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INFLUENCE OF CANNABIS AND DELTA-9-TETRAHYDROCANNABINOL ON THE BIOCHEMISTRY OF THE MALE REPRODUCTIVE ORGANS

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Abstract—Studies have been made on the effect of repeated subcutaneous administration of cannabis extract and delta-9-tetrahydrocannabinol on the fructose and citric acid contents of male reproductive organs of prepubertal as well as adult albino rats. Results indicate that both the fructose and the citric acid contents of the male reproductive organs are reduced significantly by cannabis. The reduction further appears to be dose-related to the amount of THC being administered, in case of both young and adult rats. Thus the study corroborates the previously reported antitestosteronic action of the drug.

There have been several reports indicating cannabis and its active component delta-9-tetrahydrocannabinol (delta-9-THC) to have a prominent action on the male reproductive system [1–3]. It has been reported to depress plasma testosterone levels and spermatogenesis [3, 4], along with a reduction in the weights of the accessory reproductive organs [4, 5]. Alterations in the testicular proteins and nucleic acids [6] with changes in spermatozoal biochemistry [7] have also been indicated. In the present work therefore, the effects of delta-9-THC and cannabis on the biochemistry of male gonads and accessory reproductive organs have been ascertained to indicate the action of the drug on the mechanism of sperm production and maintenance.

MATERIALS AND METHODS

1. *Animals and treatment*

The study has been done on two age groups of male animals *viz:*

(a) *Prepubertal rats.* Young male albino rats of Charles Foster strain weighing about 30 g were treated with cannabis extract or delta-9-THC for 10 consecutive days from day 11 to day 21 of age. The rats were maintained at 26 ± 1° and 12 hr of light and 12 hr of dark every day. Injections were given at 10.00 hrs every morning. The rats were sacrificed by instant decapitation 24 hr after the last injection. The treatment schedule was as follows:

Group I—Control (received vehicle only).
Group II—Delta-9-THC treated at a dose of 10 mg/kg body weight per day.
Group III—Delta-9-THC treated at a dose of 50 mg/kg body weight per day.
Group IV—Cannabis of known delta-9-THC content treated at a dose of 10 mg THC/kg body weight per day.
Group V—Cannabis of known delta-9-THC content treated at a dose of 50 mg THC/kg body weight per day.

(b) *Adult rats.* Adult male albino rats of Charles Foster strain weighing approx. 100–120 gm, obtained from the Laboratory animal house were used for the study. The rats were maintained at 26 ± 1° and 12 hr of light and 12 hr of dark each day. Delta-9-THC was injected subcutaneously for 10 consecutive days and the rats were killed by instant decapitation 24 hr after the last injection. The treatment schedule was as follows:

Group I—Control (received vehicle only).
Group II—Delta-9-THC treated at a dose of 10 mg/kg body weight per day.
Group III—Delta-9-THC treated at a dose of 25 mg/kg body weight per day.
Group IV—Delta-9-THC treated at a dose of 50 mg/kg body weight per day.

2. *Preparation of the drug*

Standard samples of cannabis (of known delta-9-THC content) and pure delta-9-THC were obtained from the United Nations Narcotics laboratory, Geneva. The cannabis was semipurified [8] in the laboratory and dried in a stream of nitrogen. Both the dried cannabis extract and the pure delta-9-THC samples were suspended in normal saline containing 6% Tween-80, and the suspensions were administered subcutaneously to the extent of 0.1 ml per rat. Control animals received equivalent volumes of saline Tween-80 vehicle for a similar period.

3. *Treatment of the tissue*

After instant decapitation of the animals the abdomen was opened up and the male reproductive organs were carefully dissected out. All adhering tissues were removed and they were placed immediately in crushed ice. Thereafter, the organs were weighed carefully on an electric balance to the nearest mg and used for the biochemical estimations.

Fructose content was estimated from whole tissues using the standard procedure of Roe *et al.* [9] and citric acid content was estimated according to the established method of Malherbe and Bone [10].

