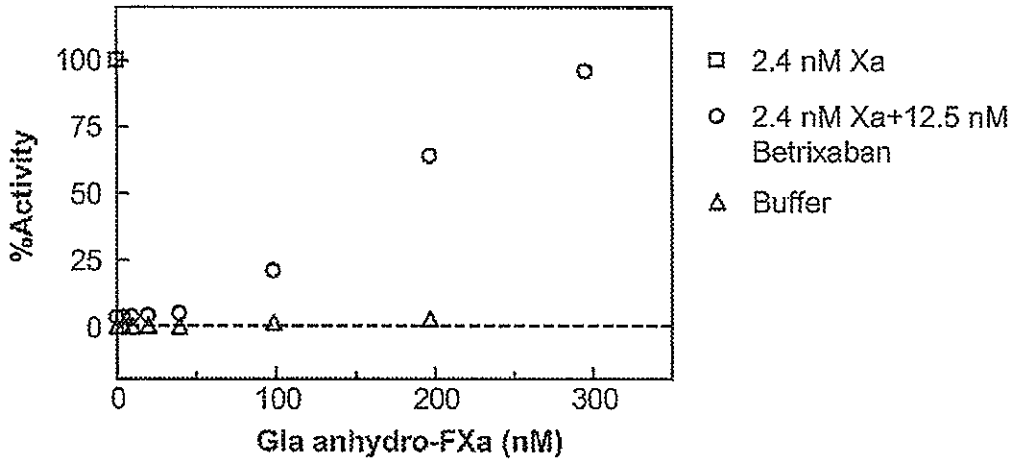

100
75
50
25
0
%Activity
0
100
200
300
Gla anhydro-FXa (nM)
2.4 nM Xa
2.4 nM Xa+12.5 nM Betrixaban
Buffer

FIG. 5

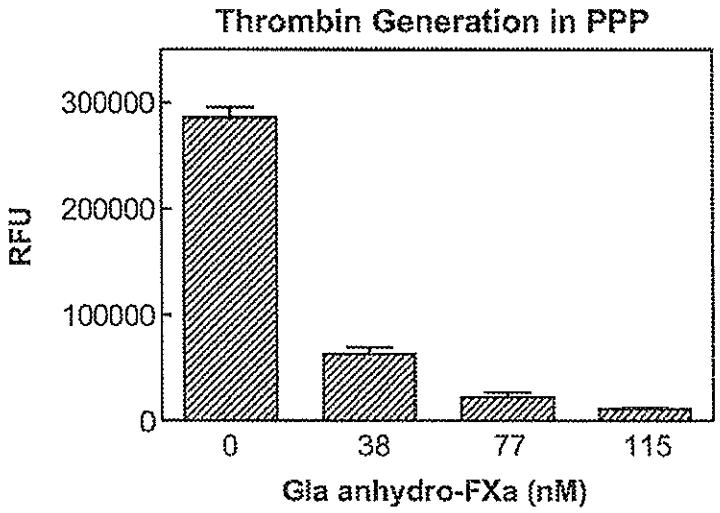

Thrombin Generation in PPP
RFU
300000
200000
100000
0
0
38
77
115
Gla anhydro-FXa (nM)

FIG. 6

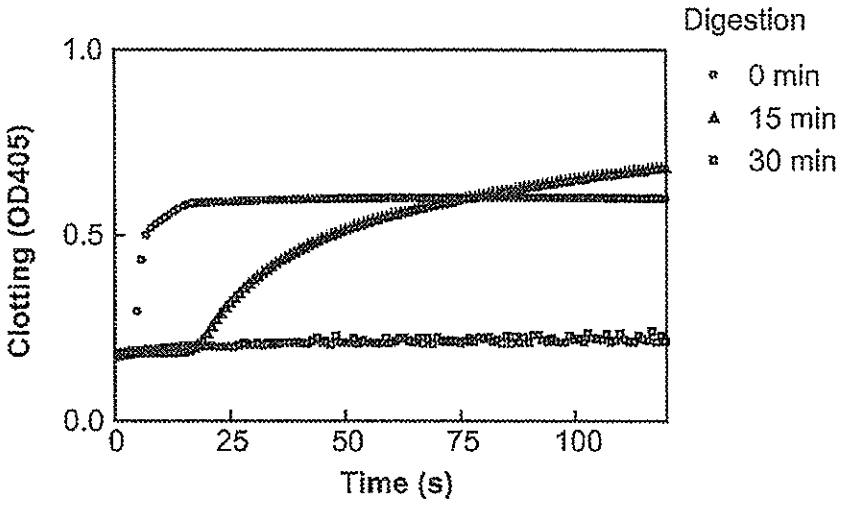

Digestion
0 min
15 min
30 min
Clotting (OD405)
1.0
0.5
0.0
0
25
50
75
100
Time (s)

