Abstract
Thesis Title: **Isolation, characterization and mechanism of action of anticancer compounds from selected plant sources**

Cancer is a deadly disease and results from several interconnected processes such as including cell proliferation, angiogenesis, cell adhesion, migration, and invasion into the surrounding tissue etc. The appearance of metastases in organs/distant from the primary tumor is the most destructive feature of cancer. Thus metastasis remains as the principal cause of the death of cancer patients despite decades of research that are aimed at restricting the tumor growth. Therefore, current thesis entitled “**Isolation, characterization and mechanism of action of anticancer compounds from selected plant sources**” explores the possibility of dietary antioxidants and antimetastatic polysaccharides that can effectively bring down oxidative stress and galectin-3, a key molecule in metastasis, which causes severity of cancer pathogenicity and death as revealed in scheme – 1. During the study, series of commonly used plant/dietary sources were screened for inhibition of H⁺, K-ATPase, antioxidant and antimetastatic cyto/DNA protective activity. *A. serpyllifolia* and *Zea mays* were selected as a potent source of antioxidants and antimetastatic pectic polysaccharides respectively from Corn – *Zea mays* were characterized and determined their efficacy in vitro and in vivo. Separation of free (ASFP) and bound phenolic (ASBP) fractions from *A. serpyllifolia* followed by demonstration of differential antioxidant activity of phenolic acid composition in them enabled us to correlate the key role and involvement of phenolic acids against various steps of reactive oxygen species mediated cancer pathogenecity. The content and nature of phenolic acids in the phenolic fractions therefore may explain their antioxidant and antiproliferative abilities to be responsible for anticancer property. *A. serpyllifolia* also found to contain andrographolide (AG) contributing to the activity. Results of the study clearly indicated the inhibition of metastatic cell growth; inhibition of cell adhesion/invasion, inhibition of tumor colony formation etc by corn pectic polysaccharide (COPP). Evaluation of molecules involved in cancer metastasis such as upregulated galectin-3, matrix metalloproteinases, phosphoglucoisomerase (PGI) and NFkB were modulated by selected dietary galectin-inhibitors.
Abstract

Studies are thus evidenced the potential inhibition of cascades of metastatic events induced by galectin-3. Structure – function analysis revealed the presence of higher levels of galactose and arabinose and their probable contribution to antimetastatic potency. Antioxidants of *A. serpyllifolia* and antimetastatic COPP was effective in inhibiting Reactive oxygen species - mediated stomach cancer by N- methyl N- nitrosourea and B16F10 melanoma cells induced lung metastasis *in vivo*, suggesting their *in vivo* efficacy against cancer. Overall data thus suggest that selected sources *A. serpyllifolia* and *Zea mays* having both antioxidants and antimetastatic components can effectively inhibit cancer spread/metastasis at multistep (Scheme-1). Thus the study highlights the need for multi-targetting components for successful inhibition or arrest of cancer/cancer metastasis.
Scheme 1: Summary of the work envisaged in the thesis

Multistep active antioxidant (antimetastatic components). Carcinogen includes reactive oxygen species (a) generated in the body due to chemical/environmental carcinogen (b) resulting in oxidation of biomolecules (c). These steps usually lead to progression of *in situ* carcinoma (d) to invasive cancer (e) and metastasis, (f–i). Tumour outgrowth (d,e) is dependent on tumour angiogenesis and is determined by the balance between tumour-cell proliferation versus apoptosis. At this step ASFP/ASBP/AG promote apoptosis and inhibit proliferation/angiogenesis of tumour cells via different antioxidant fractions from mechanisms as metastatic cell clones emerge, tumour cells express galectin-3, which contact with surrounding cells and the extracellular matrix (ECM) leads to invasion of blood or lymphatic vessels and to extravasation of tumour cells at distant sites (f–i).