injection, the solubilizer used and the handling of the animals, particularly after irradiation, were not involved in either the rate of mortality or the total mortality because if they had been, definite differences in both of these factors would have shown up in the pre- and post-irradiation methylglucamine groups. The non-irradiated control groups and the saline-methylglucamine and flavonoid injected control groups had no deaths during the experimental period or at any time thereafter up to 60 days. This indicates that the deaths obtained in the medicated irradiated groups were not due to the flavonoids themselves.

Discussion. The results herein reported concerning the ineffectiveness of parenterally administered rutin, hesperidin, hesperidin methyl chalcone, and naringin in modifying Roentgen ray irradiation mortality in guinea pigs confirm the observations of Dauer and Coon(10) who gave rutin, hesperidin methyl chalcone, and citrus vitamin P by the oral route. The results of previous investigators (2,4,7,10) as well as our own would definitely indicate that the flavonoids are incapable of modifying the radiation syndrome in mice, rats, guinea pigs, or dogs.

Summary. It has been shown that rutin, hesperidin, hesperidin methylchalcone, and naringin were ineffective in modifying Roentgen ray irradiation lethality in guinea pigs. There was an indication that post-irradiation medication with rutin may have increased the rate of mortality.

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Received October 15, 1952. P.S.E.B.M., 1952, v81.

Species Differences in Circulating 17-Hydroxycorticosteroid Concentrations.* (19980)

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Vogt(1) described a substance in adrenal vein plasma which protected adrenalectomized dogs from cold. Since then, bioassays of adrenal venous plasma have been accomplished by other workers(2,3) and various corticosteroids have been isolated from fresh adrenal tissue(4,5). By the use of recently developed qualitative and quantitative technics, considerable species differences in the steroid content of adrenal venous blood have been demonstrated. By paper-partition chromatography, Bush(6) found that the dog and cat secreted mainly 17-hydroxycorticosterone and some corticosterone; the ferret secreted both compounds in approximately equal amounts; the rat and rabbit produced mainly, if not

* This research was supported in part by a grant from the Helen Hay Whitney Foundation.

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TABLE I. 17-Hydroxycorticosteroid Plasma or Serum Concentrations in Various Species.

Species	No. of determinations	Mean, μg %	SE_M	Range
Rabbits	28	0	—	—
Rats	7	2.1	± .96	0 – 7.5
Guinea pigs	10	33.1	± 4.46	18.9–65.6
Humans:				
Children*	31	10	± 1.67	0 –26.8
Adults	13	10.9	± 1.73	3.1–21.6

* Data taken from reference 12.

entirely, corticosterone; the guinea pig mainly 17-hydroxycorticosterone but also corticosterone. 11-dehydrocorticosterone and 11-dehydro-17-hydroxycorticosterone. By chromatographic separation, large amounts of a steroid hormone identified as 17-hydroxycorticosterone have been isolated from the adrenal vein effluent of dogs(7) and smaller amounts from the adrenal venous blood of cows(8). By further refinement of this technic Nelson and Samuels(9) have developed a method for direct quantitation of circulating 17-hydroxycorticosteroids. In normal adult human subjects. they found 17-hydroxycorticosteroid concentrations of 4 to 10 μg per 100 ml of whole blood(10). Using the plasma method (9). which yields values approximately twice those of whole blood, Ely, Kelley, and Raile (11) found a mean value of 10 ± 1.67 μg per 100 ml of plasma in normal children.

In an attempt to find a laboratory animal suitable for 17-hydroxycorticosteroid studies. an investigation of the secretion of these hormones by various species was undertaken. In this report the circulating levels of these compounds in rabbits, rats, guinea pigs, and human subjects are compared.

