Bioassay of Anti-Angiogenic Activity in the Sera after Targeting Heparin-Binding Growth Factor

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Previous studies showed the heparinoid pentosanpolysulfte(PPS) can inhibit heparin-binding growth factors(HBGF) released from tumor cells and thus block tumor angiogenesis and tumor growth in animal model. TNP-40 was recently synthesized based on a fungal product and showed direct inhibition of endothelial cell proliferation in vitro model. The reason for using a bioassy versus a chemical detection method is that these semi-synthetic compounds consist of a heterogeneous mixture of different molecular masses. This various chemical composition makes a HPLC detection method very difficult-if not impossible- and renders the usual pharmacokinetic analysis useless.

In this study, we used angiogenic tumor cell line NSF-14 as a HBGF producing cell line. And we used SW-13, HUVEC cell line as target cells for the HBGF. We showed the NSF-14 cells release endothelial cell stimulating activities in vitro and addition of PPS or TNP-40 inhibited this stimulatory effect on the endothelial cell proliferation. And in vivo, 2.5 fold stimulation of endothelical cell proliferation was observed with serum from tumor-bearing mice versus control mice. Mice were sacrificed at a different time intervals after TNP-40 injection and their sera were harvested. A pharmacologically active concentration was present 12 hours later and active drug was eliminated after another 12 hours. Sera obtained from patients up to 4 hours after PPS treatment inhibited HBGF-dependent cell proliferation.

This assay system present here could be useful to determine doses and scheduling of treatment in evaluating PPS and TNP-40 as anti-tumor agents.