CHAPTER 2

OBJECTIVE OF THE PRESENT WORK

The drug molecules interact with the biomembranes on the specific receptors or on the lipid bilayer or even at the lipid-protein interfaces. Studies have revealed that midazolam has neurotoxicity. The toxicity of midazolam ranges from degradation of nerve cell membrane to neuronal death and loss on neurons. The exact mechanism for its toxicity is still being elucidated. The extent of damage caused by midazolam in the spinal cord of animal suggests that the observed neurotoxicity should arise from its interaction with the lipid part of the bilayer of the cell membrane owing to its high lipophilic nature.

Though many reports are available on the neurotoxicities of midazolam using animal models, studies on the lipid bilayer-drug interactions are scanty. It is a well established fact that the drug-lipid interaction is also an important factor in deciding the mechanism of action of a drug with the cell.

The exact mechanism and sites of action of benzodiazepines responsible for their pharmacological effects are still under study. Benzodiazepines are proposed to act on the subunits of GABA_A receptors at the postsynaptic neurons and to augment the activity of the inhibitory neurotransmitter γ-amino butyric acid.
The clinical use of these drugs involves a compromise between their benefits and toxicities. Many studies using animal models showed that spinally administered MDZ induces severe neurotoxicities, but many reports contradict these results, which leads to the present work.

The objective of the present work is to study the extent of interaction of midazolam with the lipid bilayers using planar lipid membrane and salt bridge supported lipid membrane models. Additionally it was intended to develop an electrochemical biosensor for the detection of MDZ in solution using glassy carbon supported BLM.