Cancer is the uncontrolled growth of abnormal cells in the body, which is caused by the stepwise accumulation of mutations that affect cell growth control, differentiation and survival (McCormic, 1999). Maintaining the integrity of the human genome is a big job. A vast amount of DNA must be replicated in each cell cycle and its replication must be accurate at not only the nucleotide level but also globally, to ensure that the entire genome is duplicated and that no region is replicated more than once. Mitosis cannot initiate before DNA replication is complete and the replicated sister chromatids must be held together until the appropriate moment, when the mitotic apparatus segregates one sister chromatid to each daughter cell. Mistakes in any of these steps can initiate the genetic alterations leading a cell down the lane to cancer (Diffley and Evan, 2000). The past two decades have witnessed tremendous advances in our understanding of the pathogenesis of cancer (Luo et al., 2009). Two classes of genes: proto-oncogene and tumor suppressor genes, work together to regulate cell division in normal cells. All cancers involve the malfunction of genes that control cell growth, division and death. However, most of the genetic abnormalities that affect cancer risk are not hereditary, but instead result from damage to genes (mutations) that occur throughout one’s lifetime. Aberrant activation of the cell cycle can be achieved by induction of positive regulators (often encoded by proto-oncogenes) or through inactivation of negative regulators (often encoded by tumour-suppressor genes). Induction of positive regulators is caused by overexpression or mutations leading to permanent protein activity. Inactivation of repressors is caused by deletion, mutation or promoter hypermethylation. All mechanisms can be found in human (Tessema et al., 2004). Many genes involved in cell cycle and differentiation are not cancer genes; they do not themselves induce cancer. Rather, they code for enzymes with vital normal functions, mainly to metabolize chemicals, breaking them down for excretion. These normal processes detoxify many chemicals to protect the body. In metabolizing some chemicals, however, they produce other chemicals that may damage DNA and induce cancer. Some of these genes assume different forms in different people, resulting in different rates of metabolizing various chemicals. A raised metabolic rate may decrease or increase the cancer risk of a chemical to which one is exposed, depending on whether the chemical itself or its metabolic product is carcinogenic. The study of how genetic and environmental factors interact in cancer risk is becoming a fast growing science i.e. molecular epidemiology. Variations in genetic predisposition partly
explain why some people are more susceptible than others to a particular environmental carcinogen (Mucci et al., 2001). Cancers are classified by the type of cell that resembles the tumor and, therefore, the tissue presumed to be the origin of the tumor. Main categories of cancer are carcinoma, sarcoma, lymphoma, leukemia, germ cell tumor and blastoma.

According to epidemiological studies, 80-90% of all cancers are due to environmental factors of which, lifestyle related factors are the most important and preventable. The major risk factors for cancer are tobacco, smoking, infections, dietary habits and behavioral factors. Tobacco consumption, either by way of chewing or smoking, accounts for 50% of all cancers in men. Dietary practices, reproductive and sexual practices account for 20-30% of cancers. Studies have shown that appropriate changes in lifestyle will reduce the mortality and morbidity caused due to cancer (Murthy and Mathew, 2004).

Cancer imposes a major disease burden worldwide, with considerable variations in incidence, mortality, survival, occurrence and causative factors (Rajkumar et al., 2011). According to Jemal et al. (2011), the burden of cancer is increasing in economically developing countries as a result of population aging and growth as well as, increasingly, an adoption of cancer-associated lifestyle choices including smoking, physical inactivity, and "westernized" diets. Thun et al. (2010), reported that cancer is now the third leading cause of death worldwide, with >12 million new cases and 7.6 million cancer deaths estimated to have occurred in 2008, in which 56% of the cases and 64% of the deaths were in the economically developing world (Jemal et al., 2011). By 2030, it is projected that there will be approx 26 million new cancer cases and 17 million cancer deaths per year (Riedl et al., 2011). Moreover, the global distribution of cancer and types of cancer that predominate continues to change, especially in economically developing countries. Low- and middle-income countries accounted for about half (51%) of all cancers worldwide in 1975; this proportion increased to 55% in 2007 and is projected to reach 61% by 2050. Cancers of the lung, breast, colon/rectum and prostate are no longer largely confined to western industrialized countries but are among the most common cancers worldwide (Thun et al., 2010). India is in an epidemiological transition phase and cancer is now one of the leading causes of morbidity and mortality. It is estimated that there are 2 million cancer patients in India with 0.7 million new cases each year. More than 35% of cancer
cases in men are related to the oral cavity, larynx and pharynx (all tobacco related). About 40% and 30% of cancer cases in women are cervical and breast cancer, respectively, in India (Seth et al., 2005). As the statistics of the newly diagnosed cancer cases continues to rise yearly, therefore, the management of cancer becomes very prominence area of research for scientific and medical community.

