

Cancer is one of the deadliest diseases in the world which continues to grow at an alarming rate. Among all types of cancers, breast cancer is the second leading cause of cancer death worldwide. However, in India, it is the leading cause of cancer death. The majority of the breast cancer mortality cases are primarily due to metastasis of primary cancer to different organs like bones, brain, liver, lymph nodes and lungs. Currently a variety of treatment options are available to treat cancer such as surgery, radiation therapy, chemotherapy, immunotherapy, targeted therapy, hormone therapy, stem cell transplant and precision medicine. These anti-cancer therapies are employed primarily on the basis of type, stage and affected organs. Though success of these therapy depends on various factors almost none addresses the issue of metastasis very efficiently. This is critical and needs utmost attention because, despite comparatively high success rates with primary breast cancer cases, the 5-year survival rate of metastatic breast cancer patients is only about 25%. Chemotherapeutic approaches for alleviation of breast cancer are available. However, most of these drugs under current chemotherapeutic regimen are synthetic, expensive and generate a number of side-effects in patients. Medicinal plants are rich sources of bioactive molecules and can be exploited for application as anti-cancer agents. Plant-derived compounds offer key advantages as these are eco-friendly, cost-effective, fast in action and less toxic as compared with conventional chemotherapy drugs. The current study was broadly aimed at searching plant extracts with anti-cancer activity and identifies individual bioactive compounds by exploiting the rich biodiversity of North-East India. To achieve this, extensive literature survey was done that led to the selection of three plants with traditional medicinal use. Extracts were prepared from six different parts of these plants and studied for their anti-cancer activity. Finally, two extracts *viz.* fruit extract from *Ricinus communis* L. (RCFE) and tuber extract from *Amorphophallus paeoniifolius* (Dennst.) Nicolson was selected for further characterization to unravel the molecular mechanism responsible for the activity. Both these extracts were studied for their apoptosis-promoting and metastatic-inhibiting activities using primarily two breast cancer cell lines: less metastatic, estrogen-positive MCF-7 and highly metastatic, triple-negative MDA-MB-231. In addition, effect of the extracts on other cell lines including those from non-cancerous origin was also studied to specify their activities. Attempts were made to identify some of the important bioactive molecules from both these extracts. A few selected compounds identified as constituents of RCFE were studied for

their individual anti-cancer activities against breast cancer cells. RCFE has been studied for its activity in tumor regression *in vivo* using mouse mammary carcinoma cell 4T1-mediated syngeneic model.

The entire study is described in six different chapters.

Chapter 1 introduces the demographics of cancer, highlights some well-accepted reasons for the origination and probable therapeutic options available for the disease with special emphasis on breast cancer. The chapter also emphasizes the problems of breast cancer metastasis. The chapter also demonstrates the requirement of further studies to achieve novel compounds especially from natural sources that are safe, inexpensive and highly efficient.

Chapter 2 presents a detailed up-to-date literature survey on the molecular basis of breast cancer development and indicates different pathways that can function as plausible targets for the alleviation of the disease. The role of medicinal plants in the quest of novel anti-cancer molecules is also discussed.

Chapter 3 describes the selection of medicinal plants and the extracts prepared from those plants. It also demonstrates the establishment of cell culture models for measuring cytotoxic activities of the extracts towards screening for further studies. Phytochemical screening and radical scavenging activity of the selected extracts are also reported here.

Chapter 4 depicts the anticancer activity of *Ricinus communis* L. fruit extract (RCFE) by *in vitro* and *in vivo* approaches. The effect of the extract to induce apoptosis and inhibit metastatic properties is reported using two breast cancer cell lines: MCF-7 and MDA-MB-231. The mechanistic details of these activities have also been studied. Tumor regression efficacy of RCFE is shown in 4T1 cell-induced syngeneic mouse model. The chapter also reports the presence of major compounds in RCFE as identified by HPLC and ESI-MS and the activity of individual compounds.

Chapters 5 demonstrate the anticancer activity of APTE by *in vitro* approaches using MCF-7 and MDA-MB-231 cell lines. The role of the extract in promoting apoptosis in caspase-dependent and p53 independent manner has been elaborated. The effect of the extract on inhibition of metastasis is also shown. HR-LCMS analysis of the extract suggests the presence of compounds well-documented for anti-cancer activity.

Chapter 6 represents the conclusion of the research carried out in this thesis along with the future prospects and directions of the study.