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Topic of research- “Understanding the structural and mechanistic role of heparin cofactor II in hemostasis.”

Cardiovascular diseases along with thromboembolism are the major health-care concern among developed and developing countries including India with a global mortality rate of about 30-35%. In the current time, several anticlotting drugs are available in the market categorizes under anticoagulants, antiplatelets and thrombolytic drugs which dissolves the blood clot. Despite major developments in anticoagulant medication the treatment and prevention of thrombosis remains a big challenge due to their high cost and a number of drawbacks associated with the currently available anticoagulants. However, due to drawbacks associated with their long term use and an extremely high cost the therapy is generally not available to people from modest background. Heparin cofactor II (HCII) belongs to serpin superfamily of protease inhibitors which performs inhibitory as well as non-inhibitory role in humans. It is secreted by hepatocytes and circulates systemically in blood.

Overall, this is the first study in which an alternatively spliced novel transcript of HCII has been identified in human liver. We have observed that novel transcript of HCII has been structurally different from HCII with the lack of specific RCL sequence and showed higher heparin-binding capacity unlike HCII. We have also identified mannose pentasulfate (MPS) as an activator of HCII which enhances the thrombin inhibition rate by 7-fold and also modulate the coagulation rates. HCII forms stable complex with thrombin in presence of MPS.