Anti-Tumor Effects of Heparin-Analogue which Inhibit Angiogenesis

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Angiogenesis is an essential process of cancer progression and metastasis. This new vessel formation in a growing tumor requires both proliferation and migration of endothelial cells through the host stroma and into the tumor mass. A number of polypeptide growth factors, in particular endothelial cell growth factors, have marked affinity for the glycosaminoglycan heparin and are commonly known as heparin-binding growth factors(HBGFs). This common feature of different growth factors has prompted the use of polysulfated aromatic compounds, suramin. However, because of systemic toxic effect, this drug was difficult to use. Earlier we reported that the pentosanpolysulfate(PPS) was effective in vitro against HBGFs released from tumors and in vivo the inhibit growth in animal tumor models.

Studies were carried out to assess the antitumor potential of the new heparinoid analogues, 1306. In anchorage independent growth assay using SW-13 cell and conditioned-media from MDA-MB-231 cells, dose-dependent growth inhibition was found with 1306 compound. In ahchorage dependent growth assay, no anti-proliferative activity was found against 1205 melanoma cell line, gastric cancer cell line, brain tumor cell lines, while anti-proliferative activity was found against endothelial cell proliferation. This anti-proliferative effect was reversed as the drug was eliminated in the culture system. In fibronectin attachment assay, 1306 showed no effect on cell attachment. In vivo study with 1205 melanoma cell lines, anti-tumor effect was found on the primary tumor mass growth and anti-metastasis effect was found on the metastatic nodules.

As a result of these studies, heparinoid analogue has potential therapeutic indication in blocking angiogenic growth factors.