Alcohol is a widely abused drug throughout the world with its adverse health effects. Reports clearly indicated that there has been an increase in the number of female alcoholics in many countries including India. The female gender has long been neglected in research investigations related to alcoholism. However a few isolated studies available clearly revealed that females respond differently to alcohol when compared to males. Though differential body composition, differential alcohol dehydrogenase activity, hormonal milieu and physiology of organs are attributed to the differential response of females to alcohol, the precise mechanisms and many related events are unclear. According to available literature females are more sensitive to alcoholic damage and toxicity. Unfortunately, no clear data are available on female alcoholics related to chronic alcohol toxicity. Hence, based on certain earlier reports the present study has been designed with rats as animal models with two concentration of ethanol at 4g/kg b.w/day (for females) and 10g/kg b.w/day (for males) for a period of 60 days and is aimed at investigating the alcohol induced biochemical toxic changes in rats receiving 4g ethanol/kg b.w/day in females comparable to the same with 10g ethanol/kg b.w/day receiving male rats as pronounced alcohol toxicity was confirmed in these groups.

A comprehensive analysis of the results of the present study indicated that there exists sex difference in normal levels of plasma biochemical profiles. Further it is also evident that the alcohol induced changes in female rats receiving 4g of ethanol appear to be equal to that of male rats receiving a 2.5 fold higher dose i.e., 10g ethanol. These results suggested that females are more sensitive to alcohol toxicity at lower doses.
Further it is also clear from the results that differential consumption, metabolic regulation and hormonal milieu may be responsible for the observed differential response to alcohol in female rats when compared to males.

Increased production of nitric oxide, increased oxidative stress (evident from increased lipid peroxidation) and decreased status antioxidant machinery in the present might be contributing to the observed greater sensitivity and toxicity in female alcoholic rats than males. The possibility of involvement of neuroendocrine mechanisms in these processes cannot be ruled out.

Results of the study showed that mitochondria of liver are more susceptible for alcohol action when compared to brain mitochondria in both genders. However anisotropy experiments using DPH and pyrene revealed a decrease in membrane fluidity in mitochondrial and red cell membranes from rats that were chronically administered alcohol. It is surprising to note that hepatic microsomal bilayers showed no significant changes in fluidity.

Liver is a hormone responsive organ. Estrogen receptors modulate kupffer cells in female rats causing the release of reactive oxygen species in high concentrations when compared to males. Further in males androgens have protective and free radical scavenging properties. The greater sensitivity to alcohol observed in female rats can be attributed to these hormone receptor related discrepancies. Overproduction of nitric oxide observed in the present study is also responsible for several pathological changes as well alternations in lipids and enzyme activities in alcohol toxicity observed in the present study.

To sum up differential metabolic regulation, differential composition and nervous control mechanisms, lack of androgen protection and estrogen mediation,
differential hormonal milieu and dysfunction of nitric oxide metabolism are responsible for the observed greater sensitivity of females to alcohol and alcohol toxicity.