SUMMARY AND CONCLUSIONS

(i). The activity of antioxidant enzymes viz., catalase, superoxide dismutase, glutathione reductase and glutathione peroxidase and oxidative enzymes of pentose phosphate pathway viz., glucose 6-phosphate dehydrogenase and 6-phospho-gluconate dehydrogenase were determined in different regions (cerebrum, cerebellum and brain stem) of adult brain. The results showed that enzyme activity levels were different in the three regions of the brain. The differential activity of these enzymes in various parts of brain may be responsible for different rates of ageing in various regions of brain.

(ii) Data concerning subcellular distribution of antioxidant enzymes and of oxidative enzymes of pentose phosphate pathway showed that considerable amount of activity of these enzymes occurred in particulate fraction as well as soluble fraction. Catalase was present in the post nuclear supernatant fraction.

(iii) In the three age-groups (6, 9 and 12 months) studied in the present work, the antioxidant enzyme activities (except catalase) in the particulate fractions from all the three regions of brain showed age-related changes. Glutathione peroxidase decreased with age in cerebellum and brain stem but it showed an age-related increase in cerebrum. Superoxide dismutase and glutathione reductase showed increases with age in all the three regions of the brain.

(iv) Antioxidant enzymes associated with soluble fraction mostly did not show age-related changes in all the three regions.
of brain. One exception was the case of glutathione reductase associated with soluble fraction of cerebrum which showed an increase with age.

(v) Catalase activity did not change with age.

(vi) Thus, the present results showed that these enzymes at certain sites increase, decrease or remain unchanged with age and a particular enzyme associated with different subcellular fractions may differ in its response to age.

(vii) Levels of lipid peroxide increased with age in all the three brain regions, but not at the same rate.

(viii) Biochemical and histochemical determination of lipofuscin shows: age-related accumulation of lipofuscin in the rat brain.

(ix) The effects of geriatric drugs (centrophenoxine, dimethylaminoethanol and chlorpromazine) on enzymes (catalase, superoxide dismutase, glutathione reductase, glutathione peroxidase, glucose 6-phosphate dehydrogenase and 6-phosphogluconate dehydrogenase), lipid peroxidation, lipofuscin deposits, electrocortical activity and multiunit activity were studied in the present work. The effect of these drugs seemed to be dose-dependent.

(x) Histochemical and biochemical study of the effect of all the three drugs on lipofuscin showed drug-induced reduction in the level of lipofuscin in all the three age-groups.

(xi) Dimethylaminoethanol and chlorpromazine (both in vivo and in vitro studies) treatments produced decreases in the level of lipid peroxides in all the three age-groups. Centrophenoxine did not seem to effect the level of lipid peroxides.
(xii) All the three drugs induced increases in the activities of the enzymes viz., superoxide dismutase, glutathione reductase, glutathione peroxidase, glucose 6-phosphate dehydrogenase and 6-phosphogluconate dehydrogenase in all the three brain regions of various age-groups. Catalase activity was not influenced by any of the three drugs.

(xiii) Drugs exerted their effects on antioxidant enzymes and oxidative enzymes of FPP in a dose-dependent manner. Effects of these drugs on the enzymes of soluble and particulate fractions were not similar, viz., glutathione peroxidase associated with particulate fraction showed an increase with both the doses of all the three drugs whereas soluble fraction enzyme did not show any change.

(xiv) The present data, thus, showed that centrophenoxine, dimethylexinoethanol and chlorpromazine were effective in reducing the formation of lipid peroxidation products (lipofuscin) and were also able to exert a stimulatory effect on the enzymatic defense mechanisms. The correlation between the decrease in peroxidated products and increases in antioxidant enzymes, particularly of glutathione peroxidase, suggest that reduction in peroxidation products might be brought about by drug-induced activation of the enzymatic defense mechanisms involving glutathione peroxidase. Lack of centrophenoxine's effect on lipid peroxides remains to be explained.

(xv) Stimulation of enzymatic defense mechanism by these drugs will be also significant for stabilization of cellular membranes and extension of life span because oxidative
damage is thought to be one of the important factors responsible for destabilization of cellular membranes and reduction of life span.

(xvi) In vitro studies of the effect of different concentrations of centrophenoxine on acetylcholinesterase and monoamine oxidase showed decrease in enzymatic activity.

(xvii) In the present work, electrocorticogram and multiunit activity were recorded in wakeful state of rats aged 1, 3, 6, 9, 12 and 26 months.

(xviii) One month old rats showed the presence of high voltage slow brain waves without alpha waves (8-12 Hz) and alpha waves appeared in 3 month old rats. The slow wave electrocorticogram of one month was increasingly replaced by medium-fast waves till the 6 month of age and afterwards the wave pattern remained unchanged. In very old age (26 months) the electrocorticogram showed decline in alpha waves.

(xix) Maximum rate of firing of multiunit spikes appeared at 3 months of age. A gradual decline in multiunit firing rate was observed thereafter.

(xx) Both the doses of all the three drugs (centrophenoxine, dimethylaminoethanol and chlorpromazine) influenced the electrocorticogram and multiunit activity in all the three age-groups. The effects of all the three drugs were, however, not the same. Centrophenoxine effect was different from that of dimethylaminoethanol and chlorpromazine.

(xxi) Centrophenoxine produced activation in electrocorticogram i.e., increase in frequency and acceleration of multiunit activity. Whereas dimethylaminoethanol and chlorpromazine produced deactivation of electrocorticogram i.e., slowing
of ECoG waves and deceleration of multiunit spiking.

(xxii) Chlorpromazine produced decrease in awake and rapid eye movement sleep period, whereas it produced increase in nonrapid eye movement sleep period and total sleep period.

(xxiii) From the present data on the effects of drugs on electrical activity, it can be suggested that neurons of parietal cortex were influenced by centrophenoxine in an excitatory fashion whereas dimethylaminoethanol and chlorpromazine in an inhibitory fashion at both electrocorticogram and multiunit levels.

(xxiv) It can also be suggested that age-related slowing of electrocorticogram and multiunit activity can be reversed by treatment with centrophenoxine. Present results also showed that multiunit activity signals were sensitive to the changes in electrocorticogram.