Traditional ways of cancer treatment include surgery, radiation therapy and chemotherapy. People diagnosed with cancer have various treatment options that depend on the type of cancer involved and how far it has spread. The localized malignant tumors are best managed by surgical removal (Downey, 1999), while the treatment options for advanced and metastasized tumor include chemotherapy and radiotherapy (Chay et al., 2002; Hudis, 2003; Qian et al., 2003). Chemotherapy is based on the systemic administration of anticancer drugs that are designed to kill proliferating cells, because drugs are carried through out the body by circulatory system. It aims to wipe out all the cancerous colonies within the patient’s body including metastasized cancer cells, however it is associated with various side effects, such as nausea, anemia, weakening of the immune system, diarrhea, vomiting and loosing hair (Koehnlechner, 1987; Barbounaki-Konstanatakou, 1989).

Broadly, the anticancer drugs used in chemotherapy can be categorized as plant derived product, which includes- vinca alkaloids (vincristine, vinblastine and semi-synthetic analogue vinorelbin), taxanes (paclitaxel, docetaxel), camptothecin and its analogs (topotecan, irinotecan) and podophyllotoxin derivatives (etoposide, teniposide). Further, several other natural and modified natural products in the line include - alkylating agents (nitrogen mustard, ethyleneamines, alkylsulfonate, nitrosourea), anthracyclins (daunorubicin, doxorubicin, epirubicin, idarubicin), anthracenediones (mitoxantrone) and antimetabolites (folate antagonists such as methotrexate) (Minev, 2010).

Thus, nature has been a source of medicinal products for ages and during the past many years several drugs of wide spectrum of diseases have been prepared from natural sources especialy plants (Cragg et al., 2012). About 25% of drugs in the modern pharmacopoeia are derived from plants, including several anticancer drugs currently in clinical use. These natural products, their derivatives and analogues based on these drugs constitute an arsenal against various types of neoplasms. The traditional use of plants provides valuable information for development of cancer chemopreventive molecules
A successful anticancer drug should kill or incapacitate cancer cells without causing excessive damage to normal cells. It has been found that most cancer chemotherapy drugs exert cytotoxic effects on malignant cells by inducing apoptosis (Kaufmann and Earnshaw, 2000). The life span of both normal and cancer cells is significantly affected by the rate of apoptosis (Tarapdhar et al., 2001). Induction of apoptosis in cancer cells or malignant tissues is recognized as an efficient strategy for cancer chemotherapy. Apoptosis, or programmed cell death, is an essential event that plays an important role in organism development and homeostasis (Liu et al., 2006). During apoptosis, cell experiences a cascade of events that ultimately result in nucleus condensation and DNA fragmentation (Nagata et al., 2003). Apoptotic cells can be recognised by characteristic morphological patterns e.g., cell shrinkage, condensation of cytoplasm, nuclear fragmentation, formation of apoptotic bodies and loss of cell surface structures, etc. (Christop, 2003).

Certain products from plants are known to induce apoptosis in neoplastic cells but not in normal cells. It has become increasingly evident that apoptosis is an important mode of action for many antitumor agents, including ionizing radiation, alkylating agents such as cisplatin and 1,3- bis(2-chloroethyl)-1-nitrosourea (BCNU), topoisomerase inhibitor etoposide, cytokine tumour necrosis factor (TNF), taxol and N-substituted benzamides such as metoclopramide and 3-chloroprocainamide. Apoptotic induction has been a new target for innovative mechanism based drug discovery. It is thus considered important to screen apoptotic inducers from plants, either in the form of crude extracts or as components isolated from them. Understanding the modes of action of these compounds should provide useful information for their possible application in cancer prevention and perhaps also in cancer therapy (Taraphdar et al., 2001). Due to the rapid development of resistance to chemotherapeutic drugs, the search for novel drugs is still a priority goal for cancer therapy (Demain and Vaishnav, 2011).