Materials and methods. Male and female albino rabbits weighing approximately 2 kg, male Sprague-Dawley rats weighing 250 to 350 g. and male guinea pigs weighing 300 to 550 g were used. The human subjects employed were normal young adults. Approximately 30 ml blood samples were obtained from the marginal ear veins of the rabbits and allowed to clot at 4° C. The rats and guinea pigs were rapidly anesthetized in an ethyl ether atmosphere and blood samples were obtained from the abdominal aorta into heparinized syringes. Serum and plasma samples were separated by centrifugation and stored in deep-freeze until used. Where necessary, the plasma of 2 to 3 rats or guinea pigs were pooled to make 10 to 15 ml samples for the determinations. In addition to the control studies on rabbits, certain response tests were done. One group of rabbits was given a single intramuscular injection of ACTH in a dose of 1.5 mg per pound. Another group was given a single intramuscular injection of 10 mg of cortisone per animal. Blood samples were obtained 2 hours post-injection in the ACTH-treated group, and 2, 8, 24, and 72 hours post-injection in the cortisone-treated group. Circulating 17-hydroxycorticosteroid concentrations were estimated by the plasma method of Nelson and Samuels(9).

Observations. In Table I observations concerning circulating 17-hydroxycorticosteroids in the species studied are summarized. The serum of rabbits was found to contain no detectable amount of these steroids. Rat plasma yielded concentrations of 0 to 7.5 μg per 100 ml with a mean value of 2.1 ± 0.96. Guinea pig plasma contained from 18.9 to 65.6 μg per 100 ml, with a mean of 33.1 ± 4.46 μg per 100 ml of plasma. Plasma of normal adult human subjects had a mean concentration of 10.9 ± 1.73 μg per 100 ml with a range of 3.1 to 21.6 μg.

In Table II, the 17-hydroxycorticosteroid concentrations in rabbits following the injection of ACTH and cortisone are shown. Rabbits given ACTH, 1.5 mg per pound, intramuscularly, were found to have no measurable amounts of 17-hydroxycorticosteroids 2 hours after injection. Following the intramuscular injection of 10 mg of cortisone per animal, 17-hydroxycorticosteroid concentrations as high as 52 μg per 100 ml of plasma were found after 2 hours, with as much as 7.9 μg still detectable at the end of 24 hours. These con-

TABLE II. 17-Hydroxycorticosteroid Serum Levels in Rabbits Following Injection of ACTH and Cortisone.

Hr	No. of animals	Mean, μg %	SE_M	Range
Controls	28	0	—	—
After ACTH (1.5 mg/lb I.M.)				
2	9	0	—	—
After cortisone (10 mg I.M.)				
2	3	26.3	±11.2	11.1–52.8
8	3	11.3	± 1.5	7.3–14.3
24	3	5.3	± 1.7	1.2– 7.9
72	6	0	—	—

centrations returned to zero within 72 hours in all rabbits.

Discussion. The method used here measures all steroids with the 17-hydroxy-configuration, including 17-hydroxycorticosterone, 11-dehydro- 17 -hydroxy-corticosterone, and 11-desoxy- 17 -hydroxycorticosterone (Compounds F, E, and S, respectively), but apparently does not measure other corticosteroids. The finding of negligible amounts of these compounds in the blood of rats, and none in the blood of rabbits is in agreement with the data of Bush(6) obtained by paper-partition chromatography. The absence of circulating 17-hydroxycorticosteroids might be explained either by failure of their production by the adrenal cortex or by their rapid disappearance from the circulation. The injection of ACTH in rabbits failed to produce measurable amounts of 17-hydroxycorticosteroids in their blood. On the other hand the injection of cortisone produced high concentrations, which only slowly returned to zero. These responses suggest strongly that the absence of 17-hydroxycorticosteroids in these animals is to be explained by failure of secretion of these hormones by the adrenal cortex, rather than their rapid disappearance.

Since 17-hydroxycorticosteroids, as determined by this or other presently available methods, do not exist in significant amounts in the peripheral blood of rats or rabbits these animals cannot be used for studies of these steroids. Guinea pigs, however, appear to have amounts of these steroids readily measured by the method and thus are acceptable experimental animals for such studies.

Summary. 1. Quantitative determinations of 17-hydroxycorticosteroid concentrations in the peripheral blood of rabbits, rats, guinea pigs and human subjects were made. 2. Considerable species differences in these concentrations were noted. These differences appear to be quantitative as well as qualitative. 3. Of the species observed, the guinea pig appears to be the best experimental animal for studies of 17-hydroxycorticosteroids.

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Received October 17, 1952. P.S.E.B.M., 1952, v81.