Summary and Conclusion
The aim of the present study is to identify the protective role of melatonin on polychlorinated biphenyl (Aroclor 1254) induced impairment in antioxidant system, membrane bound ATPases, creatine kinase, acetylcholinesterase (AchE) activities and amyloid beta protein levels in cerebellum, cerebral cortex and hippocampus of adult male rats. Histomorphological studies in the same regions are also investigated. To achieve this, adult male wistar rats were treated with polychlorinated biphenyls (Aroclor 1254) dissolved in corn oil at a dose of 2 mg/kg body weight intraperitoneally daily for 30 days. One group of rats was treated with melatonin intraperitoneally at a dose of 5 mg/kg body weight simultaneously for 30 days. Another group of rats was treated with melatonin intraperitoneally at a dose of 10 mg/kg body weight simultaneously for 30 days. Separate drug treated controls were also maintained in the same period. 24 hours after last treatment, the animals were sacrificed by decapitation and brain was immediately removed and dissected over ice-cold glass slides to the following regions: cerebellum, cerebral cortex and hippocampus.

The samples were homogenized to produce 10% homogenates and used for determining the biochemical parameters such as enzymatic and non enzymatic antioxidant parameters such as total superoxide dismutase (total SOD), Copper Zinc superoxide dismutase (Cu/Zn SOD), Manganese superoxide dismutase (Mn SOD), Catalase (CAT), Glutathione peroxidase (GPx), Glutathione reductase (GR), Glutathione –S-transferase (GST), Reduced glutathione (GSH), Vitamin C, Vitamin E, Lipid peroxidation (LPO), Hydrogen peroxide (H₂O₂) and Hydroxyl radical (•OH) generation.

The activities of all the antioxidant enzymes such as total SOD, Cu Zn SOD, Manganese SOD, CAT, GPx, GST, GR and the levels of non enzymatic
antioxidants such as GSH, Vitamin C, Vitamin E were significantly decreased in the brain regions such as cerebellum, cerebral cortex and hippocampus of PCB exposed animals. Simultaneous administration of melatonin (10 mg/kg body weight) in Aroclor 1254 treated rats restored the activities of all the enzymes and the levels of non enzymatic antioxidants, significantly.

Simultaneous administration of melatonin in 5mg/kg in Aroclor 1254 treated rats restored the activities of all the antioxidant enzymes except catalase and Glutathione-s-transferase, significantly.

The levels of reactive oxygen species and lipid peroxidation were increased in PCB treated animals. Simultaneous supplementation of both the doses of melatonin in PCB treated animals restored the levels, significantly.

PCB (Aroclor 1254) exposure alters the activities of antioxidant enzymes, lipid peroxidation and reactive oxygen species levels leads to cause oxidative stress in brain regions of rats. The exogenous melatonin treatment can attenuate the PCB induced oxidative stress in brain regions of experimental animals.

The biological functions of SODs are very important because they prevent oxiddative damage and inflammation, due to subsequent formation of oxygen intermediates derived from the superoxide. In its three isoforms, Cu-Zn SOD is mainly expressed in neurons. GPX4 is the only major antioxidant enzyme known to directly reduce phospholipid hydroperoxides within membranes and lipoproteins. GPx4 shows a unique cellular distribution in the brain compared to GPx1.

The mRNA expression of Cu/ Zn SOD and phospholipid hydroperoxide glutathione peroxidase (phGPx - GPx4) were also determined in cerebellum, cerebral cortex and hippocampus of PCB exposed and simultaneous melatonin
treated animals by reverse transcriptase polymerase chain reaction method (RT-PCR).

The mRNA expression of Cu/Zn SOD was significantly decreased in the brain regions such as cerebellum, cerebral cortex, hippocampus of PCB exposed animals. Simultaneous administration of melatonin in Aroclor 1254 treated rats restored the mRNA expression of Cu/Zn SOD, significantly and it has demonstrated that PCB (Aroclor 1254) exposure alters the mRNA expression of Cu/Zn SOD in brain regions of rats. The exogenous melatonin treatment can attenuate the PCB induced changes in Cu/Zn SOD mRNA expression in brain regions of experimental animals.

The mRNA expression of GPx4 were significantly decreased in the brain regions such as cerebellum, cerebral cortex, hippocampus of PCB exposed animals. Simultaneous administration of melatonin in Aroclor 1254 treated rats restored the same.

The activities of Na⁺K⁺ATPase, Ca²⁺ATPase, Mg²⁺ATPase, creatine kinase in selected brain regions and the CK level in serum were assayed. CK isoforms were also determined in serum and tissues of treated groups using Polyacrylamide gel electrophoretic system. The AchE activity was also estimated.

