Introduction
Polychlorinated biphenyl (PCB) families are persistent aromatic hydrocarbon pollutant in the environment and have diverse toxic effects in living organisms (Lloyd et al., 1975). PCBs built up in the environment and cause harmful health effects and also have extremely long half life and are strongly lipophilic. They have been used in a wide range for industrial purposes, including fire retardants, dielectrical fluids, capacitors, transformers, hydraulic fluids, paints, plasticides, gas turbines, television and air conditioners (Gray et al., 1993).

PCBs and their residues are detected in soil sediments, air, water and in variety of biota and food of animal origin (Fitzgerald, 1996) and also detected in placental cord blood (Yakushijii et al., 1978), breast milk (Frank et al., 1988), in human tissues (Calabrese, 1982) and seminal plasma (Kimbrough, 1995). The higher chlorinated PCBs are generally more resistant to biological decomposition and therefore, have a higher potential of bioaccumulation in the environment (Kamrin and Ringer, 1994).

PCBs are a group of synthetic organic chemicals that contain 209 possible individual chlorinated biphenyl compounds. These chemically related compounds are called congeners and vary in their chemical and physical properties and toxicity (see ATSDR, 1999). Toxic congeners of PCB carry between 5 and 10 chlorine atoms, mostly in the para and meta positions (Sylvestre, 1985). However, the congeners substituted at the 3, 4-orthopositions are considered the most toxic (Albro and Mckinney, 1981).

Due to their lipophilic nature, PCBs tend to accumulate in lipid rich tissues. Acute high level exposure of laboratory animals to PCBs have resulted in liver and kidney damage, neurological effects like loss of memory and learning, endocrine effects like reduced level of thyroid hormones are detected. After prolonged exposure to PCBs congeners like of 2,3,7,8-tetrachloro dibenzodioxin (TCDD),
non ortho mono and diorthochlorinated and as well as to the technical mixtures of PCBs ultimately leads to death (Zoellar et al., 2000). Neurobehavioral and developmental deficits occur in newborn and continue through school aged children who had *in utero* exposure to PCBs. Other systemic effects such as diabetes, thyroid cancer and immune system are associated with elevated serum levels of PCBs and increased cancer risks eg. Non Hodgkin’s lymphoma (see ATSDR, 1990). Sub acute and chronic exposure leads to variety of effects in animals occurring as a syndrome, progressive weight loss, alopecia, skin edema, swelling around the eyes, lymphoid and thymic involution, hepatomegally, bone marrow depression and reproductive dysfunction commonly occur together (Allen et al., 1973). Most of the systemic toxic and biological effects of PCBs are mediated by the Aryl hydrocarbon receptor (AhR) (Safe et al., 1998), as also indicated by loss of responsiveness of AhR knock-out mice to PCBs (Sugihara et al., 2001).

Numerous reports have shown that PCBs decrease dopamine levels (Seegal et al., 2002; Kang et al., 2004). PCB-induced cytotoxicities and dopamine reduction are mediated mainly by oxidative stress, impaired calcium homeostasis, by dopamine transporter (DAT)/ vesicular monoamine transporter (VMAT) inhibition and by cell death itself (Bemis and Seegal, 2004). Findings to date suggest that neuronal degeneration by PCB may be the result of dopamine homeostasis disruption through neurochemical and neurobiological processes. Kang et al., (2004) reported that Aroclor 1254 (commercial PCB mixture) causes cell death and that this is related to the depletion of stored calcium in an immortalized catecholaminergic cell-line and dopaminergic cell line (CATH, a cells).

The effect of PCBs exposure on neurochemical function in the brain have been extensively studied and regional changes in the brain neurotransmitters such
as norepinephrine (Seegal., 1985; Chu et al., 1996a), serotonin (Seegal et al., 1986; Chu et al., 1996b) and dopamine (Chu et al., 1996a; Seegal et al., 2002) have been reported. PCBs affect the uptake of neurotransmitters into synaptosomes (Mariussen and Fonnum, 2001) and cause inhibition of the vesicular monoamine transporter (VMAT₂) and DA transporter (DAT) (Mariussen and Fonnum, 2001; Bemis and Seegal, 2004). Furthermore, recent in vivo studies show that acute exposure to PCBs results in a decrease in the protein levels of DAT and VMAT₂ (Richardson and Miller, 2004). PCBs have been shown to impair serotonergic and other monoamine neurotransmitter systems in animal models as diverse as mammals, fish and clams (Khan and Thomas, 2001). PCBs are endocrine-disrupting chemicals (EDCs) in that they can bind to hormone (usually estrogen or androgen) receptors to either activate or inactivate them (Gore, 2001). The ability of PCBs to affect the estrogen receptor (ER) is generally related to their degree of chlorination, with more lightly chlorinated PCBs acting in an estrogenic manner, and those PCBs with higher (>48%) chlorination acting as weak estrogens or as ER antagonists (Kester et al., 2000).

