Abstract

Anti-Protease Activity of Heparin-like Drugs

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Background

Unfractionated heparin and other heparin-like derivatives such as low molecular weight heparin (LMWH) and heparin-derived drugs (i.e. fondaparinux) are used in the prophylaxis and treatment of diseases such as deep vein thrombosis and pulmonary embolism in and after in-situ surgical applications including cardiac bypass. Following surgery, heparin's anticoagulation effects must be reversed to prevent excessive bleeding. Currently the most widely used method for reversing heparin's anticoagulation activity is to use protamine sulfate. However, the use of protamine sulfate is associated with serious side effects, including bradycardia, hypertension, and induction of antigenic thrombocytopenia in patients with a history of heparin-induced thrombocytopenia. Our objective was to characterize the ability of various salicylamide derivatives to neutralize the anticoagulant and antiprotease actions of these heparin-like drugs.

Methods

Anticoagulant and Antiprotease activity assays:

Neutralization of Heparin by Protagmine and PMX 60056

Results

These studies demonstrate that the PolyMed series of salicylamide derivatives can neutralize the anticoagulant and anti-protease actions of LMWH and fondaparinux. Manipulation of chemical structure may allow for the identification of agents that are more effective than currently available antagonists.

Conclusion

The use of LMWHs and heparin-derived drugs (i.e. fondaparinux) is associated with serious side effects, including bradycardia, hypertension, and induction of antigenic thrombocytopenia. Our objective was to characterize the ability of various salicylamide derivatives to neutralize the anticoagulant and antiprotease actions of these heparin-like drugs.