SUMMARY AND CONCLUSIONS
Summary and Conclusions:

In the present investigation the impact of interaction of exercise training and ethanol on carbohydrate metabolism and ATPases (Mg$^{2+}$, Ca$^{2+}$) has been studied in the brain tissue with reference to aging and enzyme systems of non-oxidative and oxidative metabolism by taking male albino rat as an experimental model. Alcoholic beverages have been used and abused. Since the dawn of the history. Alcoholism is a serious problem for any age group that can have pathological effect on several important systems of the body eg: CNS, Liver, Kidney, Brain. Chronic alcohol exposure leads to brain damage and production of free radicals which ultimately leads neurodegenerative changes, such as aging. Regular exercise has been well documented health benefits and increases average life expectancy by approximately 10%. Exercise is believed to be beneficial to improve quality of life, retarding age-related decline of physiological functions and preventing age-related disease. The type of activity and the amount of exertion during exercise are important for pathological and physiological effects. Running, swimming, aerobic dancing, cycling and walking are suitable for producing these beneficial effects. Anyway, high intensity of exercise causes oxidative stress. Alcohol and sports have been linked since ancient times. Aging is a multidimensional process and usually considered to be a normal phenomenon that occurs in all members of population. If carbohydrates are in fact that causative factors responsible for senescence, the maintenance of carbohydrate metabolism would minimise damage to physiological system and consequently the process of aging could be delayed. Acute exercise enhances the ability to release energy by effective utilization of various metabolic fuels including stored ones, due to improved oxidative capacity.
The survey of literature revealed that the reports on the effect of ethanol toxicity, exercise training and aging on cellular oxidative metabolic profiles, oxidative metabolic enzymes and energy metabolic enzymes in the brain tissue of male albino rat are inconclusive and inadequate, particularly the interactive effects of exercise and alcohol. This field of research has to be explored in view of the findings of is there any beneficial aspects of exercise to alcoholics? Elderly people may be more susceptible to the oxidative stress, induced by alcohol drinking than youth. As the number of elderly drinkers in the population is quite large, who are also doing, regular exercise. The effects of regular exercise on aging and alcohol induced effects on energy metabolism deserve thorough investigation. Hence, in the present investigation the impact of treadmill exercise on two different age groups for comparison, representing the aging phenomenon has been studied in selected oxidative metabolic profiles, oxidative enzymes and ATPases by choosing wistar strain male albino rat as an experimental animal model.

The treadmill exercise was selected for this study because, it is exclusively used to evaluate the physiology of running. In this model, it is possible to imply the stress on the animal in a defined manner where the speed and angle of scope can adjust exactly. The advantage of treadmill exercise over other types is, it brings about a greater involvement of myocardial muscle mass and other organs which leads to higher maximum aerobic capacity.

Wistar strain male albino rats of two age groups (3 months and 18 months representing young and old age respectively) were maintained in the animal house at 27°C with photoperiod of 12 hours light and 12 hours darkness, were used in the present study. The survey of literature in the field of
"Exercise science and Aging" regarding selection of age and grouping of animals as mentioned in 'material and methods' section was taken into consideration to select '3 months old' rats as 'young age' and '18 months old' rats as 'old age' in this experimental design for comparison of the results. They were maintained in clean polypropylene cages and fed with standard rat pellet diet (Hindustan Lever Ltd., Mumbai) and water ad libitum.

The submaximal exercise training and ethanol administration was followed as per the protocols given by Somani and Hussain (1997). The usage of animals and animal exercise protocol in the current investigation was approved by the Institutional Animal Ethics Committee (Regd.No. 438/01/a/ CPCSEA, dated 17.7.2001) in its resolution number 9/IAEC/SVU/Zool, dated 4.3.2002.

The animals of each age (young/old) were divided into four groups. Each group consists of six animals and the division of groups is as follows.

- **Group I**: Sedentary control (SC)
- **Group II**: Exercise training (ExT)
- **Group III**: Ethanol treated (Et)
- **Group IV**: Exercise training and Ethanol treated (ExT+E)

The animals were sacrificed after 24 hours of the last exercise session by cervical dislocation. The brain tissue was excised at 4°C. After washing the tissues with ice cold normal saline, immediately immersed in liquid nitrogen under ice cold conditions.

The studies on selected oxidative metabolic profiles, oxidative metabolic enzymes and ATPases (Mg²⁺, Ca²⁺) in this study revealed as follows.
Summary and Conclusions

(1) The decrease in total carbohydrate level in the brain of ethanol treated rats of both young and old age group of rats indicate utilization of carbohydrates to meet energy demand during ethanol and exercised stress conditions.

(2) The brain glycogen concentration was increased after 2 months endurance exercise training in both age groups due to mobilization of stored reserves including carbohydrates and fats. Where as, in ethanol treated rats the glycogen content was decreased. However, with the combination treatment (ExT+Et) the glycogen content was increased, which may due to the induction of exercise training under such conditions.

(3) Elevation in glucose levels observed in old rat brain of all experimental rats than young rat, indicate low rate of glucose utilization. In the present study exercise resulted in their rapid utilization for increased energy requirements. Decreased glucose content was observed in the brain of ethanol treated of both age group of rats indicate rapid utilization, to meet energy demands during ethanol toxicity conditions. However, elevated levels of glucose content was observed in the combination treatment of both age groups which may be due to beneficial effects of exercise to minimize the toxic conditions during ethanol toxicity.

