subcutaneous route are also given for comparison. It was found that there is a linear relationship between the fall of the Na^+/K^+ ratio and the logarithm of the dose of each corticoid administered by mouth in the following ranges: aldosterone 0·06–2·00 μg; Cl–F 0·05–10·00 μg. As expected the response obtained by the oral route for each comparable dose level was less than that obtained when the same steroid was given subcutaneously. From the regression lines tabulated in the Table, the dose of each steroid which produces a 50% effect on the Na^+/K^+ ratio has been calculated, this being for the oral route 0·68 μg of aldosterone and 0·59 μg of Cl–F, and for the subcutaneous route 0·089 μg and 0·20 μg respectively.

Aldosterone, when administered by subcutaneous route, is at least twice as potent as Cl–F, as judged by comparison of the calculated dose of each steroid which produces a 50% response. In this context it is of great interest that aldosterone is *less* effective than Cl–F when given by mouth (Table). These observations reinforce the hypothesis[8] that the increased activity of some halogenated steroids as compared with 'natural' hormones may result from a slower rate of metabolization by the liver.

The conclusions to be drawn from this experiment are: (a) the oral route, though not as sensitive as the subcutaneous, can be used for the bio-assay of aldosterone-like materials in the rat; and by inference, for the assessment of aldosterone antagonists; (b) aldosterone is less effective by mouth than Cl–F; (c) the relative potency on electrolyte-regulating activity of two or more different steroids tested by the subcutaneous route should not be used as an indication of their relative potency by the oral route.

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Résumé

On démontre que chez le rat, l'administration orale de l'aldostérone et substances similaires pour essai biologique est pratiquable et sûre, bien que moins sensible que l'administration parentérale. Par inférence, il est suggéré que cette méthode est utilisable pour l'évaluation des antagonistes de l'aldostérone.

A l'inverse de leur efficacité relative par voie parentérale, l'aldostérone est par voie orale moins actif chez le rat que l'acétate de 9α-chlorocortisol pour produire l'abaissement du rapport Na^+/K^+.

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The Effect of 17α-Ethyl-19-Nortestosterone on the Estrus Cycle

17α-Ethyl-19-nortestosterone (Nilevar®)[1] is reported to show a potent anabolic[2], progestational[3], and deciduomagenic[4] activity in rats, an anti-estrogenic effect in spayed estrogen-treated rats[5], to inhibit the pituitary gland in parabiotic rats[6], and to damage the reproductive process as evidenced by the inhibition of the ovulation in rabbits[4] and by the antifertility[4] effect in rats. In the course of our investigations on the possibly protective effects of this new synthetic hormone in adult female, ethionine-treated intact rats, we have observed that the estrus cycle was completely inhibited during the time of the intramuscular administration of 0·5 mg/kg body weight, a dose being highly anabolic, but not yet androgenic[7]. Since the animals had to be killed after 13, or 22 days respectively, it cannot be said whether or when the normal cycle would have been restored after the medication has been stopped. Testosterone propionate in corresponding non-adrogenic doses[8], i.e. 0·04 mg/kg body weight, did not inhibit the estrus cycle: Only 2 out of 16 animals had a prolonged anestrus for the first 12, or 13 days respectively. All control animals treated with the vehicle (sesame oil) alone, showed no change of their normal cycles. The estrus cycle-interrupting effect of 17α-ethyl-19-nortestosterone can be explained by the known inhibition of the pituitary gland[6] and/or by the antimetabolite effect on the estrogens[5] present in the intact animal. Further detailed studies are in progress.

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Zusammenfassung

Im Verlaufe unserer Untersuchungen mit 17α-Äthyl-19-nortestosteron (Nilevar) beobachteten wir, dass bei erwachsenen weiblichen, mit diesem neuen Hormon behandelten Ratten kein Östrus mehr auftrat, während Testosteronpropionat in entsprechenden, nicht androgenen Dosen den östrischen Zyklus nicht signifikant beeinflusste.

[1] Appreciation is expressed to Dr. V. A. Drill, of G. D. Searle & Co., Chicago, Ill., USA., for generous supplies of Nilevar®.

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