FIG. 7

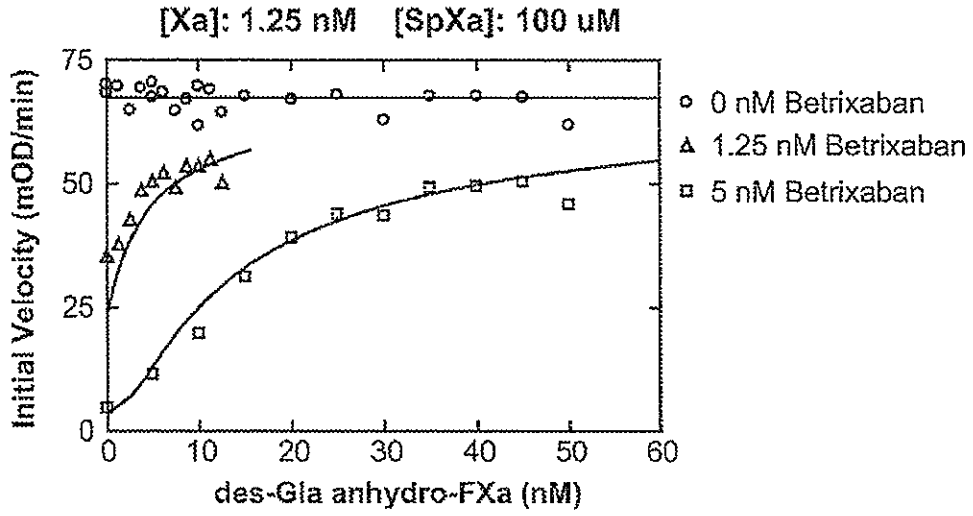

[Xa]: 1.25 nM [SpXa]: 100 uM
Initial Velocity (mOD/min)
75
50
25
0
0
10
20
30
40
50
60
des-Gla anhydro-FXa (nM)
0 nM Betrixaban
1.25 nM Betrixaban
5 nM Betrixaban

FIG. 8

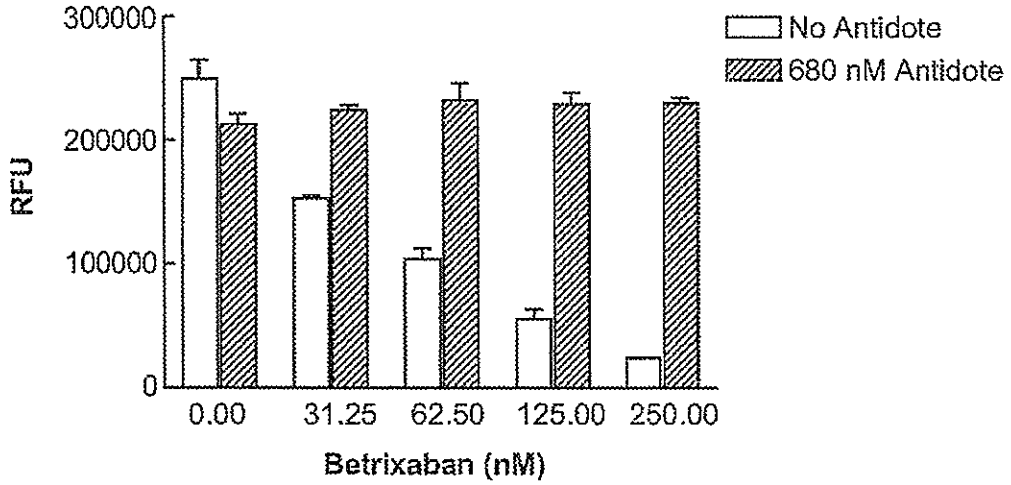

300000
200000
100000
0
RFU
0.00
31.25
62.50
125.00
250.00
Betrixaban (nM)
No Antidote
680 nM Antidote

