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ABSTRACT

A METHOD FOR INHIBITING CLOT FORMATION

The invention relates to tannins that are specific inhibitors of thrombin and are useful in the treatment of venous thrombosis, arterial fibrillation, restenosis, and arterial thrombosis and in prevention of myocardial infarction. Thrombin plays a central role in the blood coagulation cascade. The present invention relates to the isolation and identification of five tannins from the methanol extract of *Geum japonicum* which showed strong anticoagulant effect by prolonging prothrombin time, thrombin time and activated partial thrombin time significantly. They are pedunculagin, penta-O-galloyl-β-glucoside, tellimagradin, casuariin, and 5-desgalloylstachyurin. All five tannins inhibit thrombin enzymatic activity in a dose-dependent manner. Among these inhibitors, pedunculagin competitively inhibit the thrombin-induced fibrin clot, whereas others inhibit thrombin enzymatic activity in a noncompetitive manner. Tellimagradin shows the strongest inhibition with IC_{50} at concentration of 14 nM for thrombin-catalyzed hydrolysis of fibrinogen. Others give IC_{50} at concentration range of 26 nM to 150 nM. These tannins are potent and specific thrombin inhibitors and exhibit strong anticoagulant effects. Thus these compounds could be useful in prevention/treatment of cancer, cardiovascular and cerebrovascular diseases, such as atheroscalerosis, myocardial infarction and stroke.

(Figure 6 is to be published.)