CHAPTER VI

SUMMARY

Effect of various chemicals and plant alkaloids on animal system have been studied since the early days of experimental research. Some of these chemicals have toxicological impact on animal system. Caffeine, a purine derivatives also a toxic chemical at particular dose and also has pharmacological action on certain dose level. Besides this chemical is an ingredient of common food and drink. Therefore investigation of toxicity of caffeine for mammalian system is important.

There are some chemicals which have positive effect on animal body and tested for chronic poisoning of toxicant among these vitamin C is one of the compound which has anti toxic effect. This water soluble vitamin has a little or no toxicity even in large doses and therefore this chemical can be used to reduce toxic injury. Considering these present investigation has been performed to evaluate the protective nature of vitamin C against caffeine induce toxicity in mammal by taking rat as a model animal.

Present investigation was based on alteration of certain blood and tissue parameters in relation to caffeine toxicity and anti toxic effect of vitamin C.

The experiment was carried out on three groups of animals (control, caffeine treated and caffeine + ascorbic acid treated) during the period of 90 days. Caffeine was fed at the rate of 150mg/kg/day upto 90 days. In supplemented group,
ascorbic acid was fed at the dose of 300mg/kg/day for 90 days along with caffeine at the rate of 150mg/kg/day. Some blood parameters including glucose, urea, T₃, T₄ and Insulin were studied at the intervals of 10 days while cholesterol, uric acid, total protein and ascorbic acid were estimated at 30 days intervals. Level of caffeine in blood was estimated at the interval of 10 days. Organs like thyroid, kidney and liver were studied histologically and kidney by SEM at the end of the experiment.

Experimental findings revealed a gross biochemical changes of glucose and urea while cholesterol, total protein and uric acid level did not change significantly. An initial rise of blood glucose level was observed following caffeine administration, while in the later part of the experiment the level declined towards normal. For instance, the animal groups those obtained ascorbic acid and caffeine treatment showed a rise of glucose level at the early part of the experiment while remained as such for a short period and then declined. Level of urea elevated in both caffeine treated and also simultaneously caffeine and ascorbic treated rat, however, subsequently the level declined towards normal.

Protein level remained unaltered in all the groups, but at the end of the experimental period i.e. on 90 days, it declined in caffeine and ascorbic acid treated rat. Although a conspicuous change of cholesterol and uric acid were not found but the level of both showed apparently low after administration of the drug till the end of the experiment.
Insulin level showed a rise to a recognizable concentration and remained high throughout the period of experimentation.

Metabolic hormone T₃ and T₄ also changed significantly and level became low after the administration of caffeine. However the T₄ level again elevated towards normal after 70 days onwards.

Following caffeine administration concentration of caffeine in serum showed an elevation during the period of 10 to 90 day of experiment. However, it was observed that vitamin C had significantly lowering effect on blood caffeine level during the early period (upto 30 days) of experiment. Prolong use of vitamin C did not show such lowering activity rather showed an additive effect on blood caffeine level as compared to only caffeine administered group.

Histological examination revealed certain changes in vital organs like liver, kidneys and thyroid glands. Kidney showed loss of intercellular material in caffeine treated rat. However, replacement of intercellular material was visible with simultaneous application of ascorbic acid. Thyroid gland also showed similar changes. Membrane structure of erythrocytes, as studied by SEM, showed structural abnormalities like formation of teardrop cells, membrane internalization and also formation of echinocytes. Simultaneous application of ascorbic acid appeared to cause recovery as denoted by appearance of large population of discocytes.
The experiment also showed a lowering action of caffeine on serum T3 and T4 level, more significantly on T3 than T4.

As evident, a significantly higher level of insulin in blood was an indication that caffeine had stimulatory action on insulin secretion.

The present experiment also showed that thyroid follicles and kidney parenchyma were also affected following prolong use of caffeine at high doses.

Ascorbic acid appeared to act as an antitoxic factor and also played preventive role against caffeine toxicity. The present study also signified that ascorbic acid metabolized the caffeine at the early part of the experiment and level of serum caffeine remained lower in caffeine and ascorbic acid treated rat than that of only caffeine treated rat.

In some blood constituents specially on glucose, the ascorbic acid had significant positive role. There was a clear picture that ascorbic acid although not able to normalize the toxic injury to control level but it could regulate the level of different biochemical parameters to prevent their high elevation or depletion as found in the experiment. Besides ascorbic acid also had capacity to protect the cellular structure and cell injury. SEM structure of thyroid clearly indicated that ascorbic acid was able to prevent loss of intercellular structure and bound thyroid follicle in intact condition.

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It was found that toxicological manifestation of caffeine were high at the day 40 and 50 and after that toxic injury returned towards normal, but in few parameters the toxic manifestation remained as such throughout the experimental period though ascorbic acid was administered.

SEM examination of erythrocytes clearly revealed toxic injury of caffeine on RBC membrane. Formation of teardrop cells, membrane internalization, discocyte-echinocytes transformation, stomatocytogenesis were the abnormal erythrocytes in the blood after caffeine treatment while preventive role was observed following simultaneous application of ascorbic acid.

The present investigation showed that caffeine appeared as toxic at particular dose level for mammal but could alter biochemical, hormonal and microanatomical structure. However, this could be partially prevented with the simultaneous application of ascorbic acid.

The finding, therefore, clearly revealed the antitoxic role of ascorbic acid in prevention of chemotoxicity induced by caffeine.