PREFACE
The "Green revolution" and the rapid industrialization have led to self-sufficiency in food, better transportation and reduced dependence on the other countries for the common needs. However, the industrialization has led to widespread pollution with a number of chemicals being released in the environment to which man and the economic species get directly and indirectly. The commonly used chemicals are metals, pesticides, monomers, solvents, mineral dust etc. Several chemicals have been shown to affect the central nervous system and implicated in the development of serious neurological disorders. Manganese, a commonly used metal and paraquat a widely used pesticide have been implicated in Parkinson's disease and aluminum and lead in Alzheimer's disease. Such reports have aroused a great concern over the environmental illness among the health scientists world over. Role of neurotransmitters (NT), their receptors, cellular signaling in functioning of the central nervous system is well established and alterations in their levels would lead to neuropsychiatric disorders like Parkinson's disease, schizophrenia, mental retardation and depression. The intricate process of synaptic transmission involves several steps viz synthesis, release, degradation, uptake of neurotransmitters and their binding with receptors and subsequent translation of the message. Interaction of the xenobiotics with any step of this intricate process can lead to altered receptor function leading to neurobehavioral changes.
Continued exposure to lead, methyl mercury and certain solvents lead to some structural damage occurs. Exposure to low level of such chemical leads to central nervous system damage leading to functional deficit, which are often irreversible. Therefore, it would be significant to identify neurochemical markers which could help in detecting early exposure and monitoring the disease condition. It is not possible to perform neurochemical studies in living human brain and data obtained from post mortem brain specimens are not reliable due to difficulties in proper isolation and preservation of the tissue. Also choice of age, sex and stage of the diseases and monitoring of the biochemical alteration with progression of disease treatment follow up in humans are not possible. Availability of non-invasive techniques like PET, SPECT and NMR has made possible to study neurotransmitter function in vivo but their availability is a limiting factor due to their high cost. Realizing these problems scientists are attempting to characterize and validate parameters in the peripheral fluids of human as surrogate markers of dysfunction, damage or interaction involving neuron targets of toxicants. Peripheral tissues such as blood, saliva, sweat, urine and blood components and cerebrospinal fluids (CSF) have been used in recent years for such purposes. Cerebrospinal in patients after lumbar puncture poses ethical consideration and are not preferred.

Blood cells like platelets and lymphocytes are ideally suited for monitoring neurotoxic effects because of their easy accessibility and they share some common functions similar to those of neuron. Platelets and lymphocytes have been routinely used in pharmacological studies as models of nerve ending because they contain neurotransmitters and/or have receptors for neurotransmitters on their surface. Alterations in α-adrenergic receptors of lymphocytes reflect changes in patients with hypertension. Also polymorphonuclear leukocytes (PMNS) β-adrenergic receptors have been used to study changes during depressive disorders, following 14 days washout period where a decrease in receptor density in these cells has been reported by some investigators. In several neurological disorders, functions of non adrenergic system are coupled with enzyme adenylate cyclase and their stimulation leads to
increase in the intracellular adenosine cyclic 3', 5'-monophosphate (cAMP) levels. In addition, alterations in intracellular calcium signaling in lymphocytes have also been reported in affective disorders. In Parkinson's disease (PD) and Alzheimer's disease (AD), there is reduction in number of lymphocytes receptors and dopamine receptors. Altered lymphocyte benzodiazepine receptor binding has been observed in generalized anxiety disorders. The lymphocyte binding of serotonin has also been studied in patients of Alzheimer's disease, idiopathic mental retardation and autism. Further, there is some evidence of alterations in catecholamines and their receptors in blood components in schizophrenic patients. Thus, circulating lymphocytes may serve as useful peripheral marker which reflect changes in muscarinic receptors in central nervous system.

Platelets have been extensively used as an effective model to understand the functioning of the brain. Due to several similarities between platelets and neurons with respect to morphology, biochemistry and pharmacology platelets have been proposed as a peripheral model for neurons. Initially, platelets were proposed as model for presynaptic nerve terminals on account of their ability to accumulate, store and release biogenic amines such as serotonin, noradrenaline and dopamine. Subsequently, receptor binding sites for neurotransmitters (serotonin, dopamine, adrenergic, glutamate) and drugs (tricyclic antidepressants, benzodiazepine and phencyclidine) have been demonstrated on platelets. Parallel changes between platelet and brain dopamine and serotonin receptors following exposure to selected drugs and neurotoxicants acting on dopaminergic and serotonergic systems respectively have further strengthened the usefulness of platelets as a peripheral model. The 5-HT uptake mechanisms or 5-HT transporter is an important part of the 5-HT system which can be measured by the number of binding sites for antidepressant drugs located on the 5-HT-transporter in the membranes of serotonergic neurons or platelets.

Among the other important factors excitotoxicity, mitochondrial dysfunction and free radical induced oxidative stress has been implicated in pathogenesis of neurodegenerative disorders, such as Parkinson's disease, Alzheimer's disease, epilepsy and the aging brain. It has been proposed that inflammatory processes
contribute significantly to the enhanced oxidative damage observed in chronic phase of neurodegenerative processes.

The candidate has attempted to validate and investigate the status of dopamine receptor and some parameters of oxidative stress and studying markers of neurotoxicity of chemicals in platelets by their responses to neurotoxicants like metal and pesticides on blood components. The objectives of the study were to investigate the status of:

Dopamine D4 Binding sites in platelets of normal healthy controls. The effect of selected neurotoxicants viz cadmium, fenvalerate, methyl parathion on various parameters related with oxidative stress and membrane function in lymphocyte. The binding of 3H-Paroxetine on patients of drug of abuse in platelets.

It is the sincere hope of the candidate that these studies would provide valuable information on the mechanism of alteration of neurotransmitter receptors in platelets and help in developing and validating markers for neurological disorders. These studies would also strengthen the usefulness of platelets and lymphocytes as a peripheral model for central nervous system.