FIG. 9

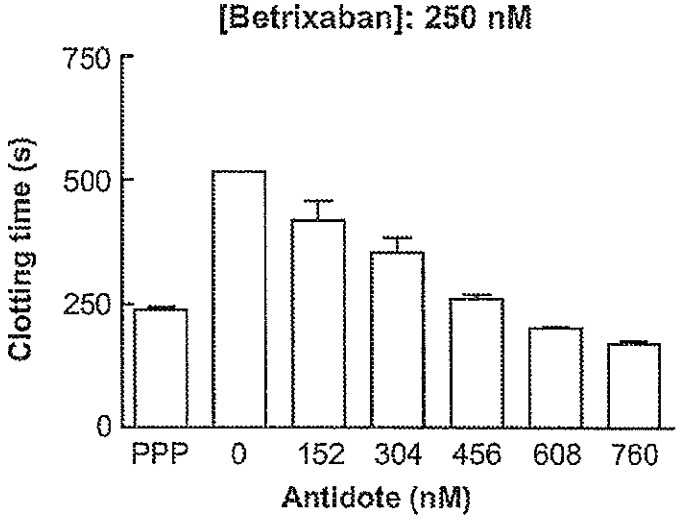

[Betrixaban]: 250 nM
Clotting time (s)
750
500
250
0
PPP
0
152
304
456
608
760
Antidote (nM)

FIG. 10

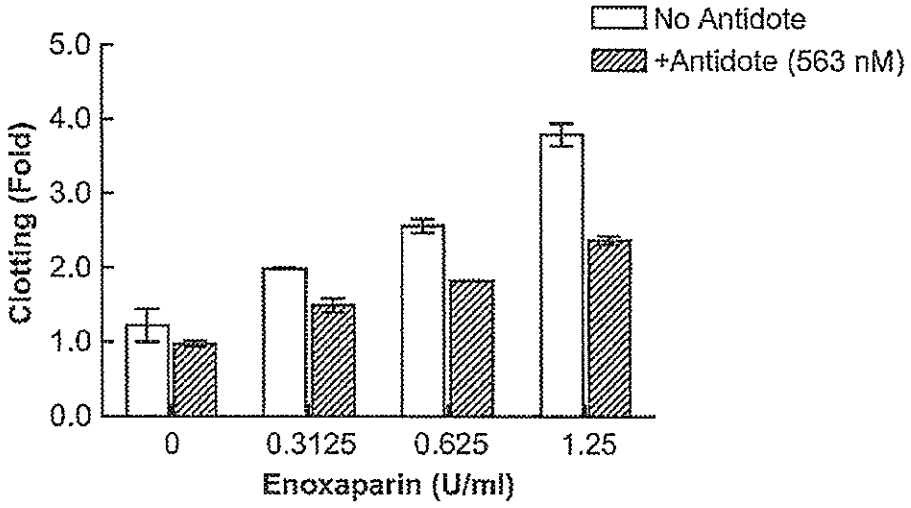

No Antidote
+Antidote (563 nM)
Clotting (Fold)
5.0
4.0
3.0
2.0
1.0
0.0
0
0.3125
0.625
1.25
Enoxaparin (U/ml)

FIG. 11

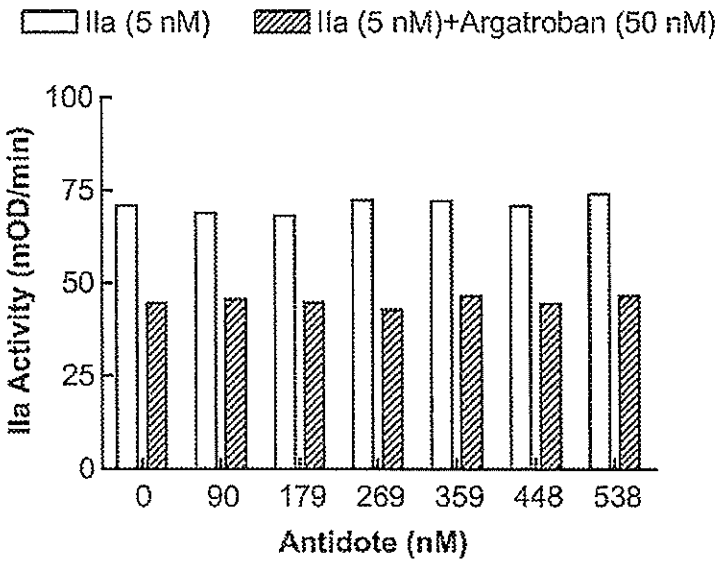

IIa (5 nM)
IIa (5 nM)+Argatroban (50 nM)
IIa Activity (mOD/min)
100
75
50
25
0
0
90
179
269
359
448
538
Antidote (nM)

