Summary and Conclusions

The mechanism of CPA side effects is established due to generation of ROS in different organs. Decreased activity of antioxidant enzymes, create a great oxidative stress, which leads to severe cellular damage. In the last decade a number of studies have focused on the protective potency of natural antioxidants against side effects induced by chemotherapeutic agents such as CPA.

Indian Ayurveda is one of the most important and widely accepted branch of natural medicines. In Ayurveda, herbal formulations are playing an important role in the prevention of a variety of diseases.

In the first part of our thesis, we studied the phytochemical profiles of extracts obtained from *P. fraternus* and *A. marmelos*. It is observed that the AEPF and AEAM are rich source of phytochemicals. Therefore, these extracts could be the potent antioxidant against oxidative stress induced by CPA.

In the current study, CPA impaired the enzymatic antioxidants in the different organs of mice. Furthermore, the increased level of toxicity markers was observed after CPA injection in normal mice. This indicates the development of side effects of CPA in the different organs (Liver, kidney and testis).

In the present study, mice were exposed to CPA toxicity and then treated by AEPF and AEAM. It was observed that the treatment of AEPF and AEAM are potent to prevent the toxicity caused by CPA. This study suggested the protective potential of AEPF and AEAM, by improving the antioxidant status of different organs against oxidative stress induced by CPA. This protective effect of AEPF and AEAM was evidenced by the ability of these extracts to increase the reduced level of intracellular enzymes in selected organs. However, the protective effect of extracts was dose dependent.
The following are the conclusions drawn from the results of the investigation:

- Hepatobiliary enzymes are present in liver under normal conditions. During hepatocytes necrosis or membrane damage, these enzymes are released into the circulation, as indicated by elevated serum enzymes level. Elevated levels of serum hepatobiliary enzymes (SGOT, SGPT, LDH, ALP and ACP), total bilirubin, cholesterol and significant reduction in albumin in CPA treated mice indicate hepatic cells damage. AEPF and AEAM administration restored hepatobiliary enzymes levels because it prevents the leakage of intracellular enzymes by stabilizing the hepatic cell membrane.

- The reduction in the activities of the SOD, CAT and increase in MDA level in liver suggests CPA-induced imbalance of antioxidant system. It also normalized activity of antioxidant enzymes by bolstering the antioxidant defense system. This might be due to the free radical scavenging/antioxidant properties of the phytochemical constituents present in extracts.

- Both extracts significantly enhanced the RBC and WBC count as compared to the CPA intoxicated mice. These observations assume great significance, as anemia is a common complication in cancer.

- Serum BUN and creatinine were found increased in CPA treated group which is a marker of nephrotoxicity. Administration of AEPF and AEAM prevented CPA-induced renal toxicity, as indicated by a steep decrease in serum BUN and creatinine levels.

- MDA level was found increased in kidney after administration of CPA. It leads to the destruction of membrane lipid with the formation of lipid radicals and increased uptake of oxygen, causing rearrangement of the unsaturated lipid. The activity of SOD and CAT were found decreased in the kidney of CPA treated group. Administration of the AEPF and AEAM attenuated the
renal disorders in CPA treated group as indicated by the levels of various parameters determined in this study.

- Reduction in GSI was an indication of CPA-induced toxicity because the weight of the testis largely depends on the mass of the spermatogenic cells. In the present study, we administered AEPF and the results found, were significantly positive as it improved all studied parameters used to determine testis injury.

- The results of present study showed the increased level of MDA and decline in the activity of SOD and CAT in testis of CPA treated group. AEPF treatment significantly reversed the upsurge in the MDA level and the antioxidant status indicating that it has some antioxidative/free radical scavenging property.

- In this study, AEAM treatment has no protection against CPA-induced adverse effects on sperm parameters and oxidative stress in testis. It might be because of presence of coumarin, which is supposed to have antifertility activity.

CPA used for cancer chemotherapy is known to produce toxic side-effects in multiple organs like liver, kidney and testis that were proved by biochemical and histopathological studies. The results strongly suggest that AEPF and AEAM may be considered a potentially useful candidate in combination of chemotherapy with CPA to combat oxidative stress mediated tissue injury. It was also found that *P. fraternus* extract is more potent than *A. marmelos* extract because it reverses the side effects in liver, kidney and testis. Overall we can conclude that, both AEPF and AEAM have potency to reduce the CPA-induced toxicity, but AEPF is more potent and can be administered along with CPA to minimize side effects of chemotherapy.