Chapter - 8

EFFECTS OF ISOPROTERENOL ON HYDROXYSTEROID DEHYDROGENASES OF PREPUTIAL GLAND OF MALE RAT

Rat skin and sebaceous glands are known to metabolize steroids (Baillie et al., 1965; 1966; Muir et al., 1970). Several metabolites of steroids have been identified in sebaceous glands and its anologues such as preputial gland of rat (Bardin et al., 1970; Richardson and Axelrod, 1971; Hodgins and Hay, 1973; Sansone and Reisner, 1974) and in costovertebral glands of hamster (Takayasu and Adachi, 1972). Balogh (1966) and Muir et al. (1970) have reported on the histochemical localization of hydroxysteroid dehydrogenases in the preputial gland.

Histochemical localization and effects of castration on hydroxysteroid dehydrogenase activities of the preputial gland are reported in Chapter-3. Much has been said about the involvement of androgens in functional activities of the accessory glands of reproduction. Recent studies by Singhal et al. (1971) reported that c-AMP exhibits andromimetic effects. Isoproterenol, a β-adrenergic agent, is known to increase, c-AMP levels in accessory sex organs of rats

(Tsang and Singhal, 1976) and mice (Zepp and Thomas,1976; 1978). There are no reports on the effects of isoproterenol on preputial gland or any other sebaceous gland or its analogues. Since the gland is androgen dependent any change in the androgen metabolism of the gland will result in altered functional activity of the gland. The present study was carried out with a view to investigate the possible influence of isoproterenol on steroid metabolism of preputial glands of male rats.

MATERIALS AND METHODS

Male albino rats weighing 120-140 gms were used for the present investigation. Rats were divided into two groups : One group consisted of untreated rats as controls and Second group consisted of isoproterenol treated animals. Isoproterenol (25 mg/Kg body weight, i.p.) was injected twice a day for 10 days and the animals were sacrificed after 12 hours of last injection. Preputial glands were removed free of blood and other tissues and kept on a chuck of cryostat maintained at -20°C and 9 to 12 μ thick sections were cut. The sections were processed for histochemical demonstration of 17-β hydroxysteroid dehydrogenase (17β-HSDH) activity with testosterone as substrate (Kellogg and Glenner, 1960), 3β-hydroxysteroid dehydrogenase (3β-HSDH)

104

EXPLANATIONS FOR FIGURES

Figs.1 to 6 Photomicrographs of sections of the rat preputial gland showing histochemical localization of activities of hydroxysteroid dehydrogenases. 125X

Fig.1 17β-HSDH(T) activity in the section of the preputial gland obtained from normal rat.

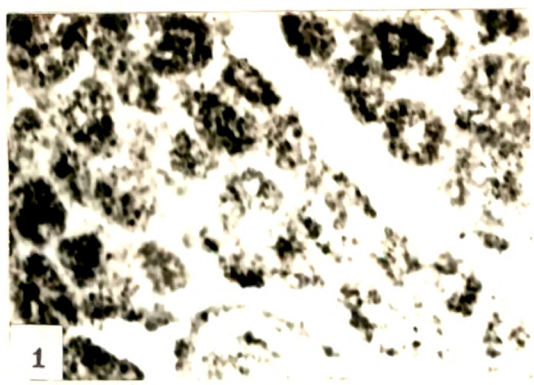
Fig.2 17β-HSDH(T) activity in the section of the preputial gland obtained from isoproterenol treated rat.

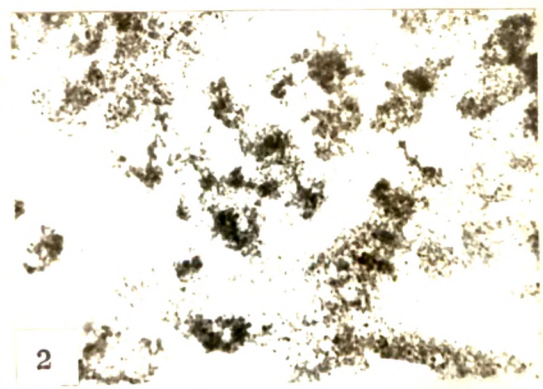
Fig.3 3β-HSDH(DHEA) activity in the section of the preputial gland obtained from normal rat.

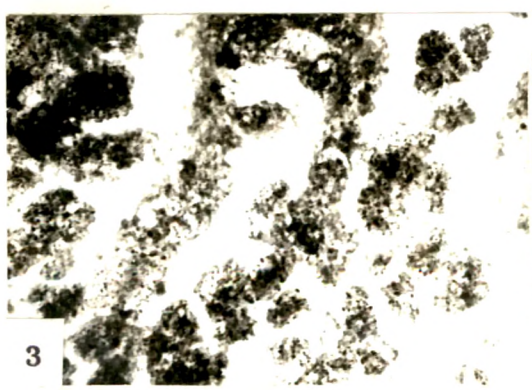
Fig.4 3β-HSDH (DHEA) activity in the section of the preputial gland obtained from isoproterenol treated rat.

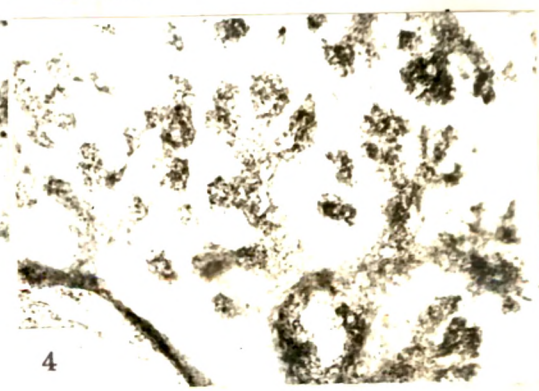
Fig.5 3α-HSDH activity in the section of the preputial gland obtained from normal rat.

