INTRODUCTION

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Cancer is one of the most dreaded disease of the 20th century and spreading further with continuance and increasing incidence in 21st century. World Health Organization in its 1990 report stated that cancer occupied the second position in the list of killer diseases in industrially advanced countries. A combination of life style, exposure to environmental carcinogens and the overall balance between inherited resistance and sensitivity genes is likely to determine the susceptibility of an individual to cancer. Invasion and metastasis are the most insidious and life-threatening aspects of cancer (Sporn, 1996).

Tumorigenesis associated with metastasis formation accounts for 90% of cancer deaths, and represents one of the prime causes of human mortality (Weiss, 1985; Mareel et al., 1993; Sporn, 1996). In general, cancer arises from the stepwise accumulation of genetic changes and the progressive alterations in gene expression, disengaging cells from homeostatic constraints that normally keep the tissue balance in the healthy adult. Several defined events have been described as common to cancer cells including self-sufficiency in proliferation signals, insensitivity to growth inhibitory signals, evasion from cell death, limitless replicative potential, aberrant angiogenesis, as well as tissue invasion and metastasis (Hanahan and Weinberg, 2000).

Metastatic disease is the hallmark of malignant cancer. Metastasis is the spread of cancer cells from a primary tumour to vital organs and distant sites in the cancer patient's body. The design of more effective therapies to treat metastatic cancer requires better understanding of the molecular events and cellular processes that are involved in the process of metastatic formation. Successful formation of metastatic foci consists of several highly complex and interdependent steps. These include separation from the
primary site, circulation through blood or lymph, adhesion to the basement membrane, invasion and proliferation at distant sites (Fidler et al., 1974). Since each step is rate limiting, failure to complete any of these events completely disrupts metastasis formation. Any drug, which can interrupt any of these steps in the cascade, will be useful in the inhibition of tumour metastasis.

Multidisciplinary scientific investigations are making best efforts to combat this disease, but the sure-shot, perfect cure is yet to be brought into world medicine. Modern researches aim to eradicate the death and suffering from cancer, to cure cancer once it starts and ultimately to prevent cancer. Therefore high priority is given to research promoting continuous development of sophisticated molecular technologies and clinical application of these technologies to prevention, diagnosis and treatment of cancer (Boder, 1993).

Most of the cytoreductive cancer chemotherapeutic agents are highly toxic towards normal cells and hence the drug dose which can be used for cancer therapy is limited. Side effects such as nausea, vomiting, mucosal ulceration, interstitial pulmonary fibrosis, hepatic toxicity, lymphocytopenia and alopecia (Belli et al., 1967; Glick et al., 1982) and other symptoms act as discouraging factors for patients subjected to such therapy. Higher doses of administration of chemotherapeutical agents produce severe urotoxicity with haemorrhagic cystitis on urinary bladder (Hutter et al., 1973). Radiotherapy is one of the widely accepted therapeutical approaches in cancer. However whole body radiation with a dose of more than 100 rads cause acute effects including hematopoietic syndrome and gastrointestinal syndromes, which involves nausea, vomiting, diarrhea, decreased count of various blood elements such as red blood cells,
granulocytes, lymphocytes and platelets (Manuch et al., 1995). Unfortunately there is no specific drug at present, which can effectively reduce these effects. Therefore it is imperative to look for less toxic but effective therapeutics. Development of effective and nontoxic cancer therapeutics are essential.

Natural product research continues to explore a variety of lead structures, which may be used as templates for the development of new drugs by the pharmaceutical industry. In recent years many natural compounds derived from plants and or crude plant extracts have been proved to have protective effect against toxic effects of many chemicals and to combat a variety of ailments. Plants have a long history of use in the treatment of cancer (Pettit et al., 1994). The need to find a safe and highly effective cure for neoplastic diseases remains a major challenge for modern medicine. A wide variety of natural compounds appear to possess significant cytotoxic as well as chemopreventive activity. Extracts of plants used in traditional medicine also have a similar property. Many more screening studies are necessary using plant extracts and compounds isolated from them. Naturally occurring compounds that are included in the diet are non-toxic and may partially regulate programmed cell death in several tissues and organs. Elaborate studies with such compounds with respect to their abilities to inhibit metastatic tumour progression and understanding their mechanism of action may provide valuable information for their possible application in cancer therapy. Flavones, flavanols, isoflavones, catechins and tannins present in many plants have also been shown to possess anti cancer activities. Furthermore some of the herbal medicines and their constituents have been reported to inhibit metastatic tumour progression (Leyon and Kuttan, 2005).
The possibility that cancers viewed by immune system as non-self was postulated by Burnet in 1957 (Burnet, 1957). The concept of immune surveillance states that a physiological function of immune system is to recognize and destroy the clones of transferred cell before they grow into tumours and to kill tumours after they are formed. Evidence indicates that the healthy immune system is necessary for control of malignant disease and that immune suppression associated with cancer contributes to its progression. Tumours have developed strategies to successfully evade the host immune system, and various molecular and cellular mechanisms responsible for tumour evasion have been identified (Theresa and Whiteside, 2006). The fate of the host-tumour interactions depends on the balance between the intrinsic metastatic potential of the tumour and strength of the host immune response (Cooper et al., 2001). Therapeutic strategies are being designed to correct the immune imbalance, deliver adequate in vivo stimulation, transfer effector T cells capable of in vivo expansion and provide protection for the immune effector cells re-populating in the host. Survival of these cells and long-term memory development in patients with malignancy are necessary for improving clinical benefits of cancer immunotherapies (Theresa and Whiteside, 2006).

Immunomodulation is another type of the immuno-therapeutic modalities in clinical immunology. It may be defined as the augmentation of the host nonspecific or specific immune response through the use of a wide variety of biologically active substances. Immunomodulatory responses of an organism acts by interfering with its regulatory mechanism. These responses are antigen independent and may directly induce production of mediators and effector molecules by the immuno competent cell. The
primary target of the immunomodulatory compound is believed to be macrophages, which play a key role in the generation of immune response.

Terpenoids are the class of compounds widely distributed in plant kingdom (Steinmetz and Potter, 1991). Many of them have shown to inhibit chemically induced tumours (Tanaka et al., 2000). Although terpenoids are widely used for medicinal purpose in many Asian countries, their biogenesis and pleiotropic actions has not impacted on the practice of western medicines (Nanjoo et al., 1998).

Present study was aimed to investigate the immunomodulatory and antimetastatic activity of some of the naturally occurring terpenoids using in vitro and in vivo models. Antioxidant, antitumour, radioprotective and chemo protective activity of these terpenoids were also analysed in the present study.