Paraquat is Not a Direct Hepatotoxin at Low Level of Exposure

Varaporn Podprasart ** and Krongtong Yoovathaworn *

**Graduate Program in Toxicology and *Department of Pharmacology, Faculty of Science, Mahidol University, Bangkok 10400, Thailand

Abstract

Paraquat (PQ) is a well-known toxic herbicide widely used in agricultural countries. Though pulmonary toxicity is a main cause of death in patients after PQ exposure, many reports showed that PQ also causes liver damage and can be classified as a "direct hepatotoxicant". There were only few studies focusing on the toxicity of PQ on the liver after repeated exposure which mimics the human occupational exposure, or identifying the risk factors for PQ-induced hepatotoxicity. It is, therefore, interesting to investigate specifically on the PQ-induced liver damage after continuous exposure for a certain period of time. This study is established to examine the dose- and time-effect of PQ, in male *Wistar* rats, on the liver, by determining the change of liver enzyme markers including AST, ALT, AP, and also total bilirubin, total protein and albumin. Dose-response of PQ was studied in rats by subcutaneous injection of paraquat dichloride at the doses of 4.0, 5.0, and 6.0 mg/kg BW/d, 7 days. All PQ-treated rats had a significant decrease in BW, showed slow movement, and less response to the stimuli when compared with the untreated rats. All hepatic enzyme markers, total bilirubin, total protein, as well as albumin in the plasma obtained from the rats receiving PQ at these doses were not significantly different from the control group. PQ at the dose of 4.0 mg/kg/d was selected to determine the time-course of effect on the liver. The treated animals were sacrificed on days 3, 7, and 10 after PQ administration. The results obtained from this experiment were similar to the previous experiment. It may be concluded that repeated subcutaneous exposure to PQ at the doses up to 6.0 mg/kg/d for 7 days or 4.0 mg/kg/d up to 10 days did not cause either frank cytotoxic hepatic injury or disturb liver synthetic function even the highest dose used produced more than 50% mortality. These results are not in agreement with a number of previous studies, both in human and animal models that showed hepatotoxicity after exposure to PQ at high dose. However, the hexobarbital sleeping time in rats treated with PQ was significantly longer than that of the untreated animals. As hexobarbital sleeping time is one of the markers of drug- or xenobiotic-metabolizing enzyme activity, further study will explore the mechanism underlying the changes in the biological response to drugs in correlation with distribution of this pesticide.

Keywords: Paraquat, hepatotoxicant, liver function