CPA is extensively used as an anticancer chemotherapeutic drug in childhood and adult malignancies, as well as an immunosuppressive agent for organ transplantation, leukemia, Hodgkin’s disease, etc. (Dollery, 1999). CPA undergoes bioactivation by hepatic microsomal cytochrome P450 mixed function oxidase system (Marinello et al., 1984). The principal alkylating metabolite, phosphoramide mustard, is responsible for its therapeutic activity. However, despite its wide spectrum of clinical uses, CPA also possesses adverse effects, including hepato, nephro and reproductive toxicity in humans and experimental animals (Fraiser et al., 1991).

The liver is particularly vulnerable to toxicity produced by reactive metabolites because it is the major site of xenobiotic metabolism. Many compounds, including clinically useful drugs, may induce cellular damage in the liver through metabolic activation of the chemical to highly reactive compounds such as free radicals causing oxidative stress (Kumar et al., 1997).

Hepatic tissues are the primary site for the microsomal activation of the drugs. Studies reveal the hepatic injury resulting from treatment with CPA (Honjo et al., 1988), may be due to acrolein, a by-product in the bioactivation of CPA. It is well known that phosphoramide mustard and acrolein are two metabolites of CPA produced by the liver microsomal enzymes (Ludeman, 1999). Acrolein causes liver dysfunction by binding to cytochrome enzymes, hepatic macromolecules and nucleic acids (DeLeve, 1996). Hepatic activation of CPA leading to the formation of toxic metabolite caused damage to the kidney and liver tissues as shown by decreased SGOT and SGPT. Histopathological studies proved that CPA causes damage to the organs like heart, kidney and liver (Senthilkumar et al., 2006). This might be due to membrane damaging potential of the CPA’s metabolites. Various studies have indicated that CPA administration to rats resulted in a significant increase in the
activities of serum SGOT, SGPT, ALP and LDH (Mathew and Kuttan, 1997; Al-Nasser, 1998; Ghosh et al., 1999).

Investigation also reports that chemotherapeutic agents are capable of causing nephrotoxicity (McDonald et al., 1991; Rossi, 1997). One of the main adverse side effects of CPA chemotherapy is Nephrotoxicity. CPA causes nephrotoxicity by alkylation of renal cells by Cys sulfhydryl group of acrolein. Renal cell alkylation leads variable reduction of glomerular filtration rate as well as tubular dysfunction, resulting from renal failure. CPA also generates the free radicals which lead to oxidative stress resulting in renal damage (Singh et al., 2014). The activity of ALP increases in the serum, which is also a marker for the kidney damage. CPA also induced renal damage characterized by increases in the level of LDH, BUN and creatinine (Caglar et al., 2002). The increased serum urea and creatinine evidence the renal toxicity due to CPA (Senthilkumar et al., 2006).

CPA therapy is a common continuing problem in the treatment of a variety of glomerular diseases leading to gonadal toxicity as a side effect of the drug. The consequences of infertility can have great physical and emotional impact on both men and women. Unfortunately, treatment with cytotoxic chemotherapy is associated with gonadal damage in men. It has been studied that at lower doses of alkylating agents, recovery of spermatogenesis occurs within 1 to 3 years; however, at higher doses, infertility may be prolonged or even permanent (Shetty and Meistrich, 2005). It has been reported that CPA chemotherapy results in azoospermia in all men during the treatment period; among them 67% recovered to normospermic levels within 5 years, whereas 5% remained oligospermic (Meistrich, 1999; Howell and Shalet, 2005). The effect of CPA treatment on sperm count suggests that fertility may be affected. CPA treatment affects the male reproductive tissue weight, testicular histology and sperm count. The impact of CPA exposure on male germ cells was translated into increases in pre-implantation and post-implantation loss with a resulting decrease in the number of live fetuses per litter. CPA treated in young male cancer patients have been reported to cause infertility and toxicity to the gonads. Once the cancer is controlled,
quality of life, which often includes the ability to have a normal child, then becomes a major concern (Meirow and Schenker, 1995; Schover, 2005). The cytotoxic effect of CPA targets rapidly dividing cells, so testis is especially a good target for damaging effects. It has been reported that low dose administration of CPA may decrease reproductive organ weights (Das et al., 2002), impair male fertility (Trasler et al., 1986) and alter growth and development of the next generation (Higuchi et al., 1995). A number of studies have reported that reduction in body weight, weight of the testis, sperm count, motility, histological changes in testis after 5th week of last injection in CPA (200 mg/kg) treated mice was an indication of drug toxicity (Elangovan et al., 2006; Carmely et al., 2009).

CPA therapeutic dose of human (750 mg/m²) equivalent to mouse (210–220 mg/kg) were found severe as compared to the lower dose which affected initially but were recovered at later stage (Elangovan et al., 2006). Recent studies suggest that CPA generates reactive oxygen species (ROS) like superoxide anion, hydroxyl radical and hydrogen peroxide (H₂O₂) during its oxidative metabolism and depresses the antioxidant defence mechanisms in the liver (Stankiewicz et al., 2002; Bhattacharya et al., 2003). These free radicals attack soluble cell compounds as well as membranes, eventually leading to the impairment of cell functioning and cytolysis (Bergendi et al., 1999). Biological compounds with antioxidant properties have shown to contribute in protecting the cells and tissues against deleterious effects of ROS and other free radicals induced by CPA (Navarova et al., 1999; Manda and Bhatia, 2003).

