S U M M A R Y

1) The general survey of the effects of these environmental carcinogens and mutagens like DMN, DENA and NTG, on protein and RNA synthesis in mitochondria from diverse sources reveals that the plant system is more sensitive rather than the animal system. The environmental carcinogens under study inhibit RNA synthesis more strongly than mitochondrial protein synthesis. Among the two nitrosoamines, DENA is a more potent inhibitor of macromolecular synthesis than DMN.

2) The inhibition of protein and RNA synthesis in isolated plant mitochondria by nitroso compound under study is due to the nonavailability of precursors for RNA synthesis arising out of altered permeability of the mitochondrial membrane and that the presence of NTG is essential to exert its inhibitory effect. DMN induced inhibition of mitochondrial protein and RNA synthesis are completely reversible whereas NTG induced inhibition is partially released.

3) During the isolation of mitochondria, from seeds germinated in presence of DMN, excess DMN on the mitochondrial surface is removed completely, although the intramitochondrial DMN may not be removed. When such mitochondria are incubated <u>in vitro</u> in presence of radioactive nucleic acid precursors, an already modified and activated template is utilized for biosynthetic purpose resulting in a stimulated macromolecular synthesis. But in case of <u>in vivo</u> incorporation, inspite of template activation, the restricted nonavailability of radioactive precursor leads to a resultant effect which is finally reflected as

inhibition of protein synthesis.

4) DDT has no effect on *in vitro* mitochondrial protein synthesis independently but inhibits *in vitro* microsomal protein synthesis. However, inhibition of microsomal protein synthesis would lead to inhibition of *in vivo* mitochondrial protein synthesis.

5) Different experiments support the fact that incorporation of radioactive dNTP into mitochondrial DNA is truly due to mitochondrial DNA synthesizing machinery.

6) Different specific inhibitors of DNA polymerase viz. PALPO, PAA, araCTP have no effect on plant mitochondrial DNA synthesis whereas EtBr inhibits at higher concentration.

7) Similar to mitochondrial RNA synthesis, DNA synthesis is also inhibited by carcinogens and/or mutagens under study. NTG induced inhibition of DNA synthesis is partially released after thorough washing of NTG from mitochondrial membrane whereas DMN induced inhibition is completely released. It has been suggested that nitroso compound may alter the permeability of the mitochondrial membrane thus interfering with uptake of radioactive precursors during DNA synthesis.

8) Homogeneous polymerase isolated from a variety of sources are more or less inactivated in presence of high concentration of NTG. Inhibition of *E. coli* polymerase and AMV-DNA polymerase activities by NTG is released with increasing concentration of the enzyme respectively. These release of inhibition suggest

that NTG may inhibit enzyme activity by binding with the enzyme protein itself.

9) In presence of DMN and DENA the activity of homogeneous DNA polymerase is not inhibited but rather stimulated. Again when calf-thymus DNA (template) is pretreated with DMN or DENA before assay, the stimulation of enzyme activity increases with increasing time of pretreatment.

10) It appears that there is no specific enzyme(s) system in plant mitochondrial extract which can transform the carcinogen to an active metabolite. Even if there is such a conversion, the active metabolite fails to inhibit DNA polymerase I in an in vitro reaction.

11) So far nucleic acid synthesis in plant mitochondria is concerned, mode of action of nitrosamine (DENA & DMN) is essentially different from that of nitrosamide (NTG). While the former inhibits at the membrane level of mitochondria only, the latter inhibits both at the level of membrane as well as DNA polymerase enzyme.
