82V0001

RABBITS

The model of doxorubicin cardiotoxicity caused rabbits to experience discomfort. Drugs that reduce the discomfort have been reported to interfere with the changes in molecular markers during the development of doxorubicin cardiotoxicity. Since we were testing doxorubicin cardiotoxicity, those drugs were not administered.

Species: Rabbit
affected: 6
Col. E

MICE

Injections of cisplatin and GPX-325 caused discomfort in the mice. Four days after the injections of cisplatin and GPX-325, blood was collected from the mice for measuring creatinine and blood urea nitrogen to identify the cisplatin induced nephrotoxicity and its reversal by GPX-325.

Compounds that might lessen the discomfort and pain may alter the effect of GPX-325. Therefore, these compounds were not injected.

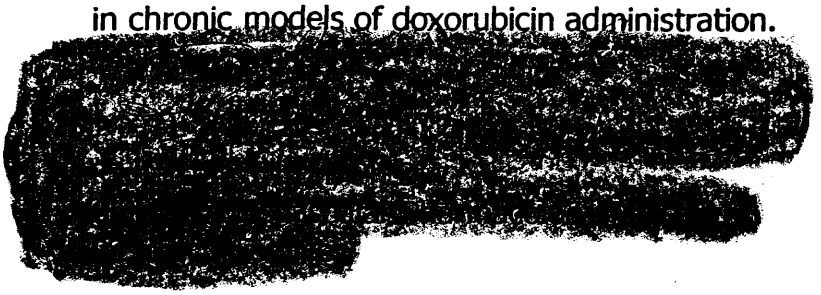
Species: Mice
affected: 126
Col. E

(b)(6)
(b)(7)(C)

October 25, 1999

82V0001

Our laboratory developed a chronic rabbit model of doxorubicin cardiotoxicity to investigate the mechanisms of cardiac lesions produced by doxorubicin. This entailed injecting 1 mg/kg doxorubicin i.v. twice/week for 8 consecutive weeks. In addition to development of cardiotoxicity, this chronic regimen of doxorubicin administration was associated with a variable (no change to moderate) amount weight loss and appetite suppression. Also, there was a transient hair loss in some rabbits that was reversible. There were no attempts to reverse the hair loss or appetite suppression. It is unclear whether anabolic steroids would prevent weight loss in doxorubicin treated rabbits. Anabolic steroids may, however, confound or mask analysis of cardiac lesions produced by doxorubicin and invalidate the study design. Other therapeutic possibilities such as vitamin B complex have unproven efficacy to prevent weight loss or appetite suppression in chronic models of doxorubicin administration.



(6)(6)
(6)(7)(C)

Species: NZW Rabbit

Number affected: 5 from column E and 10 from column B