CRAB HEPARINOIDS STIMULATE THE SYNTHESIS OF THE ANTITHROMBOTIC HEPARAN SULFATE THROUGH THE INTERACTION WITH THE EXTRACELLULAR MATRIX OF ENDOTHELIAL CELLS

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In invertebrates, glycosaminoglycans similar to mammalian heparin with structural peculiarities has been named heparinoids. Natural heparinoids containing a high degree of 2-O-sulfated β–D-glucuronate units were isolated from the crab Goniopsis cruentata. We now report the effect and interaction of these compounds with the extracellular matrix (ECM) of rabbit aortic endothelial cells (RAEC). Crab heparinoids(CH) were able to stimulate the synthesis of antithrombotic heparan sulfate(HS) in RAEC suggesting that this stimulus may be due their interaction with the ECM. Competition assays between CH and heparin using a fluorescence method showed that CH partially compete for the same heparin binding sites in RAEC. CH and Heparin were biotinylated and the binding to RAEC assayed using cytochemistry techniques and analyses in confocal microscopy. The binding of biotinylated CH to RAEC showed to be dose dependent with a KD of 87,5-119,4nM to cell binding and a high affinity binding to extracellular matrix with a KD of 28-37,5nM. Furthermore, these compounds were detected bound only to the ECM of RAEC and co-localized with fibronectin. Then, we can conclude that CH and heparin stimulate the synthesis of the antithrombotic HS through the interaction with the same binding site(s) of the ECM.

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