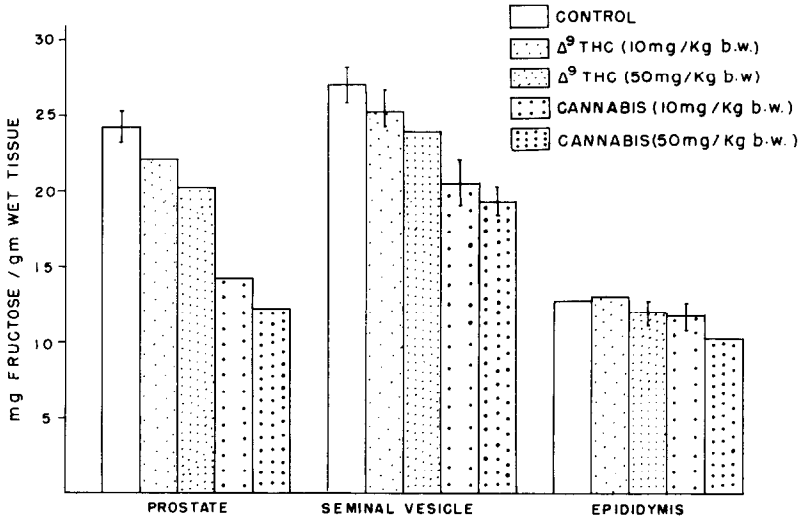

Fig. 1. Delta-9-THC and cannabis-induced changes on the fructose content of reproductive tissues in young male rats.

RESULTS AND DISCUSSION

Figure 1 indicates the changes in fructose content of prostate, seminal vesicle and epididymis on treatment with delta-9-THC and cannabis for a 10 day period in young, prepubertal rats. It is evident from the figure that there is a dose-dependent reduction in the fructose levels on treatment with delta-9-THC or cannabis. Cannabis extract containing an equivalent amount of delta-9-THC appears to be more effective than pure delta-9-THC, indicating that other cannabinoid components have a similar effect on the fructose level as well.

Figure 2, signifying the effect of delta-9-THC and cannabis on the citric acid contents of prostate, seminal vesicle and epididymis in young rats, also indicates a similar trend of results in the case of the first two organs. Epididymal citric acid content however, does not appear to be much affected.

Figure 3 shows the effect of pure delta-9-THC on the fructose level of the adult male reproductive organs after a period of treatment of ten consecutive days. It is evident from the study that there is a reduction in the fructose content of testis, epididymis and prostate which correlates directly with increasing dosage of delta-9-THC. Similar results are observed

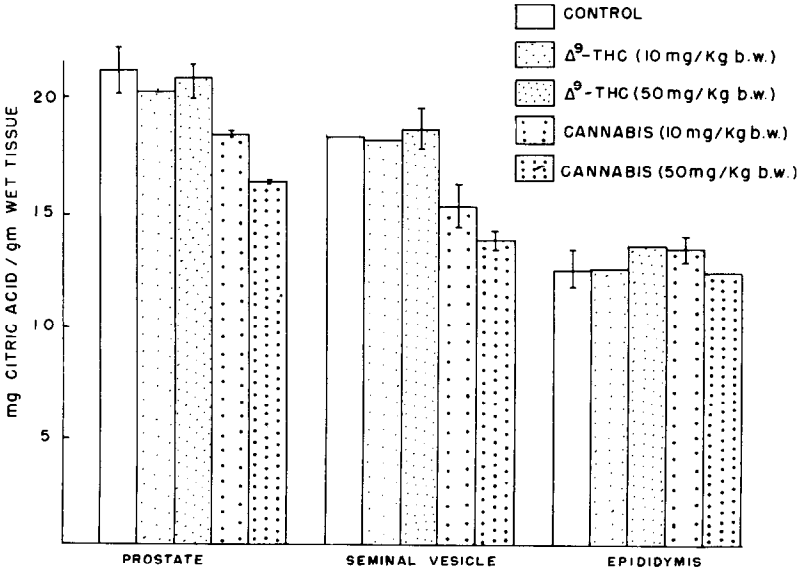

Fig. 2. Delta-9-THC and cannabis : role on citric acid contents in reproductive tissues of young male rats.

