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Effect of Phthalic Acid Esters on Gonadal Function in Male Rats

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Phthalic acid esters are widely used as plasticizers in the manufacture of a variety of plastic products. Di-(2-ethylhexyl)phthalate (DEHP), one of the most used plasticizers, is known to be widely distributed in the environment having been detected in various forms of marine life (MAYER et al. 1972), soil sample (OGNER et al. 1970), and in both animal (NAZIR et al. 1971) and human tissue (JAEGER and RUBIN 1972).

Although DEHP has been found to exhibit a extremely low order of acute toxicity in rodent species (AUTIAN 1973), the administration of DEHP to rats has been shown to result in testicular atrophy (SHAFFER et al. 1945, OISHI and HIRAGA 1975, GRAY et al. 1977, FUKUHARA and TAKABATAKE 1977). In addition, SINGH et al. (1974) demonstrated that the high dose of DEHP produced a distinct reduction of fertility in male mice.

This communication presents the result of investigation undertaken in the contex of a target organ study on the hormonal changes produced in the rat testis following DEHP treatment.

MATERIALS AND METHODS

DEHP used was the guaranteed reagent of Tokyo Kasei Co., Ltd. (Tokyo). Male Wistar rats weighing 330-420g, were purchased from CLEA JAPAN Co. (Tokyo). The rats were housed individually in air-controlled room (temperature, 23-25°C; relative humidity, 50-60%) and supplied stock diet and water ad libitum. DEHP (1.25 g/kg/day) or olive oil (control) was injected intraperitoneally into rat for 5 days. Both DEHP-injected and control rats were divided into two groups following 24 hr of last injection: group A, testicular venous blood was collected by the method of OHSAWA (1970) under pentobarbital anesthesia (Nembutal; Abott Laboratories, IL., ca. 30 mg/kg ip); group B, 100 I.U.

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of human chorionic gonadotropin (hCG), Teikoku Zoki Co. (Tokyo), was injected intravenously into rat and testicular venous blood was collected following 15 min of hCG administration under pentobarbital anesthesia. Testicular venous plasma was separated with centrifugation and testosterone concentration was measured fluorometrically (OHSAWA et al. 1970).

RESULTS AND DISCUSSION

Table 1 shows the concentration of testosterone in testicular venous plasma and testosterone secretion in response to hCG stimulation. Testosterone concentration was significantly lower than that of control and its secretion following hCG stimulation was also lower. The administration of 100 I.U. of hCG made maximum stimulation within 15 min in rats (OISHI et al. 1974), and so the administrated dose of hCG in present experiment was sufficiently. HCG has a interstitial cell stimulating hormone-like action, and administration of hCG activates cholesterol side-chain cleavage enzyme and stimulates the synthesis of pregnenolone from cholesterol (FORCHIELLI et al. 1969). DEHP, therefore, might inhibit the biosynthetic process of testosterone from cholesterol rather than that of cholesterol from acetate.

The decrease of testosterone secretion after DEHP administration might result in the reduction of testis weight and fertility. The investigation of these possibilities must be the subject of future research.

TABLE 1
Effect of DEHP on testosterone concentration in testicular venous plasma, and its secretion following hCG stimulation.

	Control	DEHP
Resting state	0.41±0.04(10)	0.29±0.04(9)*
hCG stimulation	1.36±0.15(7)	0.96±0.09(10)*

The results are expressed as μg/ml and the mean±S.E. for the numbers in parentheses. *$p<0.05$.

REFERENCES

AUTIAN, J.: Environ. Health Perspect. 4, 3 (1973).

FORCHIELLI, E., K. M. J. MENSON and R. I. DORFMAN: The Gonads (Ed., K. W. MCKERNS). Amsterdam: North-Holland Publishing Co. 1969.

FUKUHARA and TAKABATAKE: J. Toxicol. Sci. 2, 11 (1977).

GRAY, T. J. B., K. R. BUTTERWORTH, I. F. GRAUNT, P. GRASSO and S.D. GANGOLLI: Fd. Cosmet. Toxicol. 15,389 (1977).

JAEGER, R. J. and R. J. RUBIN: New Engl. J. Med. 287, 1114 (1972).

MAYER, F. L. JR., D. L. STALLING and J. L. JOHNSON: Nature 238, 411 (1972).

NAZIR, D. J., A. P. ALCARAZ, B. A. BIERL, M. BEROZA and P. P. NAZIR: Biochemistry 10, 4228 (1971).

OGNER, G. and M. SCHNITZER: Science 170, 317 (1970).

OHSAWA, N.: Folia Endocrinol. Jap. 46, 645 (1970).

OHSAWA, N., K. KAGEYAMA, and H. IBAYASHI: Excerpta Medica 210, 102 (1970).

OISHI, S., K. KAGEYAMA and N. OHSAWA: Folia Endocrinol. Jap. 50, 146 (1974).

OISHI, S. and K. HIRAGA: Ann. Rep. Tokyo Metr. Res. P. H.: 26-2, 131 (1974).

SHAFFER, C. B., C. P. CARPENTER and H. F. SMYTH: J. Ind. Hyg. Toxicol. 29, 35 (1945).