The activities of all the membrane bound ATPases, creatine kinase and acetylcholine esterase were significantly decreased in the brain regions such as cerebellum, cerebral cortex and hippocampus of PCB exposed animals. Simultaneous administration of melatonin in Aroclor 1254 treated rats restored the activities of all the enzymes significantly. The CK level and CK isoforms such as CK BB, CK MM and CK MB were increased in serum. The CK BB (brain specific) level was decreased in all the three brain regions. Simultaneous
administration of melatonin restored the CK isozymes, and serum CK level, significantly.

Many amyloid diseases are characterized by protein aggregations linked to oxidative stress. Amyloid precursor protein (APP) is an integral membrane protein expressed in many tissues and concentrated in the synapses of neurons. APP is the precursor molecule whose proteolysis generates amyloid beta a 39-43 amino acid peptide whose amyloid fibrillar form is the primary component of amyloid plaques found in the brain of Alzheimer’s disease patients. Oxidative stress promotes intracellular accumulation of Abeta through enhancing the amyloidogenic pathway.

The level of beta amyloid protein was significantly increased in the brain regions such as cerebellum, cerebral cortex and hippocampus of PCB exposed animals. Simultaneous administration of melatonin in Aroclor 1254 treated rats restored the level, significantly.

The level of melatonin was significantly decreased in serum and selected brain regions such as cerebellum, cerebral cortex and hippocampus of PCB exposed animals. Simultaneous administration of melatonin in both doses (5 mg or 10 mg/ kg body weight) in Aroclor 1254 treated rats restored the melatonin levels in both serum and brain regions, significantly.

PCB (Aroclor 1254) exposure increases expression of beta amyloid protein in brain regions of rats. The exogenous melatonin treatment can attenuate the PCB induced changes in the expression of beta amyloid protein in brain regions of experimental animals. PCB affects the melatonin level in serum and also in selected brain regions and the exogenous administration of melatonin (5 mg or 10 mg/ kg body weight) protects the PCB induced changes, significantly.
To determine the histomorphological changes in cerebellum, cerebral cortex and hippocampus the same groups were maintained separately described in previous experiments. 24 hours after the last treatment, animals were sacrificed by administering thiopental sodium intraperitonealy and were perfused transcardially. From the perfused animal, the head was separated and stored in 10% formal saline and after 2 or 3 days the brain was removed. The cerebral hemisphere was cut into 3 coronal slices. Later the tissue sections were processed for paraffin sectioning and paraffin tissue blocks were made. The paraffin tissue blocks were cut into 10μM thickness using rotary microtome and the sections were stained for haematoxylin and eosin staining. The cortical, cerebellum and hippocampal cellular morphology were analyzed and recorded.

The neuronal morphology of selected brain regions such as cerebellum, cerebral cortex and hippocampus were entirely changed in PCB exposed groups. Neuronal morphology of cerebral cortical layers, pyramidal cells of hippocampal layers and the Purkinje cellular layer in cerebellum were morphologically changed in PCB treated groups. Simultaneous administration of both the doses of melatonin restored the PCB induced morphological changes.

Thus, the melatonin protects the PCB (Aroclor 1254) induced oxidative damage in rat cerebellum, cerebral cortex and hippocampus.
CONCLUSION

The central nervous system is sensitive to PCBs. Oxidative stress and formation of free radicals are the major factors of the cytopathology of many neurodegenerative disorders, where neuron displays oxidation and upregulation of oxidative defenses. PCB (Aroclor 1254) exposure alters the activities of antioxidant enzymes, lipid peroxidation and reactive oxygen species levels lead to cause oxidative stress in rat brain regions. Studies show increased amyloid beta protein expression and it leads to induce oxidative stress. In the present study, PCB increases expression of beta amyloid protein in brain regions of rats. The present study has demonstrated that exogenous melatonin in both doses (5 mg/kg and 10 mg/kg) protects PCB (Aroclor 1254) induced oxidative stress and amyloid beta protein expression in selected brain regions.

In the present study, PCB also affects the membrane bound enzymes, creatine kinase and acetyl cholinesterase status by inducing reactive oxygen species. The exogenous melatonin protects the PCB induced changes, significantly. PCB affect the melatonin level in serum and in selected brain regions such as cerebellum, cerebral cortex and hippocampus. PCB exposure alters the neuronal morphology of all the selected brain regions and induce neuronal degeneration in all the three regions. Exogenous melatonin administration in both doses protects PCB induced changes.

It is concluded from the study, melatonin protects the PCB (Aroclor 1254) induced oxidative damage by decreasing the reactive oxygen species level in brain regions. Melatonin protects the free radicals induced alterations in membrane bound ATPases, creatine kinase and acetyl cholinesterase activities in the same. Melatonin, which possesses characteristics of an antioxidant, is the leading candidate for the prevention and treatment of neurological disorders.