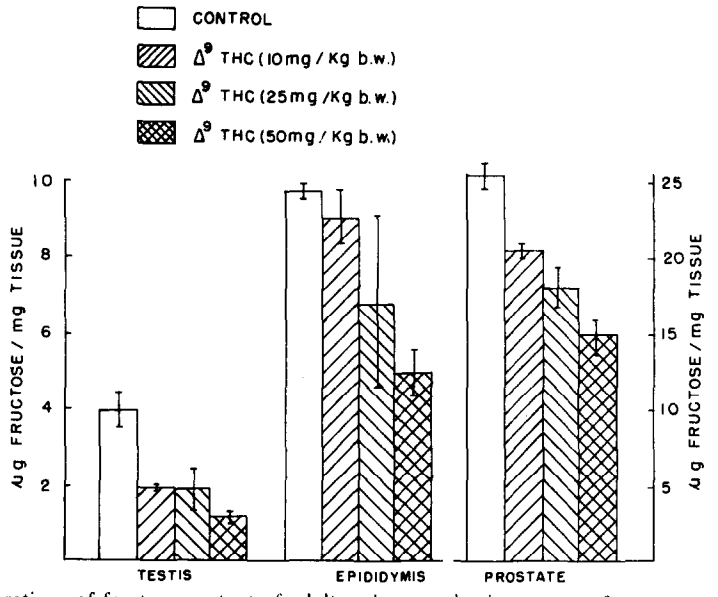

Fig. 3. Alterations of fructose content of adult male reproductive organs after treatment with delta-9-THC.

in the case of citric acid contents of epididymis and prostate (Fig. 4).

From the foregoing results it is evident that the two important gross biochemical components, *viz* fructose and citric acid, contents of male reproductive tissues in both prepubertal and adult male rats, are altered after treatment with THC. Fructose is an important indicator of male reproductive function as it is produced by the accessory glands, and found in abundance in the ejaculate. In rats the dorsolateral prostates are the main source of fructose [11]. Formation of fructose however, is hormone dependent. Testosterone stimulates the production and secretion of fructose [12] and this in turn is controlled by the circulating gonadotrophins [13]. Therefore, as delta-9-THC has already been reported to depress circu-

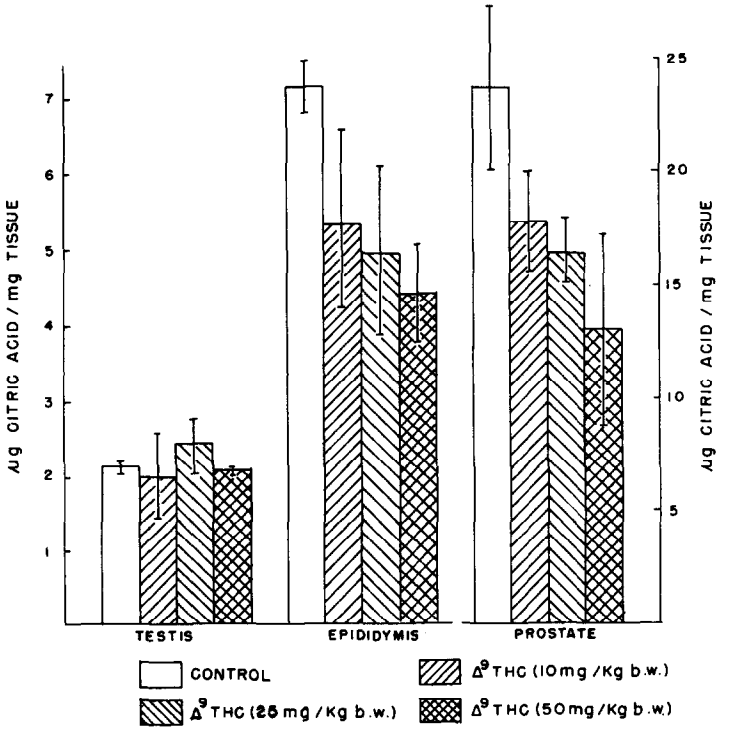

Fig. 4. Alteration of citric acid content of adult male reproductive organs after treatment with delta-9-THC.

lating testosterone levels [3, 4], the reduction of fructose content by the drug may be due to the change in the hormonal profile.