FIG. 12

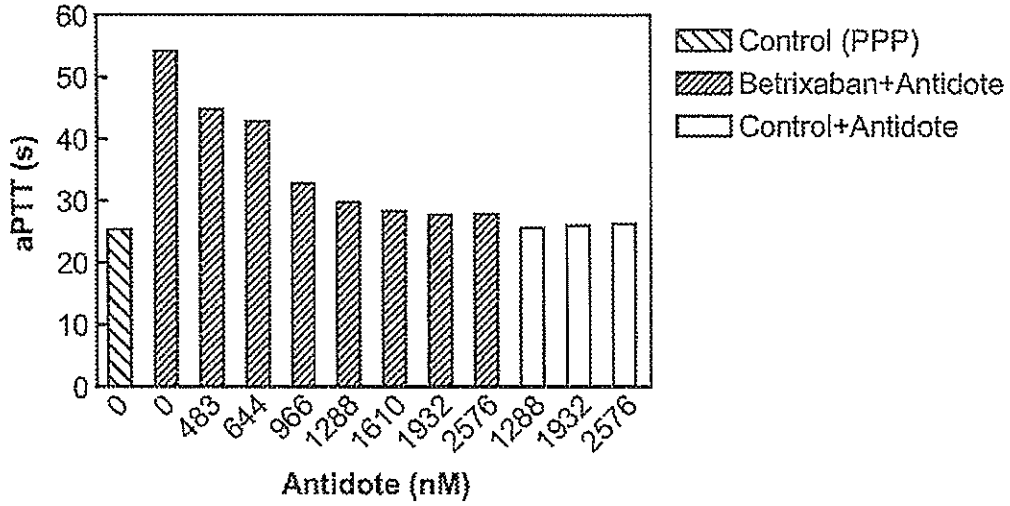

Control (PPP)
Betrixaban+Antidote
Control+Antidote
aPTT (s)
60
50
40
30
20
10
0
0
0
483
644
966
1288
1610
1932
2576
1288
1932
2576
Antidote (nM)

