INTRODUCTION

1.0 INTRODUCTION

Plants constitute an important source of medicines and play a key role in world health. In almost all regions and cultures of the world, from ancient times till today, plants have been used as medicines. Today's medicinal plants are important to the global economy, as approximately 80 per cent of traditional medicine preparations involve the use of plants or plant extracts. There is an increasing demand for herbal medicines in recent years due to their fewer side effects in comparison to synthetic drugs (Banerjee and Shrivastava, 2008).

India is the largest producer of medicinal herbs and is appropriately called the botanical garden of the world. Exploration of the unknown medicinal plants and the uses of known ones are attempted in various regions of India (Karuppaiaraih and Sekar, 2006). The traditional Indian medicine, Ayurveda, has a long history and is one of the great living traditions. Considerable research on the pharmacognosy, chemistry, pharmacology and clinical therapeutics has been carried out on Ayurvedic medicinal plants of India (Patwardhan, 2005).

Traditional medicine is an evolutionary process as communities and individuals continue to discover new techniques that can transform practices. Ethnopharmacology and drug discovery using natural resources remain important issues in the current scenario. Many infectious diseases are known to be treated with herbal remedies throughout the history of mankind (Zaidan *et al.*, 2005).

Oxygen and reactive oxygen species (ROS) are among the major sources of primary catalysts that initiate oxidation *in vivo* and *in vitro*

(Kumarappan and Mandal, 2008). ROS are highly reactive transient chemical species, which are produced by activated neutrophils during the inflammatory response. Normal cellular metabolism appears to be a primary source for endogenous ROS. Release of ROS from these cellular processes, and their evasion from antioxidant pathways, wherein the production of damaging ROS exceeds the capacity of the body's antioxidant defenses to detoxify them, leads to a condition known as oxidative stress (Karakoc *et al.*, 2007).

Oxidative stress is defined as a condition that is characterized by the accumulation on non-enzymatic oxidative damage to molecules that threaten the normal function of the cell or the organism, and has been linked to several cellular toxicity processes (Tung *et al.*, 2008). It is implicated in the development of many diseases such as macular degeneration, cardiac disease, premature aging and cancer (Andrade and Burgess, 2007).

Cancer is a major health burden in all developed countries. In all types of cancer, genetic alterations give rise to changes in expression, activation or localization of regulatory proteins in the cells. They then affect the signaling pathways that alter their response to regulatory stimuli and allow the unrestricted cell growth. Angiogenesis is a critical process for the development and progression of cancer prevention and treatment. Apoptosis has been accepted as a fundamental component in the pathogenesis of cancer and the suppression of apoptotic process. Chemotherapeutic treatment strategies attempt directly to inhibit proliferation of cancer cells or selectively remove transformed cells by inducing apoptosis or eliminating the cause of the growth advantage (Balasubashini *et al.*, 2006).

Apoptosis or programmed cell death is a distinct intrinsic cell death program that occurs in various physiological and pathological situations. It is

characterized by typical morphological and biochemical hallmarks, including cell shrinkage, nuclear DNA fragmentation and membrane blebbing. Proteolytic enzymes such as caspases play an important role as effector molecules in apoptosis, including cytotoxic therapy induced cell death. Activation of apoptotic pathways is a key mechanism by which cytotoxic drugs kill tumor cells. Defects in apoptosis signaling contribute to resistance of tumors. It leads to the mitochondrial (intrinsic) pathway, in addition signaling through death receptor (extrinsic) pathway, contributes to sensitivity of tumor cells towards cytotoxic treatments (Debatin, 2004).

Natural products have been traditionally accepted as remedies, due to the popular belief that they produce fewer adverse side effects. Therefore, understanding the potential beneficial or adverse influence of natural products extensively used by human population is very important to implement public health safety measures. One such naturally occurring product is silymarin, active constituent in a widely consumed dietary supplement, milk thistle extract. The human populations in Europe have used silymarin as a liver tonic. Silymarin has potent anticancer effects on several cancers and is a strong antioxidant with the activity to inhibit malondialdehyde DNA adduct formation (Ramakrishnan *et al.*, 2008).

The plant chosen for the present study is *Triticum aestivum,* commonly called as wheat grass. It belongs to the family *Poaceae*. Wheat grass can be effectively used for skin diseases and ulcerative wounds, by retarding bacterial action, promotes cell activity and normal growth. It helps to purify blood due to its high vitamin and mineral content and it enhances heart and lung function. (http://www.wheat-grassjuice.com/)

Earlier studies conducted in our laboratory revealed antioxidant and anticancer activity of *Triticum aestivum* in 4^{th} day plant. These studies

showed that the extract of *Triticum aestivum* leaves could counteract the oxidative stress imposed by H_2O_2 in several *in vitro* systems and also *in vivo* (Vidya, 2007). It was additionally observed that the leaf extract also exhibited anticancer effect against Hep2 (laryngeal carcinoma) cells, while not influencing the action of etoposide, a standard chemotherapeutic agent, on the cancer cells (Thiruselvi, 2008). These observations raised the query of the effect of the extract on the stress induced by etoposide on non-cancerous cells. The present study was designed to answer this query.

With this background, the present study was formulated with the following objectives:-

- To study the effect of the treatment of leaf extract of *Triticum aestivum* on primary chick embryo fibroblasts
- To characterize the cellular and nuclear events occurring during the cell death process induced by oxidative stress in primary chick embryo fibroblasts
- To evaluate the combined effect of oxidative stress and *Triticum aestivum* leaf extracts on the apoptotic events in primary chick embryo fibroblasts.

The literature pertaining to this study was reviewed and a brief account of the same is presented in the next chapter.