Citric acid is the other most important biochemical component of the male reproductive organ which has a direct correlation with the activity of the testicular hormones [14]. Castration or removal of the pituitary causes depletion of citric acid, which can be restored by administering testosterone or gonadotrophins [15]. Hence, in this case, delta-9-THC or cannabis induced depletion of citric acid levels may also be due to depressed testosterone levels in the serum [3, 4].

From the foregoing discussion, therefore, it may be inferred that cannabis as well as delta-9-THC appears to alter the biochemical milieu of the male reproductive system similarly as it does in the case of the female reproductive system [16–20]. This may subsequently lead to malfunctioning at the level of sperm production, maturation or transport.

REFERENCES

1. M. E. Corcoran, Z. Amit, C. W. Malsbury, and S. Daykin, *Res. Commun. Chem. Pathol. Pharmacol.* **7**, 779 (1974).
2. J. Harclerode, S. E. Nyquist, B. Nazar and D. Lowe, in *Advances in the Biosciences*, Volumes 22 and 23, p. 395 Marihuana: Biological effects. Eds. G. G. Nahas and D. M. Paton. Pergamon Press (1978).
3. R. C. Kolodny, W. H. Masters, R. M. Kolodner and G. Toro, *N. Engl. J. Med.* **290**, 872 (1974).
4. H. F. S. Huang, G. G. Nahas and W. C. Hembree, *Fed. Proc.* **37**, 739 (1978).
5. V. P. Dixit, V. N. Sharma and N. K. Lohiya, *Eur. J. Pharmacol,* **26**, 111 (1974).
6. A. Jakubovic and P. L. Mcgeer, in *Marihuana Chemistry, Biochemistry and Cellular Effects*, pp. 223, Ed. G. G. Nahas. Springer Verlag. (1976).
7. I. Chakravarty, G. Shah, A. R. Sheth and J. J. Ghosh, *J. Biosci.* **1**, 289 (1979).
8. J. W. Fairbairn and J. A. Liebmann, *J. Pharm. Pharmac.* **25**, 150 (1973).
9. J. H. Roe, *J. biol. Chem.* **107**, 15 (1934).
10. H. W. Malherbe and A. D. Bone, *Biochem. J.* **45**, 377 (1949).
11. G. F. Humphery and T. Mann, *Biochem. J.* **44**, 97 (1949).
12. T. Mann and U. Parsons, *Nature, Lond.* **160**, 294 (1947).
13. D. Price, T. Mann and C. Lutwak-Mann, *Anat. Rec.* **122**, 363 (1955).
14. G. F. Humphery and T. Mann, *Biochem. J.* **44**, 97 (1949).
15. T. Mann and U. Parsons, *Biochem. J.* **46**, 440 (1950).
16. I. Chakravarty, D. Sengupta, P. Bhattacharya and J. J. Ghosh, *Biochem. Pharmacol.* **25**, 377 (1976).
17. I. Chakravarty and J. J. Ghosh, *Biochem. Pharmacol.* **26**, 859 (1977).
18. I. Chakravarty, D. Sengupta, P. Bhattacharya and J. J. Ghosh, *Toxicol. Appl. Pharmacol.* **34**, 513 (1975).
19. G. I. Fijimoto, A. B. Kostellow, R. Rosenbaum, G. A. Morrill and E. Bloch, in *Advances in the Biosciences*, Volumes **22** and **23**. Marihuana: Biological effects. (Eds. G. G. Nahas and D. M. Paton) pp. 441, Pergamon Press (1978).
20. I. Chakravarty, P. G. Shah, A. R. Sheth and J. J. Ghosh, *J. Reprod. Fertil.* **57**, 113 (1979).