

The content of the various fractions of 17-hydroxycorticosteroids in the urine of healthy monkeys (Macaca rhesus) was studied by adsorption chromatography in a thin layer of kieselguhr. Besides cortisol, which accounts for about 20-25% of the total quantity of metabolites determined, cortisone, tetrahydrocortisol, tetrahydrocortisone and, in some cases, 11-deoxycorticosterone, 17-hydroxy-11-deoxycorticosterone, and its tetrahydro metabolite, were found. Age differences in the character of cortisol metabolism were discovered in the monkeys.

KEY WORDS: cortisone; hormone metabolism; 17-hydroxycorticosteroids.

Monkeys are nowadays used increasingly for the production of experimental models of various forms of pathology. The literature on adrenal function in monkeys consists chiefly of information on the biosynthesis of corticosteroids and their levels in the blood and urine [2-4, 12-15]. Hormone metabolism, however, although largely determining their biological effectiveness, has not yet been adequately studied.

It was therefore decided to study glucocorticoid metabolism in Macaca rhesus, the species most frequently used experimentally.

EXPERIMENTAL METHOD

Eight sexually immature and six sexually mature monkeys weighing 2-4 and 6-8 kg respectively were used. Corticosteroids isolated from 24-h samples of urine collected from the animals were fractionated by adsorption chromatography in a thin layer of kieselguhr gF 254 [5, 11]. Preliminary experiments showed that optimal fractionation of the steroids takes place if they are applied to a kieselguhr layer 0.3 mm thick, which is then activated at 80°C for 30 min. The steroids were separated in a chloroform-methanol-water (93:6.5:0.5) system. The nature of the compounds isolated was identified from their chromatographic mobility, the Porter-Silber reaction, and the reaction with tetrazolium blue and choline.

EXPERIMENTAL RESULTS

As was shown previously [1, 10], the urine of healthy monkeys contains cortisol, cortisone, and their tetrahydro derivatives.

A chromatogram of steroids from extracts of the monkeys' urine is illustrated in Fig. 1. Tetrahydrocortisol (THF), tetrahydrocortisone (THE), cortisol (F), and cortisone (E) were clearly separated. These compounds were found in the urine of all the monkeys. Some animals also excreted 11-deoxycorticosterone, 17-hydroxy-11-deoxycorticosterone, and its tetrahydro derivative (THS) with their urine.

The content of cortisol and its metabolites in the urine of the sexually mature monkeys was higher than in the urine of the sexually immature animals (Table 1). These differences were due principally to the difference in weight of the animals, for when calculated per kg body weight closely similar values were obtained. The comparatively wide scatter of the individual values found in these investigations agrees with the reports in the literature of considerable fluctuations in the level of the total 17-hydroxycorticosteroids in the urine of monkeys [12, 14].

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TABLE 1. Daily Excretion of Cortisol and Its Metabolites (in μg) in Monkeys (*M. rhesus*) ($\bar{x} \pm \bar{Sx}$)

Monkeys	F	E	THF	THE	$\frac{F}{E+THE+THF}$
Sexually immature	$39,2 \pm 8,6$	$33,1 \pm 3,0$	$56,8 \pm 7,5$	$62,3 \pm 15,6$	0,25
Sexually mature	$77,4 \pm 4,7$	$103,9 \pm 8,7$	$129,1 \pm 7,6$	$154,1 \pm 10,7$	0,20

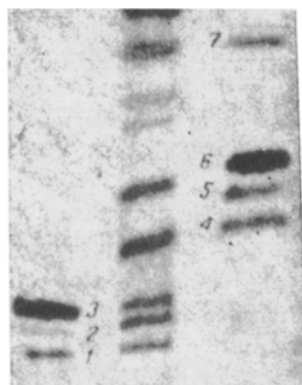


Fig. 1. Chromatogram of corticosteroids from the urine of healthy monkeys (*M. rhesus*). "Witnesses" of corticosteroids: 1) tetrahydrocortisol; 2) tetrahydrocortisone; 3) cortisol; 4) cortisone; 5) corticosteroid; 6) 17-hydroxy-11-deoxycorticosterone; 7) deoxycorticosterone.

Cortisol accounts for about 25% of the total content of its metabolites in the urine of sexually immature animals and about 20% in that of the sexually mature monkeys, whereas in adult human urine it does not exceed 10% [6-9]. This fact indicates that cortisol is metabolized to a lesser degree in monkeys.

To estimate the direction of the inactivation and metabolism of cortisol in the monkeys, coefficients reflecting the activity of dehydrogenation processes at the eleventh carbon atom of the steroid molecule and reduction of the A ring were calculated. The ratio $F/(E + THE)$, characterizing the degree of dehydrogenation of cortisol, was 0.41 in the immature and 0.3 in the mature monkeys. The ratio $(F + E)/(THF + FHE)$, characterizing the intensity of conversion of the hormones into biologically inactive tetrahydroderivatives, was 0.60 and 0.64, respectively. These results suggest that the activity of the dehydrogenase responsible for converting cortisol into cortisone is more closely linked with age than the activity of the reductase catalyzing the formation of tetrahydrocortisol and tetrahydrocortisone.

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