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Oral Effectiveness of Testosterone Propionate Plus Bile Acid.*

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(Introduced by A. C. Ivy.)

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Bile acids facilitate the absorption of cholesterol,[1] certain of the fat soluble vitamins,[2-4] and certain drugs[5-7] from the intestinal tract. The similarity in chemical structure between male sex hormones and some of these substances suggests that the administration of bile acids by mouth may enhance the oral activity of the male sex hormone. Such a procedure has been used in the human[8-10] and in the monkey.[11] The studies in the human were such that evaluation of the response to therapy was based largely on subjective factors. The evidence in the monkey was based on the fact that one monkey failed to show postcastration bleeding when treated with testosterone propionate and bile acids by mouth. The purpose of the present study, therefore, was to investigate this question by using a well-established assay method.

Testosterone propionate was the hormone used in the previously quoted reports, and also in this study. This substance is not particularly active by mouth when compared with methyl testosterone, however, it does possess slight oral potency.[12] Desoxycholic acid was the bile acid chosen for this study. This substance has been shown to be the most effective in promoting intestinal absorption of the above mentioned compounds.[1, 2, 6]

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1 Schoenheimer, R., *Biochem. Z.*, 1924, **147**, 258.

2 Greaves, J. D., and Schmidt, C. L. A., *J. Biol. Chem.*, 1933, **102**, 101.

3 Greaves, J. D., and Schmidt, C. L. A., PROC. SOC. EXP. BIOL. AND MED., 1937, **37**, 40.

4 Cohn, E. T., and Schmidt, C. L. A., PROC. SOC. EXP. BIOL. AND MED., 1939, **41**, 443.

5 Wieland, H., and Sorge, H., *Hoppe-Seyler's Z. f. Physiol. Chem.*, 1916, **97**, 1.

6 Kolda, J., *Compt. Rend. de la Soc. de Biol.*, 1926, **94**, 216.

7 Langecker, H., *Arch. du Exp. Pharm. and Path.*, 1928, **136**, 257.

8 Abarbanel, A. R., *Am. J. Ob. and Gyn.*, 1940, **39**, 243.

9 Silberman, E., Radman, H. M., and Abarbanel, A. R., *Am. J. Ob. and Gyn.*, 1940, **39**, 332.

10 Abarbanel, A. R., *Endocrinology*, 1940, **26**, 765.

11 Abarbanel, A. R., PROC. SOC. EXP. BIOL. AND MED., 1940, **44**, 452.

12 Miescher, K., and Tschopp, E., *Schwtz. Med. Wchnschr.*, 1938, **68**, 1258.

Male albino rats of 125-150 g in weight were castrated, and oral administration of the various substances was begun on the day after castration. The animals were divided into 4 groups: (1) those receiving 0.1 mg of testosterone propionate per day, (2) those receiving 0.1 mg of testosterone propionate plus 0.5 mg of desoxycholic acid per day, (3) those receiving 1.0 mg of testosterone propionate per day, and (4) those receiving 1.0 mg of testosterone propionate plus 0.5 mg of desoxycholic acid per day.

The oral administration of these substances was continued for 10 days. At the end of this period the animals were sacrificed, and the prostates and seminal vesicles were dissected out and weighed. In the earlier part of the study, 0.6 mg of the bile acid was given per day. However, the animals in this group lost considerable weight and so the dose was reduced to 0.5 mg per day.

It can be seen (Table I) that there is no significant difference

TABLE I.
Oral Effectiveness of Test. Prop. Plus Bile Acid.

Dose Test. Prop., mg/day	Dose bile acid, mg/day	No. Anim.	Avg wt Anim., g	Avg wt prostates, mg	Avg wt Sem. V., mg
0.1	None	8	155.2	20.5	41.4
0.1	0.5-0.6	8	130.1	21.4	37.2
1.0	None	9	144.5	42.2	46.3
1.0	0.5	8	144.1	41.2	45.5

between the weights of the prostates in the bile acid treated animals and those which received only testosterone propionate. It can also be seen that the response of the prostate is increased with the increase in dosage of the hormone. There is no great change in the seminal vesicle response, but these structures are known to be less responsive to androgens than the prostates. Therefore, it must be concluded from these data, that desoxycholic acid does not enhance the oral effectiveness of testosterone propionate in the rat. Gastrointestinal absorption is not necessarily the same in the rat as in the human or in the monkey. These results, therefore, do not necessarily apply to these latter animals. However, until more adequate data on the human or monkey is presented, these findings at least cast doubt on the clinical value of combining bile acids with testosterone propionate for oral administration.