Thesis Title THE SEARCH FOR THE EFFECTIVE PARAQUAT ANTIDOTE COMBINATIONS

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ABSTRACT

Paraquat toxicity had been studied by using the commercial product available in the market known as Gramoxone 27.6%. It was found that paraquat caused many pathophysiological changes probably due to the consequence of free radical (O^-_2) that was generated. Dose depended weight loss, increased haematocrit, and elevated blood glucose in serum were detected. It is interesting to observe that the paraquat treated animals would have poor prognosis, if their blood glucose levels were more than 260 mg% . There were also generalized inflammation, especially in brain, heart, lung, liver, and kidney. Attempts have been made to search for the effective paraquat antidote combinations. Fresh Aloe vera gel was used for the

anti-inflammatory purpose. In rats, fresh Aloe vera gel 1 cc/rat, following paraquat intraperitoneal administration for 2 hr., three times daily for 7 days can delay the percent death during 2^{nd} - 6^{th} days of experiments but on the 7^{th}day the percent death of animals was equal to that of control while in mice fresh Aloe vera gel 0.25 cc/mice followiing paraquat oral administration for 6 and 24 hr., twice daily for 7 days can decrease the percent death on day 7 from 60% to 26% and 60% to 33%, respectively. Ultracarbon was used for the prevention of paraquat absorption through the gastrointestinal tract. The maximum effective dose of Ultracarbon was found by varying doses and time intervals of administration following paraquat challenge. It was found that the maximum effective dose of Ultracarbon was 2500 mg/kg BW. of rats administered 30 minutes following paraquat oral administration. At this dose and time interval, Ultracarbon can reduce the percent death from 90% to 10%. Tricortin a phospholipid preparation extracted from bovine cerebral cortex combined with B12 was used to improve the repairment of the damaged cell . It was found that Tricortin at the dose of 645 mcg/kg BW., injected intramuscularly 24 hr. after paraquat oral administration, and it was given twice daily for 7 days can reduce the percent death both in rats and mice from

60% to 20% and 40% to 10%, respectively. In this study, drug combination has been evaluated by giving Ultracarbon 1200 mg/kg after paraquat administration for 0.5 hr followed by Tricortin injected after paraquat administration for 24 hr., every day for 7 days. It was found that at this treatment schedule the percent death can be reduced from 100% to 0%.The combination of fresh Aloe vera gel and Ultracarbon was less effective than using Ultracarbon alone. The results from this preliminary study suggested that the most effective treatment should be the combination of Ultracarbon with Tricortin, because when Ultracarbon or Tricortin was given alone, the reductions in percent death were 100% to 60%, and 100% to 80%, respectively. Though, Tricortin can reduce the mortality of paraquat treated animals, its mechanism of protective effect is not known, further studies are needed to elucidate its precise mechanism of action.