Comparision of the Anticoagulant and Antithrombotic Activities of Fucosylated Chondroitin Sulfate with Novel Oral Anticoagulants.

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Oral anticoagulation for the long-term treatment and prevention of thromboembolic diseases as well as for stroke prevention in atrial fibrillation has been accomplished by vitamin K antagonists for the last half century. Although effective under optimal conditions, the imminent risk of a recurrent event vs. the risk of bleeding due to the narrow therapeutic window, numerous food- and drug interactions, and the need for regular monitoring complicate the long-term use of these drugs, leading to the development of new oral pharmacological agents, such as FXa and thrombin direct inhibitors Rivoraxaban and Dabigatran etexilate.

Preparation of new compounds by chemical synthesis is limited, partly for economic reasons. Fucosylated chondroitin sulfate (fucCS) is a natural sulfated polysaccharide extracted from sea cucumber. We have shown that oral administration of fucCS to rats inhibits thrombus formation in experimental models of venous and arterial thrombosis and increases plasma clotting time, assessed by aPTT, thrombin time and anti-IIa activity. In the present work, we compare the effect of fucCS with dabigatran etexilate and rivoraxaban after oral administration to rats in coagulation, thrombosis and bleeding. Our results show that dabigatran and fucCS completely inhibits thrombus formation only at 18 mg/kg in a vena cava thrombosis model, while dabigatran and rivoraxaban alter aPTT, TT and PT values in lower doses than fucCS (about 3 fold). However, dabigatran and rivoraxaban exhibit intense bleeding in a bleeding time model, while fucCS has no effect in blood loss. These results indicate that fucCS could be an interesting alternative to oral anticoagulants.

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