FIG. 13

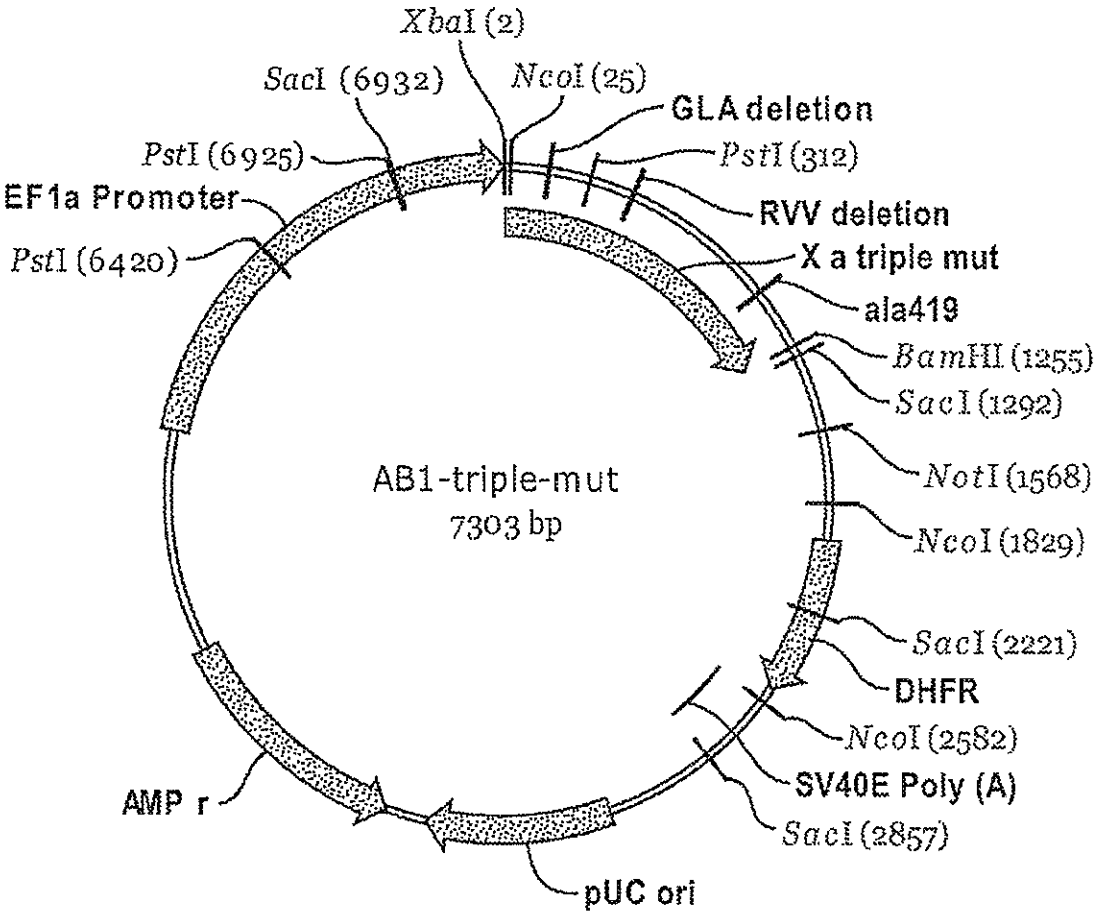

XbaI (2)
SacI (6932)
NcoI (25)
GLA deletion
PstI (6925)
PstI (312)
EF1a Promoter
RVV deletion
PstI (6420)
X a triple mut
ala419
BamHI (1255)
SacI (1292)
AB1-triple-mut
7303 bp
NotI (1568)
NcoI (1829)
SacI (2221)
DHFR
NcoI (2582)
SV40E Poly (A)
SacI (2857)
AMP r
pUC ori