(4) The formation of pyruvate, an important intermediary compound of glycolysis was found to be low during aging indicating its immediate conversion to lactate in the brain tissue studied.
The decreased levels of pyruvate and elevated levels of lactate during aging indicate possible oxygen deficiency in the intracellular milieu with advancement of age and reduced uptake of oxygen in view of preventing hypoxic conditions in the brain tissue. A possible diversion of the metabolic pathway at phosphoenol pyruvate level or its conversion to lactate during aging is suggested which make the brain to depend on anaerobic metabolism due to remarkable drop in aerobic segment as a consequence of decreased oxygen uptake (or) utility. The decreased mobilization of pyruvate into Kreb’s cycle due to inhibition of several oxidative enzymes results in its conversion to lactate. Endurance training resulted in a significant increase in lactate and decreased pyruvate utilization through anaerobic pathways.

The pyruvate levels were elevated in the brain of ethanol treated rats of both young and old age group of rats indicate the decreased feeding of pyruvic acid into tricarboxilic acid (TCA) cycle. Evidently decreased succinate dehydrogenase activity levels were noticed in the, ethanol treated rat, in the present study.

(5) The elevated level of total protein content in the brain of exercise trained rats, which may be due to decreased proteolysis and increased generation of energy by ATPases where endurance exercise enhances the ability to release energy by effective utilization of various metabolic fuels including stored ones, due to improved oxidative capacity, and enhances the oxidative phosphorylation leading to the elevation of high energy phosphate reserves, such increase in energy availability may
stimulate the free amino acids for the synthesis of protein. Hence elevated level of protein content was observed.

Total protein content was slightly decreased in the brain of old age group and ethanol treated rats. The diminishment of proteins suggest that aging and ethanol toxicity induces rapid degradation of proteins (which may be decreased due to protein synthesis (or) increased proteolysis) may be explained in terms of accelerated proteolytic activity. Combination treatment showed slight elevated total protein content, suggesting the beneficial effect of exercise under induced alcoholic conditions.

(6) Decreased free amino acid content was observed in the brain of exercise trained rats which may be due to increased rate of amino acid utilization for protein synthesis. Elevated levels of free amino acids were observed in old age group which may be due to increased proteolysis (or) decreased uptake of amino acids into protein synthesis and enhanced catabolism during advancement in age, might be the factors responsible for elevated amino acid content in the present study.

(7) In this present investigation a decline in NAD dependent LDH activity was observed with advancement of age, which indicate poor clearance of lactate (or) an increased conversion of pyruvate to lactate as the LDH activity was estimated in the direction of pyruvate to lactate formation. The decreased LDH activity in old rats indicates the prevalence of hypoxic (or) anoxic conditions in old age rats. In contrast to this, an increase in LDH activity in exercised rats presents a possible shift in the anaerobiosis to aerobiosis metabolism which
indicates increased conversion of lactate to pyruvate. With the combination treatment LDH activity was enhanced which may due to involvement of intracellular lactate shuttle to transport lactate in the mitochondrial matrix followed by oxidation to pyruvate, thus the oxidative stress due to ethanol toxicity in the brain tissue may be overcome by exercise induced upregulation of LDH activity.

(8) The citric acid cycle enzymes SDH and MDH were assayed, as markers of mitochondrial oxidative capacity. The SDH activity was remarkably decreased with advancement of age, suggests the deceleration of TCA cycle operation due to aging. An increase in this enzyme activity in exercised rats reveals increased mitochondrial oxidative potential and energy synthesis utilizing fats as substrates by endurance exercise training. This observation in increased SDH activity was more in young age than the old age. A disturbed oxidative metabolism was reported due to ethanol toxicity. However, this was restored with the combination treatment of the exercise training. Thus it seems exercise beneficial to restore the lost SDH activity. The increase in MDH activity in the combination of exercise and ethanol treatment also indicate higher utilization of malate which was diminished with ethanol toxicity. Thus, the upregulation of oxidative metabolism with high turnover of energy substances leads to high energy out put which is required during aging as well as in exercise.

(9) The mitochondrial ATPase is a complex enzyme system. An age dependent decrease was noticed in the activities of brain ATPases (Mg\(^{2+}\), Ca\(^{2+}\)) in the present investigation. The decrease in the ATPases
during aging may be attributed to reduced oxidative metabolism leading to reduced ATP synthesis due to reduced TCA cycle oxidation and respiratory chain efficiency. In general, the specific activities of Mg$^{2+}$-ATPases, and Ca$^{2+}$-ATPases were elevated in brain tissue after exercise which implies stimulation of a series of energy consuming reactions in intermediary metabolism. The drop in the activity caused by aging was elevated by exercise training in brain tissue of both young and old rats. However a decrease in the activity of Mg$^{2+}$ and Ca$^{2+}$-ATPases due to alcohol treatment was observed. In the combination treatment (Ex+Et) the ATPases were increased in the brain tissue, clearly indicates, exercise may be beneficial in energy metabolism.

To sumup, the findings from the present study suggests that both aging and exercise training influence the changes in carbohydrate metabolism in the brain that was selected during this program. The differential response of this tissue studied to exercise training, ethanol treatment and combination treatment on carbohydrate metabolic profiles as well as on oxidative metabolic enzyme systems reflects the specific physiological response of the tissue.

To conclude, the present findings suggest that 2 months endurance treadmill exercise training with the selected intensity that was adapted may be beneficial in countering the age associated and ethanol induced alterations in carbohydrate metabolic profiles, and energy metabolic enzyme activities in wistar strain male albino rats. The LDH, SDH, MDH enzyme activities and ATPases activities are upregulated due to combination treatment in brain tissue of both age groups. The augmentation of these enzyme systems due to 2
months treadmill exercise training will provide a significant advantage to overcome various pathological and physiological processes that occur in brain tissue due to old age. This investigation draw a conclusion stating that this much of intensity treadmill exercise to the old age as well as young age male subjects may be beneficial, especially for the alcoholic subjects to improve the metabolic efficiency and thereby to improve the health status and life span.