SULFATED POLYSACCHARIDES AND THE STIMULUS IN THE SYNTHESIS OF ANTITHROMBOTIC ENDOTHELIAL HEPARAN SULFATE: STUDIES ON THE CELLULAR MECHANISM

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Antithrombotic drugs, such as fucans from marine brown algae are capable to stimulate the synthesis of an antithrombotic heparan sulfate (HS) in endothelial cells (EC) through interaction with the extracellular matrix. In this work we investigated the cellular mechanism related to the increase in the synthesis of HS by heparin (Hep) and fucan A (FucA) (Plant Science 132, 215, 1998). EC exposed to these drugs for different periods of time (2-30 min) show an increase from 1.3 to 2.4 times in the amounts of nitric oxide (NO) compared to controls, whereas cells treated with L-NAME (NO inhibitor) showed a decreased on the stimulus. Exposure of EC to Hep or FucA in the presence of inhibitors of tyrosine kinases, calcium/calmodulin, PKC, PI3K, PLC led to a reduction around 20 to 60% in HS synthesis. Using western blot analysis and specific antibodies to different tyrosine kinases we observed an increase in FAK, Src and ERK phosphorylation when the cells were treated with Hep or FucA for 15 minutes. The combined data suggest that NO, calcium and Ras are involved in the increase in HS synthesis by Hep and FucA. (supported by Fapesp, CNPq, CAPES).