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27 July 76

EMETIC FORMULATION OF PARAQUAT

As promised, I enclose a summary of all the survival data we now have on dogs and monkeys.

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TOXICITY OF GRAMOXONE FORMULATED WITH PP 796

Monkeys

Experimental

Male cynomolgus monkeys (*Macaca fascicularis*), body weights in the range 3.5-5 kg, were used.

The paraquat dosing solution consisted of the appropriate volume of Gramoxone W diluted into a total volume of 20 ml and contained 10 g "Complan". To test the effect of PP 796, this was added to the dosing solution such that the animals received 2 mg/kg body weight. 8 monkeys were dosed with Gramoxone W and 8 with Gramoxone W plus PP 796.

Results

All 8 of the animals dosed with Gramoxone W died whilst only 2 out of 8 of the Gramoxone/PP 796 group died. The animals that survived all vomited in the first hour after dosing.

Dogs

Experimental

Male beagle dogs, body weights in the range 9-12 kg were used. Animals were dosed with diluted Gramoxone W and "Complan". PP 796 was added to test the effect of emesis at a dose level of approximately 3 mg/kg body weight. In experiment 1, the equivalent of 20 mg of paraquat cation/kg body weight was used in a total dosing volume of approximately 50 ml, containing 6 g "Complan". In experiment 2, the paraquat dose was increased to 30 mg of cation/kg body weight.

Results

Experiment 1: 3 out of 4 dogs dosed with Gramoxone W (20 mg PQ/kg) alone, died whereas none of the dogs dosed with Gramoxone W plus PP 796 died. All the surviving animals treated with the emetic formulation vomited within an hour of being dosed.

Experiment 2: 3 out of 4 dogs dosed with Gramoxone W (30 mg PQ/kg) alone died whereas none of the dogs dosed with Gramoxone W plus PP 796 died. All the surviving animals treated with the emetic formulation vomited within an hour of being dosed.

Summary

A dose of Gramoxone which normally kills 75-100% of a group of monkeys or dogs is not fatal when formulated with the emetic PP 796 such that vomiting occurs within the first hour of dosing.