FIG. 14

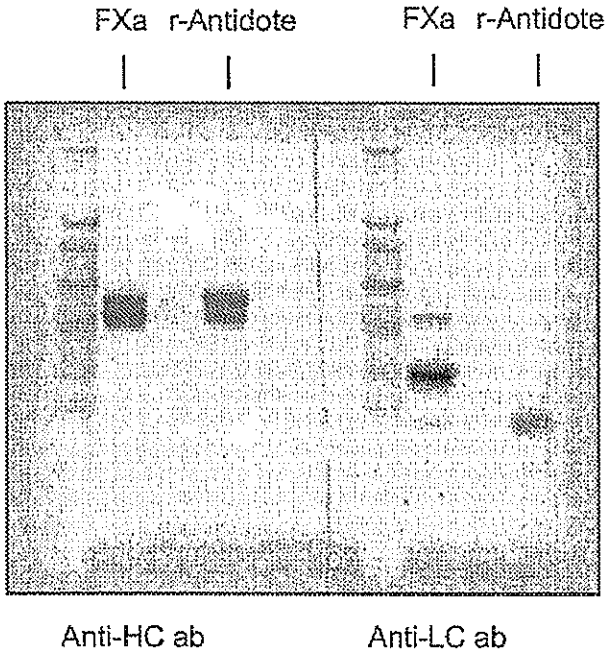

FXa
r-Antidote
FXa
r-Antidote
Anti-HC ab
Anti-LC ab

FIG. 15

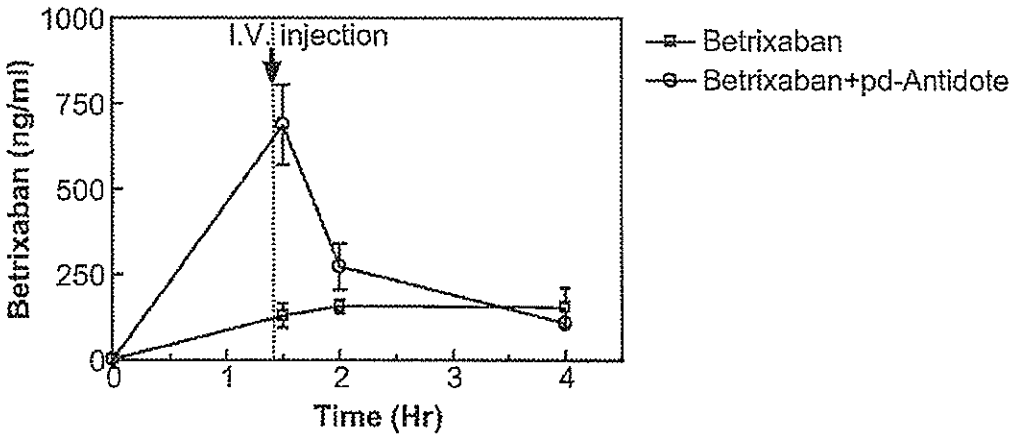

1000
750
500
250
0
Betrixaban (ng/ml)
I.V. injection
0
1
2
3
4
Time (Hr)
Betrixaban
Betrixaban+pd-Antidote