In the reproductive system, PCBs can increase or decrease uterine weight, depending on the PCB and affect basal and gonadotropin-releasing hormone (GnRH)- induced gonadotropin release from the anterior pituitary gland (Khan and Thomas, 1997). In female rats, perinatal exposure to PCBs alters sexual behavior (Chung and Clemens, 1999). Neonatal PCBs can affect aromatase levels in the brain, the enzyme that is responsible for the conversion of testosterone to estradiol and plays a critical role in the development of gender-appropriate sexual behavior (Hany et al., 1999). Male rats exposed to PCBs have altered testis and other reproductive tissue weights, and decreased serum testosterone levels (Hany et al., 1999; Venkataraman et al., 2004a).
Studies using experimental animals indicate that exposure to PCB mixtures or congeners alter motor activity (Schantz et al., 1992), neurological development and cognitive function (Holene et al., 1995). Oxidative stress is believed mainly to be responsible for PCB-induced cytotoxicity and PCB mediated intracellular GSH depletion can alter normal antioxidant defense systems. PCB has been shown to generate transient reactive oxygen species (ROS) (Mariussen et al., 2002).

Oxidative modification of brain proteins may disturb neuronal functions by decreasing activities of key metabolic enzymes and affecting cellular signaling systems (Konorev et al., 1998). Organ specific enzymes are used in the assessment of tissue destruction in various disease states and Creatine kinase (CK, EC 2.7.3.2) is used as a reliable marker in the assessment of myocardial, muscular and cerebral damage. CKs are sensitive to oxidative damage and might be one of the targets for reactive oxygen species in the brain in neurodegenerative disease (Aksenov et al., 2000).

The cholinergic system plays a crucial role in cognitive function (Everitt and Robins, 1997), in which choline esterases are ubiquitous constituents. Acetylcholine (ACh) is a very important neurotransmitter for central nervous system (CNS) function. Its action is dependent on its metabolizing enzyme, acetylcholinesterase which was found to be involved in the release of ACh and to be co-released from the dopaminergic neurons (Klegeris et al., 1995). Moreover, Appleyard (1995), has reported that AChE induces long term potentiation in hippocampal pyramidal neurons, suggesting that AChE might enhance cognitive function. Additionally, there is some evidence in the literature showing that the activity of AchE inhibited by free radical formation (Tsakiris et al., 2000). Studies show that inhibition of AChE activity leads to accumulation of ACh, cholinergic hyperactivity, convulsions, and status epilepticus (Olney et al., 1986).
Many amyloid diseases are characterized by protein aggregations linked to oxidative stress. Such diseases including those of the brain, muscle, and blood vessels exhibit plaques containing β-amyloid (Aβ) (Misonou et al., 2000; Tamagno et al., 2008). Aβ is a 39-43 amino acid peptide produced by proteolytic cleavage of amyloid precursor protein (APP) at the amino terminus within the lipid bilayer by γ-secretase. APP is a ubiquitously expressed transmembrane glycoprotein.

Endogenous melatonin is involved in many physiological functions, among them sleep promotion, circadian regulation, modulation of immune responsiveness and control of reproductive activity in seasonally reproductive animals (Pandiperumal et al., 2006). In addition, pharmacological amounts of melatonin effectively reduces oxidative stress through a number of mechanisms (Reiter et al., 2007a). Melatonin possesses an electron-rich aromatic indole ring and functions as an electron donor, thereby reducing and repairing electrophilic radicals (Martinez et al., 2005).

The efficacy of melatonin in functioning in this capacity relates to its direct free radical scavenging actions, its ability to enchance the activities of antioxidant enzymes, its stimulatory actions on the synthesis of another important intracellular antioxidant, glutathione, its efficacy in reducing electron leakage from the mitochondrial electron transport chain, and its synergistic interactions with other antioxidants (Reiter et al., 2007a).

Hence, the present study was initiated to elucidate the impact of exogenous melatonin on PCB (Aroclor 1254) induced oxidative damage and its effects in cerebellum, cerebral cortex and hippocampus of adult male rat brain. This study may determine the clinical usefulness of melatonin against PCB induced modulation in brain free radical mechanism.