Abnormal angiogenesis and evasion of apoptosis are hallmarks of cancer. Accordingly, antiangiogenic and pro-apoptotic therapies are effective strategies for cancer treatment. Hence we investigated the anti-angiogenic and pro-apoptotic efficacy of phytochemicals isolated from three plants, among which the ethyl acetate extracts of *E. jambolana* and *M. paradisiaca* exhibited the best anti-angiogenic and pro-apoptotic activities. In addition a purified plant compound, anacardic acid (A1) from *Anacardium occidentale* known to be both anti-angiogenic and pro-apoptotic was used in TRAIL sensitization studies. TRAIL, an apoptosis inducing cytokine currently in phase II clinical trial, was investigated for its ability to induce apoptosis in eight different human tumor cell lines out of which three cell lines were highly resistant. A1 was used to sensitize the resistant cells to TRAIL by treating them with suboptimal dose of A1 which up-regulated the expression of both DR4 and DR5 receptors observed in the cellular, protein and mRNA levels was corroborated by the activation of p53 as well as phosphorylation of p38 and JNK MAP kinases and concomitant inactivation of NFκB and ERK signaling cascades. A1 also modulated expression of Bax, Bcl-2 and CAD along with the abatement of tumor angiogenesis in EAT mouse model. Thus, post A1 treatment, the TRAIL resistant cells turned into TRAIL sensitive cells.

Vascular endothelial growth factor (VEGF) and the angiopoietins (ANG) are the two crucial growth factors responsible for tumor angiogenesis. Cytokines, angiopoietin-1 (Ang1) and Ang2 function through the signalling via vascular receptor tyrosine kinase Tie2. The overexpression profile of Tie2 receptor in human tumor biopsies and cell lines was ascertained by immunohistochemistry (IHC) and qPCR respectively. IHC staining of human ductal breast carcinoma biopsies revealed overexpression of Tie-2 receptors as the grade of cancer progressed. Whereas the qPCR results showed overexpression of Tie-2 receptors in MDA-MB-231 and U-87MG cell lines out of the 4 cell lines tested. Recombinant sTie2 protein was expressed using the baculovirus expression system and used in construction of scFv cDNA. scFv-sTie2 protein was expressed and purified from transformed HB2151 cells. A modified dot blot assay was used to pick out the positive clones expressing the scFv-sTie2 protein. The DNA sequencing of scFv gene revealed an 823bp sequence that was translated to an amino acid sequence and subjected to 3D structure prediction analysis and molecular docking analysis with Tie2 receptor. Bioactivity of the scFv-sTie2 was studied by inhibition of Ang2 induced neovascularization in rat corneal micropocket assay.

Ultimately, scFv-sTie2 was further used in the nanomedicine based cancer therapy to enhance the specificity of liposomes to the tumor cells and augment the delivery of encapsulated anacardic acid (A1) to bring about apoptosis of tumor cells and thus Tie2 is an effective target to be exploited for targeting in nanomedicine. The drug delivery efficacy and cytotoxicity was enhanced when PEGylated liposomes were used. Further, the dual fluorescent scFv-sTie2 immunoliposomes clearly showed in vitro that they could bind to the overexpressed Tie2 receptors on the cell surface and help in liposome internalization and payload delivery by receptor mediated endocytosis.