Thesis Title Behavioral and Neurobiochemical Effects of Chronic Exposure to Low Dose of Paraquat in Rats.

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ABSTRACT

The neurotoxic effects of chronic exposure to subcutaneous administration of low dose of paraquat on the motor behaviors and the alterations of the neurotrasmitter levels(dopamine, norepinephrine, 5-hydroxytryptamine and its metabolites, 5-hydroxy-indoleacetic acid) in various brain regions of male, Wistar rats were studied. Subcutaneous administration of paraquat 1, 2 and 3 mg/kg, 5 days per week for 8 weeks altered the total ambulatory and stereotypic activities in 20 minutes recorded by the open-field test. These alterations were dose- and time-dependent. There were no other obvious toxic effects of paraquat observed. The rotational behaviors were determined in the paraquat-treated groups as compare to control. It was found that there was no alteration in this motor

behavior. In addition, the levels of dopamine in both paraquat-treated and control were not significantly different. The chronic exposure to 3-mg/kg dose of paraquat results in the significant lower body weight, motor performance and the norepinephrine levels in the hypothalamus as compare to control. The less body weight in paraquat-treated group as compare to control group may be related to the decreases in norepinephrine levels in the hypothalamus, which was previously suggested to have some role in feeding control. Hypothalamus appeared to be the area, among various discrete brain areas, that paraquat can easily pass into the brain due to its insufficient blood-brain barrier.

The results of this study indicated that chronic exposure to paraquat can induce the neurotoxic effects with no detectable dopaminergic damage in the striatum, and there may be some noradrenergic system disturbance in the hypothalamus. The open-field test is one of the most sensitive method that can detect the adverse effects of paraquat at low doses. Further studies are needed to elucidate the specific sites and mechanisms of paraquat induced the decreases in motor behavioral activities.