Several studies suggest that antioxidant supplementation can influence the response to chemotherapy as well as the development of adverse side effects that result from treatment with antineoplastic agents (Weijl et al., 1997; Oh et al., 2007; Shanmugarajan et al., 2008; Parka et al., 2009). Traditionally used medicinal plants are considered to be rich source of antioxidants. The role of oxidants in various human diseases has dramatically increased over the past 20 years. This increasing
knowledge is being translated into efforts to develop novel antioxidants as potential therapeutics for a wide range of human diseases.

Fortunately, cells possess antioxidant molecules, which can react with ROS and neutralize them before they inflict damage on vital components. Glutathione, ascorbic acid, α-tocopherol, thioredoxin and a number of antioxidant enzymes (like superoxide dismutase, glutathione peroxidase, catalase etc.) are the endogenous agents which can detoxify ROS (Halliwell, 1996). But when the endogenous antioxidant mechanisms are overwhelmed by ROS, oxidative stress occurs and ultimately lead to necrotic or apoptotic cell death (Chandra et al., 2000). To avoid these unwanted pathophysiological changes, supplementation of antioxidants from outside is necessary.

The use of herbal extracts in the treatment of human diseases is becoming very popular worldwide. Scientific approaches further magnify the reliability of the use of herbal extracts as complimentary medicine. Medicinal plants have been the mainstay of traditional herbal medicine amongst rural dwellers worldwide since antiquity to date. Hippocrates (460–377 BC), one of the ancient authors, who described medicinal natural products of plant and animal origins, listed approximately 400 different plant species for medicinal purposes. According to WHO medicinal plants contain number of phytoconstituents, which are used for therapeutic purposes. These phytoconstituents are well known to protect the plant against microbial infections or infestations by pests (Abo et al., 1999; Liu, 2004; Nwze et al., 2004; Doughari et al., 2009). Plants are well known home remedies for 80% rural population and gaining acceptance even among the urban settlements, probably due to the increasing inefficacy of many modern drugs in the controlling of many infections such as typhoid, fever, gonorrhoea, tuberculosis, asthma, constipation, esophageal cancer and hypertension (Van den Bogaard and Stobberingh, 2000; Lederberg et al., 2003). Phytoconstituents present in medicinal plants have been reported in minimizing side effects of drugs (Lowan, 1993).
The genus *Phyllanthus* has long been used in folk medicine to treat, kidney and urinary bladder disturbances, intestinal infections, diabetes and hepatitis B. In recent years, the interest in the plants of the genus *Phyllanthus* has increased considerably, especially regarding their therapeutic potential for the management of many diseases. Several reasons contribute to this, such as: (1) their greater distribution in many tropical and subtropical countries, (2) the great number of species in this genus, (3) their broad therapeutic use in folk medicine, and (4) the greater diversity of secondary metabolites present in such plants. Administration of *P. fraternus* to rats completely protected increased levels of lipid peroxides and decreased content of phospholipid composition. These results are in agreement with the earlier reports demonstrating the protective effect of *P. fraternus* against CCl₄ (Padma and Setty, 1997; Manjrekar et al., 2008) and chronic alcoholism (Sebastian and Setty, 1999). Nimesulide (Chatterjee and Sil, 2006), allyl alcohol induced oxidative stress in liver mitochondria (Sailaja and Setty, 2006) induced oxidative stress.

Genus *Phyllanthus* (Euphorbiaceae) comprises more than 600 species which are widely distributed throughout tropical and subtropical countries (Calixto et al., 1998). The infusion of leaves, stems and roots have long been used in traditional medicine to treat several diseases. The effect of extracts or active principles of this plant has been investigated in several biological models (Ogata et al., 1992; Shead et al., 1992; Unander et al., 1995, Calixto et al., 1998). Phytochemical studies from the leaves of *P. fraternus* have reported the presence of alkaloids, triterpenoids, glycosides, flavonoids, tannins and several lignans namely phyllanthin, hypophyllanthin, niranthin, nirtetralin and phyltetralin (Anjaneyulu et al., 1973; Khatoon et al., 2006). It has been recognized that the use of natural products is an important preventive approach to minimize the pathological consequences of oxidative stress.

Earlier studies have shown that the alcoholic extract of *Aegle marmelos* leaves protects against histamine-induced contractions in guinea pig ileum and tracheal chain (Arul et al., 2004). *A. marmelos* is reported to have antidiarrhoeal, antiproliferative, anti-inflammatory, antipyretic, and hypoglycemic and antioxidant.
The leaves are reported to be antidiabetic and antilipidemic in rats (Narender et al. 2007). Leaves are applied to inflamed parts and are very efficacious in the form of poultice to ulcers. Juice of fresh leaves has a laxative action and also employed in asthmatic complaints, ophthalmia and other eye affections. Decoction of leaves is used as a febrifuge and expectorant. Medicated oil prepared from leaves gives relief from cold and respiratory infections. Leaves are also used in abscess, backache, abdominal disorders, vomiting, cut and wounds, dropsy, beriberi, weakness of heart, cholera, diarrhea, cardio tonic, blood sugar, injuries caused by animals, nervous disorders, hair tonic, acute bronchitis, child birth etc. (George et al., 2003).