

S56-1 Blood coagulation factors and anticoagulant drugs: Present state and perspectives

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Now, factor Xa is widely noticed as one of very interesting coagulation factor in the field of thrombosis and haemostasis. It is because several pharmaceutical companies are now developing synthetic anti-factor Xa and anti-thrombin medicines, and these are expected as new synthetic anti-coagulants in addition to heparin and warfarin in future. In this lecture, I will first describe the recent developments of mechanism of blood coagulation and the regulation. Then, I will focus the new synthetic anti-coagulant medicines such as anti-factor Xa and anti-thrombin medicine that will be solved several clinical disadvantages of warfarin. Both synthetic anti-factor Xa and anti-thrombin medicines have clear mechanism for inhibiting both factor Xa and thrombin activities, because these directly inhibit either the active site of either factor Xa or thrombin. Warfarin has no specific inhibitory activities, since warfarin do inhibit the Gla formations of all seven vitamin K-dependent coagulation factors and has complicate anti-coagulant mechanism, since it simultaneously inhibits both vitamin K-dependent coagulation factors and anti-coagulation factors such as protein C and protein Z. Heparin also has no specific activity, since it bind to both thrombin, factor Xa, and TFPI in plasma. New ant-thrombin and anti-factor Xa medicines have high specific activities to inhibit thrombin or factor Xa, respectively. Thus, we could hope a new era which we could select one of warfarin, heparin, and new developing synthetic anti-thrombin and anti-factor Xa medicines in future. I will shortly introduce these several new drugs which are now developing by several companies in Japan.

Recently several researchers have discovered that Gla-domain of factor X binds to adenovirus 5 to infect the liver, and the study on the polymerization of the abnormal antithrombin molecule by X-ray structure revealed the molecular mechanism of serpin diseases which could understand the mechanism of Alzheimer disease. I will describe the relationship of factor X and adenovirus infection, and folding disease of abnormal antithrombin molecule to understand the general mechanism of folding disease.