PREFACE

Cancer is one of the most serious clinical problems worldwide and affects not only developed countries but also developing countries as well, is one of the major causes of death in humans around the world. Cancer is the uncontrolled growth of cells coupled with malignant behavior, invasion and metastasis. It is thought to be caused by the interaction between genetic susceptibility and environmental toxins. Cancer can affect people of all ages, and a few types of cancer are more common in children, the overall risk of developing cancer increases with age. In 2007 cancer caused about 13% of all human deaths worldwide (7.9 million). Rates are still rising as more people live to an old age and lifestyles change in the developing world (Jemal et al 2011)

Treatment of cancer can be done by surgery, radiation and chemotherapy. However, complete cure through surgery and radiation, are generally only successful if the cancer is found at an early localized stage. Once the disease has progressed to locally advanced cancer or metastatic cancer, these therapies are less successful. The more effective anticancer therapies are required for most patients to achieve a complete eradication of the disease.

Chemotherapy emerged in 1940s from toxicological studies of nitrogen mustard-based war gas (Chabner et al, 1996). In the development of new therapeutic agents, several problems raised, including improved and durable antitumor efficiency, reduction of toxicities that can prevent effective dosing of potentially effective drugs, and prevention of drug resistance caused by the genomic instability of tumors. (Jackson, 2000). Chemotherapeutic drugs alone or in combination with other additional treatments as antiangiogenic and antimitastatic are needed to compact disseminated cancer that cannot be cured solely by surgical excision. Gene therapy, hormone therapy, photodynamic therapy, alogenic transplant etc. are some of the emerging treatment methods against cancer (Carolyn et al., 2006). But none of these methods are free from
side effects. The problems in the current treatment methods have lead to the search for better treatment methods for the effective curing of this dreadful disease.

The development of a cancer cell from a normal cell is through progression of various stages. It involves initiation in which single cell gets initiated for clonal expansion to form premalignant lesion. These initiated cells will have defect in maturation, escapes from senescence and have altered dependence on growth factors and hormones. Then their promotion involves activation of cell surface receptors, activation/inhibition of cytosolic enzymes and nuclear transcription factors, stimulation, proliferation, inhibition of apoptotic cell death etc. Progression is accelerated by additional exposure to genotoxic agents inducing genetic instability, non random sequential chromosomal aberrations and malignant conversion produces, multifocal change producing premalignant lesions. There will be up regulation of transcriptional activity and expression of modified cell surface molecules, gene amplification, and alteration in cell cycle regulatory genes, secreted proteases and methylation of DNA. These changes facilitate migration and invasion of cancer cells.

Apoptosis or programmed cell death is the essential process for maintaining normal physiology. Induction of apoptosis, programmed cell death is one approach to cancer therapy. Apoptotic cell death is a physiological mechanism that eliminates unwanted cells by triggering the cell’s intrinsic suicide program. Impairment of apoptosis is related to cell immortality and carcinogenesis, thus, the induction of apoptosis in neoplastic cells is therefore, important in cancer treatment. The word “apoptosis” is used to describe a common series of morphological changes involving the nucleus, cytoplasm and plasma membrane that accompanied the death of cells from a variety of tissue sources. Oxidative stress is characterized by an increase in reactive oxygen species, as a result of insufficient antioxidant defense. Overproduction of reactive oxygen species deregulates the apoptosis leading to cancer, cardiovascular diseases and many neurodegenerative disorders. Hence, a balance between the reactive oxygen species formation and antioxidant activity are essential for the normal functions of the body.

Cancer is still a serious health problem and has a major social and economic impact worldwide. Despite recent advances in diagnosis, prevention, and therapy, cancer
still affects quality of life in patients due to some limitations of these current medical practices. Consequently, more and more people resort to alternative medicine, which is defined as health care practices used instead of standard ones. Herbal medicine, one type of the alternative medicine, is based on the use of plants or plant extracts to treat diseases and promote health and has been offered especially for cancer treatment over the last century.

Plant-derived natural phytochemicals and plant extracts have gained significant recognition in the management of several human clinical conditions since they can act on specific and/or multiple molecular and cellular targets. Plants have been a prime source of highly effective phytochemicals, which offer great potential in the fight against cancer by inhibiting the process of carcinogenesis through the upregulation of cytoprotective genes that encode for carcinogen detoxifying enzymes and antioxidant enzymes and through inhibition of aberrant cell signal transduction pathways.

Medicinal plants are the most important source of life saving drugs for the majority of the world’s population. It is estimated that 70-80% of people worldwide rely chiefly on traditional, largely herbal, medicines to meet their primary health care needs. (Farnsworth et.al., 1991). The global demand for herbal medicine is not very large, but growing. (Srivastava, 2000).

Plants are a tremendous source for the discovery of new products of medicinal value for drug development. Today several distinct chemicals derived from plants are important drugs, currently used in one or more countries in the world. Many of the drugs sold today are simple synthetic modifications or copies of the naturally obtained substances. In past years there has been a rapidly increasing interest in plant secondary metabolites. (Verpoorte et al., 1999). So many pharmaceutical and other industrial products based on plants are now available (Staba, 1985). There are approximately 60% of medicinal plants are used in the traditional system of medicine (Ayurveda, Siddhaand Unani). It is estimated that more than 90% of the plant species used by industry is collected from natural habitats and more than 70% of plants used in drug industry involved destructive harvesting and very few are in cultivation. The evolving commercial importance of secondary metabolites has in recent years resulted in a great interest in secondary metabolism, particularly in the possibility of altering the production of
bioactive plant metabolites by means of tissue culture technology. (Mulabagal et al 2004). Through biotechnological application such as micro-propagation large scale production of these plants is possible inside the laboratory. In cultures, factory type production of these phyto chemicals can be carried out throughout the year, unaffected by the season and the risk of crop failure due to natural hazards and danger of extinction of some species due to their mass extraction from natural populations are eliminated.

Dasamoola is an important combination of ten roots and used in the formulations such as Dasamoolakwatha, Dasamoolarishta, Dasamoolatpalak ghrta and Dasamoolaghrrta (Ayurvedic Formulary, 1978). Dasamoola is described as anti-pyretic, anti-inflammatory and anti-odema. The decoction of the root is administered in catarrhal fever, inflammatory infections within the chest, cough and many other diseases caused by vata, pitta and kapha. It is also useful in cases of anorexia, aversion to food, cardiac diseases, colic, coryza, cough, headache, hiccups, insanity, epilepsy and tympanitis. (Gupta et al., 1989)

In the present study, we examined the anti cancer and apoptosis-inducing activities of the two medicinal plants Solanum xanthocarpum Scrad and Wendl and Tribulus terrestris L. used for the preparation of Dasamoola. In vitro plants were raised through micropropagation, their cytotoxic, and antioxidant activities were compared with wild plants. Preliminary phytochemical screening was done by HPTLC and HPLC method. Investigations for anticancer activities were done on Dalton’s lymphoma ascites, Ehrlich ascites carcinoma and MCF 7 human breast cancer cell lines which have not been previously investigated. These plants were also screened for cardioprotective, nephroprotective and gastroprotective activities against chemotherapy induced side effects. The results suggest that investigations if extended, could lead to the discovery of new anticancer agents with selective cytotoxic effects on cancer cells.