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Introduction:
Andexanet alfa (AA, Portola Pharmaceuticals, San Francisco, CA) represents a modified factor Xa agent which is approved antidote for apixaban and rivaroxaban. Andexanet alfa may also neutralize the anti-Xa effects of betrixaban and edoxaban. This study aims to compare the relative neutralization of these four anti-Xa agents by andexanet alfa in different matrices.

Methods:
Andexanet alfa was diluted at 10 mg/ml. Apixaban (A), betrixaban (B), edoxaban (E) and rivaroxaban (R) were diluted in pH 8.4, 0.5 M tris buffer (TB), blood bank plasma (BBP) and in 5% albuminated buffer (AB) at 0.062 - 1.0 ug/ml. Anti-Xa activities of all four agents were measured in three systems and the reversibility indices of AA were profiled. The reversibility index (RI50) of anti-Xa effects by AA was determined at 25 - 100 ug/ml.

Results:
Each of the four agents produced varying degrees of inhibition of anti-Xa at 0.062 – 1.0 ug/ml, the IC50 ranged 0.61 - 1.53 ug/ml in BBP, 0.47 - 1.28 ug/ml in AB and 0.49 - 1.4 ug/ml in TB. Andexanet alfa produced a concentration dependent reversal of all four anti-Xa agents. In the BBP, the RI50 values for A (192 ug/ml), B (32 ug/ml), E (152 ug/ml) and R (85 ug/ml). In the AB, the RI50 values for A (140 ug/ml), B (46 ug/ml), E (176 ug/ml) and R (58 ug/ml). In the TB, the RI50 values for A (154 ug/ml), B (79 ug/ml), E (>400 ug/ml) and R (110 ug/ml).

Conclusion:
Each of the four anti-Xa agents exhibit varying degrees of matrix independent anti-Xa potencies in different systems, the collective order follows edoxaban > apixaban > betrixaban > rivaroxaban. Andexanet alfa produced matrix dependent differential neutralization of the anti-Xa effects of these agents. Individualized dosing of andexanet alfa may be required to obtain desirable clinical results.