FIG. 16

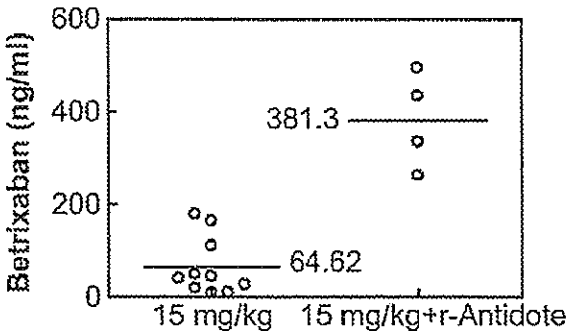


FIG. 17A

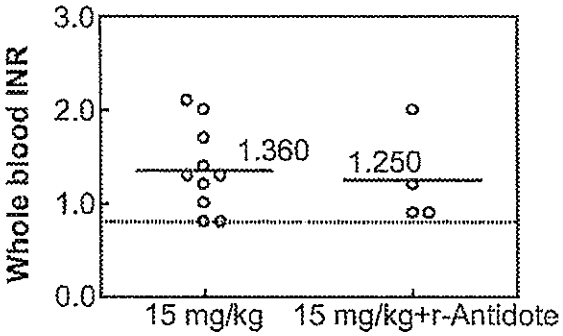


FIG. 17B

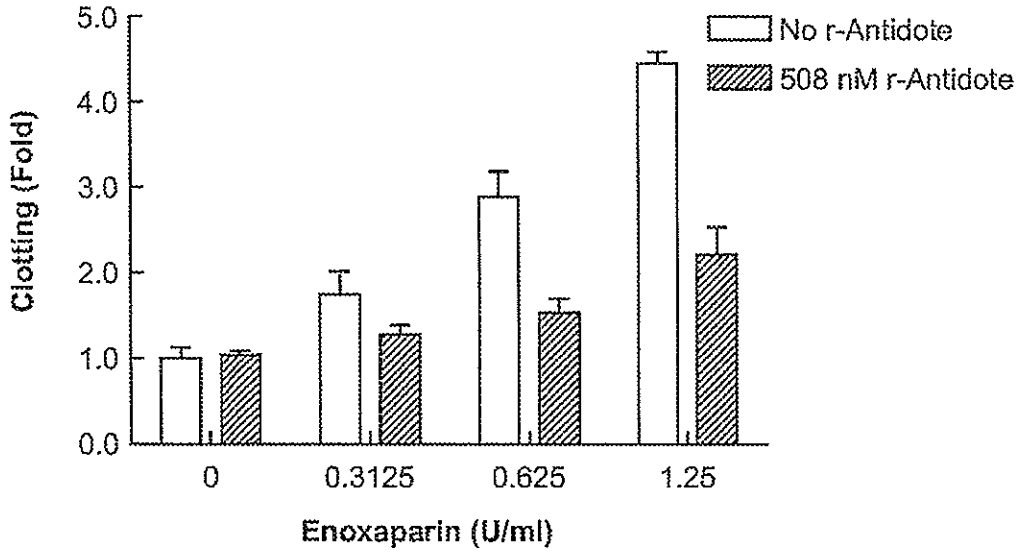


FIG. 18

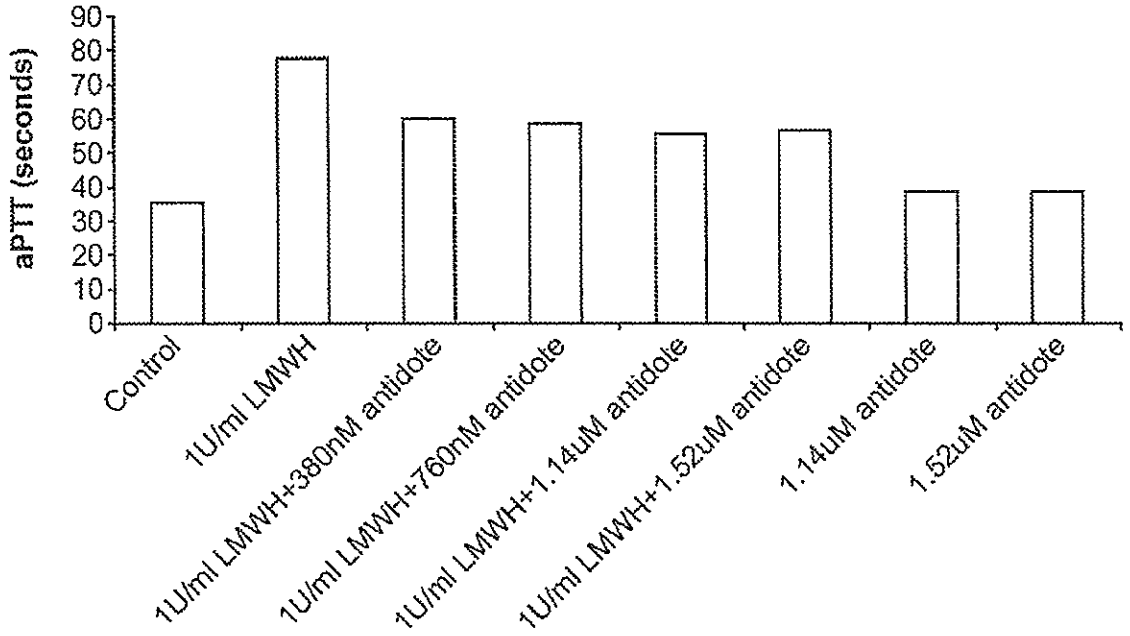

aPTT (seconds)
90
80
70
60
50
40
30
20
10
0
Control
1U/ml LMWH
1U/ml LMWH+380nM antidote
1U/ml LMWH+760nM antidote
1U/ml LMWH+1.14uM antidote
1U/ml LMWH+1.52uM antidote
1.14uM antidote
1.52uM antidote