There exists high hope for effective treatment of different cancers by systematic screening of a variety of natural products. There are reports showing that plant extracts display anti-tumor/anti-cancer/anti-proliferative effects on cultured human cancer/tumor cell lines (Sandhya et al., 2006; Sandhya and Mishra, 2006). Medicinal plants provide an inexhaustible source of anticancer drugs in terms of both variety and mechanism of action. The acetone extract of *Buxus sempervirens* showed cytotoxic activity towards all the five
studied breast cancer cell lines (MCF7, MCF10CA1a, T47D, BT-20 and MDA-MB-435) with an IC\textsubscript{50} values ranging from 7.74 µg/ml to 12.5 µg/ml (Ait-Mohamed \textit{et al.} 2011). Wang \textit{et al.} (2011) reported that Tubeimoside I, extract from Chinese herbal medicine \textit{Bolbostemma paniculatum} (MAXIM.) FRANQUET belonging to Cucurbitaceae is a potent anti-tumor agent for a variety of human cancers. Lim \textit{et al.} (2011) stated that the seeds of \textit{Acalypha wilkesiana} have been known to be used by traditional healers in Southwest Nigeria together with other plants as a powder mixture to treat patients with breast tumors and inflammation. They further revealed that ethyl acetate extract of this plant possessed significant antiproliferative effects against both U87MG and A549 with GI\textsubscript{50} ranging from 28.03 to 89.63 µg/ml respectively. \textit{Moringa oleifera} leaf extract was studied using human tumor (KB) cell line as a model system and observed that cytotoxicity was associated with induction of apoptosis as well as morphological changes and DNA fragmentation (Sreelatha \textit{et al.}, 2011). Based upon the background of diversified therapeutic values of plants and their uses in cancer disease in folklore/traditional Indian system of medicine coupled with the fact that anticancer potential of \textit{Erythrina suberosa} and \textit{Anagallis arvensis} have not yet been explored, the present investigation was designed to study the same, employing different assays.

\textit{Erythrina suberosa} Roxb. belongs to the family Fabaceae. Plants of this genus are known to have cytotoxic activity (Nkengfack \textit{et al.}, 2001; Balachandran and Govindarajan, 2005). In India, \textit{E. suberosa} Roxb. has been used as a very important medicinal plant for the treatment of various ailments. The ethanol extract of the leaves has been reported to have anti-tumor activity (Dhar \textit{et al.}, 1968). Other parts of this plant that are widely used are roots, leaves, seeds and bark. The main ingredients of \textit{E. suberosa} Roxb. are waxes, sterols, lectins and isoflavonoids (Singh \textit{et al.}, 1970, Bharracharyya \textit{et al.}, 1986; Tanaka \textit{et al.}, 2001). In the present study, stem and stem bark of \textit{E. suberosa} Roxb. have been used.

\textit{Anagallis arvensis} L. belongs to the family Primulaceae and its whole plant extract is reported to have antifungal activity (Nene and Thapliyal, 1965; Ali-Shtayeh and Abu-Ghdeib, 1999). In indigenous medicine, the plant is used for the treatment of gout, dropsy and cerebral infections (Kaul, 1997). Main ingredients of \textit{A. arvensis} L. are Saponins, Triterpenoids, Flavanoids, Arvenins and Tannins (Yamada \textit{et al.}, 1978a; Amoros \textit{et al.}, 1978b; Yamada \textit{et al.}, 1978c; Tanaka \textit{et al.}, 2001).
1987, 1988; Shoji et al., 1994a, 1994b). In the present study, whole plant of *A. arvensis* L. has been used.

The main objectives of current research are:

Estimation of anticarcinogenic activity of different isolates of *Erythrina suberosa* Roxb. and *Anagallis arvensis* L. using:

- Sulforhodamine B Assay
- MTT assay
- BrdU incorporation assay
- *In vivo* studies using murine models:
  - Ehrlich Ascites Carcinoma (EAC)
  - Sarcoma-180 (Ascites)
  - Sarcoma-180 (Solid)
  - Lymphoid leukemia (L1210)
- Mechanistic studies of promising isolates using different techniques:
  - Microscopic studies
    - Light microscopy
    - Fluorescence microscopy
    - Scanning electron microscopy
  - Cell cycle analysis
  - Annexin V/PI lebelling
  - Changes in Bcl-2 levels
  - Change in mitochondrial membrane potential ($\Delta \Psi_m$)
  - Changes in cytochrome c levels
  - Reactive Oxygen Species (ROS) detection
  - Nitric oxide (NO) production
  - Estimation of Caspases activity
  - DNA fragmentation assay