RATIONALE

OF WORK

Ultrastructural studies of target organs of animals treated with chemical carcinogen have revealed the effect brought about by these chemicals on subcellular organelles e.g. mitochondria, endoplasmic reticulum etc. It is generally argued that these cytological effects represent toxic injury (93, 94). However, biochemical effects along with the cytological effects cannot be ruled out. Information on the biosynthetic capacities of subcellular organelles, specifically mitochondria is grossly lacking.

Nitroso compounds have been found to be highly mutagenic in prokaryotes. It is therefore worthwhile to see how it affects mitochondrial functions, considering the similarities involved between mitochondria and prokaryotes. Such studies would also prove relevant in relation to biogenesis of mitochondria.

Our knowledge of chemical mutagenesis has largely proceeded through studies on animal system. However, the plant ecosystem has by and large been neglected. It is possible that environmental mutagen may contribute in a small way towards spontaneous mutation in plants. It is also important to note that the results obtained on the effect of chemical mutagen in animal experiments cannot be extrapolated for plant system. This is attributed to the differential effects of mutagens in animal and plant system.

The higher rate of alkylation of mitochondrial DNA in comparison to nuclear DNA in various rat tissue as observed by

Wunderlich and associates (83, 84) is yet another interesting aspect on the effect of chemical carcinogen on sub-cellular functions. Based on this observation a cytoplasmic mutation hypothesis has been advanced, the validity of which remains to be tested.

Apart from the serious concern that have been triggered by these compound in relation to environmental pollution, nitroso compounds on the other hand have been of great practical significance in plant breeding, to enhance crop yield. Extrachromosomal mutation in plants contribute significantly towards the genotypic expression (64) and hence result of present research work, it is hoped, would also contribute in a way towards a better understanding of the biochemical mechanisms of extrachromosomal mutation.

In addition, higher plants have been found to be an extremely convenient test system for screening mutagenic activity of potential carcinogen. Studying the effects of nitroso compounds in germinating seeds of Vigna sinensis (Linn.) Savi, a dicotyledon, at the subcellular level would further enrich our knowledge of the test systems involving germinating seeds in relation to mutagenic efficiency of proximate or ultimate carcinogens.

In order to evolve a mechanistic approach to explain how biosynthetic capacities of mitochondria are impaired by environmental mutagen, some well studied and highly purified enzymes of DNA synthesizing machinery need to be tested with a variety of alkylating agent.

Polychlorinated biphenyl of which DDT is a well studied member also happens to be an environmental carcinogen. It would be interesting to see how this typically different class of environmental carcinogen impairs biosynthetic functions at the subcellular level in both plant and animal systems.

Based on the above reasonings, the work embodied in the present thesis has been carried out along the following lines :-

(i) Mitochondrial protein and ribonucleic acid synthesis in presence of different environmental carcinogens.

(ii) Studies on mitochondrial protein synthesis in plant and animal in presence of carcinogenic pesticide e.g. DDT.

(iii) Inhibition of *in vitro* DNA synthesis in plant mitochondria by environmental carcinogens.

(iv) *In vitro* DNA synthesis by purified polymerases : mode of action of nitroso compounds on the process.