FIG. 19

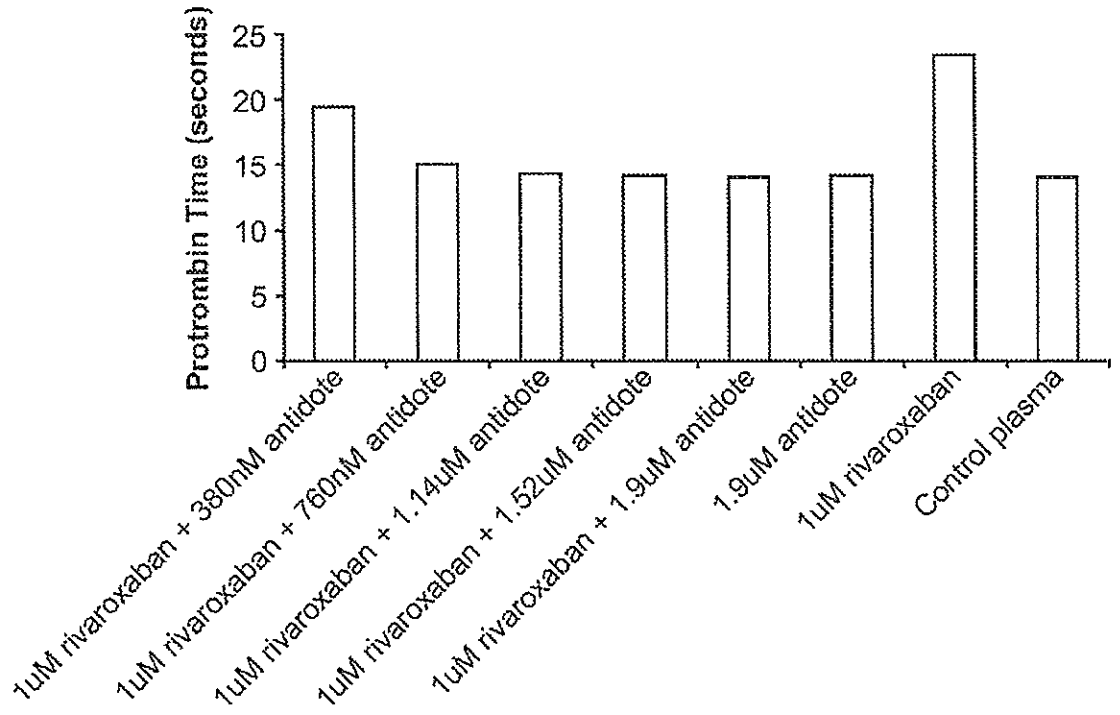

Protrombin Time (seconds)
25
20
15
10
5
0
1uM rivaroxaban + 380nM antidote
1uM rivaroxaban + 760nM antidote
1uM rivaroxaban + 1.14uM antidote
1uM rivaroxaban + 1.52uM antidote
1uM rivaroxaban + 1.9uM antidote
1.9uM antidote
1uM rivaroxaban
Control plasma

FIG. 20

```
atggggcgcccactgcaccctcgtcctgctcagtgcctccctggcaggcctcctgctgctc
 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
tgccagaaccagggcaaatgtaaagacggcctgggggaatacacctgcacctgtttagaa
 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
gactgtgaccagttctgccacgaggaacagaacttctgtggtgtgctcctgcgcccgcggg
 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
ttcaaggtgagggtaggggaccggaacacggagcaggaggagggcggtgaggcggtgcac
 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
gccgtgctccggctcaagaccccatcaccttccgcatgaacgtggcgcctgcctgcctc
 A  V  L  R  L  K  T  P  I  T  F  R  M  N  V  A  P  A  C  L
ccgagcgtgactgggccgagtccacgctgatgacgcagaagacggggattgtgagcggc
 P  E  R  D  W  A  E  S  T  L  M  T  Q  K  T  G  I  V  S  G
ttcgggcgcacccacgagaagggccggcagtccaccaggctcaagatgctggaggtgccc
 F  G  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  F  I  I  T  Q  N  M  F
tgtgccggctacgacaccaagcaggaggatgcctgccaggggacgcaggggccgcac
 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
aggtccatgaaaaccaggggcttgcccaaggccaagagccatgccccggaggtcataacg
 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

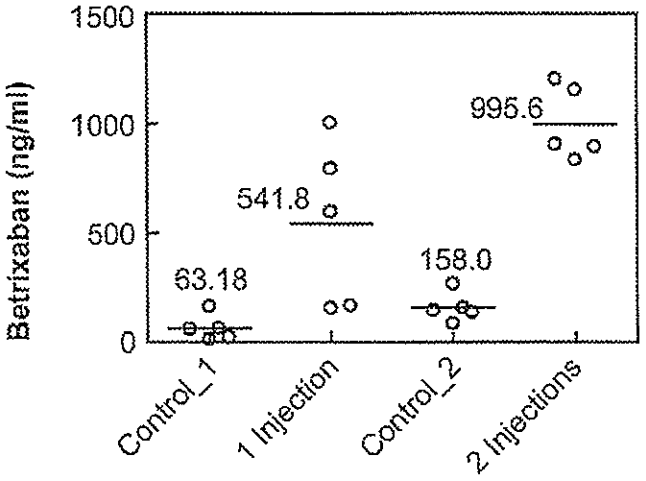


FIG. 22A

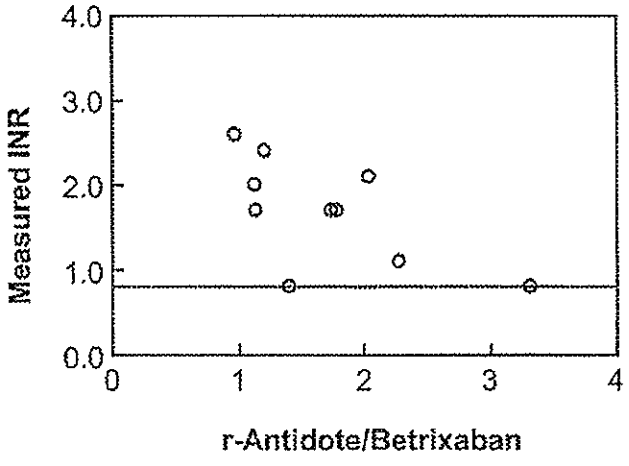


FIG. 22B