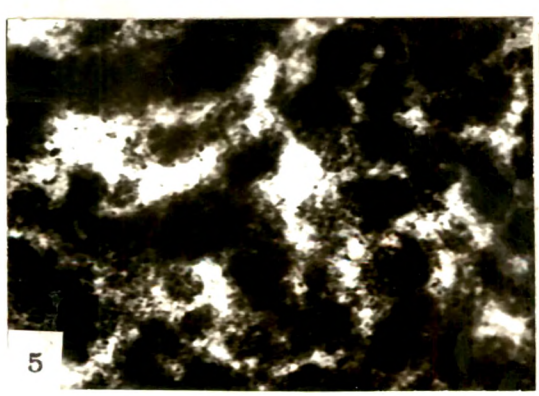
Fig.6 3α-HSDH activity in the section of the preputial gland obtained from isoproterenol treated rat.

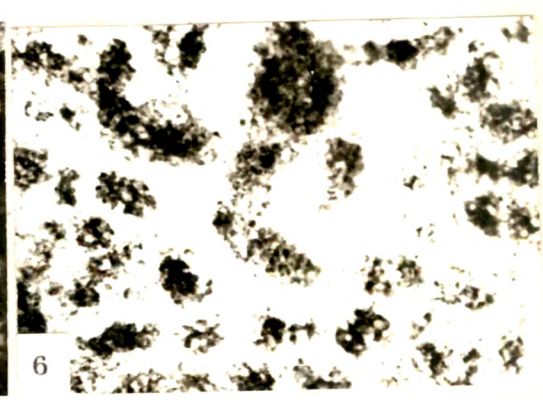

1


2


3


4


5


6

activity using dehydroepiandrosterone as substrate (Wattenberg, 1958) and 3α-hydroxysteroid dehydrogenase (3α-HSDH) activity using androsterone as substrate (Balogh, 1966).

RESULTS

As reported earlier in Chapter-3, the intensity of 3α-HSDH reactivity was found to be highest among the HSDHs studied. 3α-HSDH depicted centripetal localization, 17β -HSDH showed more activity in the peripheral cells and 3β-HSDH exhibited uniform distribution in the acini. Irrespective of distribution pattern the intensity of reactivities of these enzymes was in order of 3α-HSDH > 3β-HSDH > 17β-HSDH. Intraperitoneal administration of isoproterenol for 10 days resulted in decreased intensity of all the three steroid dehydrogenases to a considerable extent. (Figs. 1 to 6).

DISCUSSION

Hydroxysteroid dehydrogenases are important for interconversion of steroids. Gomez and Hsia (1968) have opined that an active catabolic pathway of steroid metabolism is likely to effect the hormonal microenvironment of a tissue. Moreover, hydroxysteroid dehydrogenases are also important in the conversion of hormonally inactive compounds

to more active ones. Activities of hydroxysteroid dehydrogenases in androgen target tissues depend on the circulating levels of androgens. It has been reported in Chapter-3 that castration led to reduction in the activities of hydroxysteroid dehydrogenases and that it was mainly due to non-availability of testosterone.

It has been reported that main product of dehydroepiandrosterone metabolism in the rat preputial gland is androstenedione, 17-oxosteroids and 17-β hydroxysteroids are being formed from testosterone and androstenedione respectively (Hodgins and Hay, 1973). Conversion of androstenedione to dehydroepiandrosterone is catalyzed by 3β--hydroxysteroid dehydrogenase and that of testosterone to oxosteroids by 17-β-hydroxysteroid dehydrogenase. Reduction in the activities of 17-β-HSDH, 3β-HSDH and 3α-HSDH reported here clearly indicated that isoproterenol treatment did not only influence the metabolic pathways of dehydroepiandrosterone and testosterone in the gland but also adversely affected the pathway of steroid catabolism leading to the formation of excretory products by reducing 3α-HSDH activity.

Isoproterenol, a β-adrenergic agent, is reported to increase hepatic microsomal hydroxylase activity (Gielen and Nebert, 1972). Drugs and steroids are hydroxylated by a

common enzyme system in rat liver microsomes (Conney et al., 1967; 1973). Liver is a principal site for steroid inactivation. Increased hepatic hydroxylase activity in turn would increase catabolism of steroids in liver. Increased rate of hydroxylation of testosterone would decrease the biological effectiveness of testosterone and circulating levels of testosterone. Isoproterenol and pesticides are reported to induce microsomal hydroxylase activity and catabolism of testosterone (Conney et al., 1973). Since hydroxysteroid dehydrogenase activity in the target tissue depends on the circulating level of testosterone, possible decreased circulating level of testosterone due to isoproterenol treatment might cause observed reduction in the activities of hydroxysteroid dehydrogenases in the preputial gland. This suggestion gets further support from the work of Levin et al. (1969), who have injected phenobarbital, a drug which also increases microsomal hydroxylase activity in immature rats, and reported that the drug inhibits the growth promoting effects of exogenously administered testosterone on the seminal vesicles. Fahim et al. (1970) have also found decreased weight and RNA content of male accessory sex organs after phenobarbital treatment. It has also been observed that isoproterenol treatment for ten days caused a tremendous reduction in the weight of the seminal vesicles

of rats (unpublished observations).

It seems that isoproterenol affects the microsomal hydroxylase system of the liver involved in testosterone catabolism and this in turn affects the gland. Alternatively, it is possible that isoproterenol might have some direct effect on the endogenous steroid metabolism of the gland by increasing the c-AMP concentrations in the gland. It is not possible, however at this stage, to determine the relative importance of the direct effect of isoproterenol (by increasing c-AMP conc.) on the gland.