SCOPE OF RESEARCH
Brain is one of the important organs required for normal functioning of man. It controls our thoughts, behaviour, learning and memory—in essence, everything that is regarded as civilization today. In addition, it is also the controller of movements and co-ordinator of various activities of the living system.

Brain is made up of two major cell types, namely, neurons and glia. Neurons are the seat of major activities of the brain like neurotransmission, neurosecretion and neurotrophism. Damage to the brain is largely irreversible due to the limited regenerative capability of the neurons. Thus, unlike other organs, any toxic insult to the brain can lead to permanent damage resulting in malfunctioning of the brain. Thus, assessment of brain damage caused by toxic insult is an important issue which is gaining increasing importance in recent years following increased industrialization.

Damage to the brain may occur by man-made toxic compounds which are being added to the environment in the form of industrial chemicals, pesticides etc. In addition, various environmental toxins have also been implicated in the aetiopathogenesis of several neurodegenerative disorders, like Parkinson's disease, Alzheimer's disease etc. Drugs may also have deleterious effects on CNS. Considering the tremendous health hazard posed by these compounds to human
health, it is necessary to screen these large number of compounds to determine their possible neurotoxic potential. The neurotoxic compounds have to be further investigated for their mechanism of toxic action in the CNS, which would enable the development of appropriate therapeutic and prophylactic measures. A suitable model system which can be used for rapid evaluation of neurotoxicity would be required to achieve these goals.

In vivo models using experimental animals are used to assess the neurotoxic potential of various compounds. In vivo experiments are both time consuming and expensive. Thus, in vitro methods are useful alternatives to in vivo models for evaluation of toxicity.

While in vitro methods cannot replace in vivo experiments, in vitro methods have several advantages over in vivo experiments. A large number of compounds can be screened within a given time. Species, strain and sex-related differences in neurotoxic effects can be evaluated rapidly. Further, the direct interaction of the toxicants with the components of the nervous system can be assessed directly.

Various in vitro models consisting of neuronal cultures, synaptosomal preparation, brain homogenate and slices of particular regions of the brain have been used for assessment of neurotoxicity of several compounds with limited success.
Since brain is a heterogenous organ with diverse functions which are controlled by different regions, the in vitro models have to be representative of many regions of the brain. Toxicants may have differential action on various regions of the brain and hence slices of a particular brain region have limited use. Thus, an effective in vitro model which is representative of most of the regions of the brain for the evaluation of neurotoxicity, is lacking.

The present study was carried out to develop a suitable in vitro model for rapid screening of a variety of compounds. Sagittal slices of mouse or rat brain were used as an in vitro model for neurotoxicity evaluation. Sagittal slices contain most of the brain regions present anteroposteriorly.

The efficacy of the in vitro model was evaluated by examining a range of well studied neurotoxicants having diverse modes of action. The neurotoxins studied include, acrylamide and 2,5-hexanedione, known to cause peripheral neuropathy; 1 - methyl -4-phenyl-1,2,3,6 - tetrahydropyridine (MPTP)-a selective dopaminergic toxin and a variety of excitatory amino acids implicated in various neurodegenerative disorders. In addition to determining the selectivity and sensitivity of the in vitro model comprising of sagittal slices of brain, experiments were also carried out to evaluate the molecular mechanism underlying the toxic insult.