

Effect of Butylparaben on Ovarian Weight of C3H Albino Mice

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ABSTRACT

Butylparaben is a widely used compound as a preservative in many pharmaceuticals and personal care products (PPCP). The high rate of human exposure to this chemical has been of growing concern as it is found to exhibit estrogenic activity in many *in vivo* and *in vitro* studies. Studies have shown that butylparaben exhibits reproductive toxicity affecting organs like uterus, ovary, testis and mammary glands. *In vivo* effect of butylparaben on ovarian weight has mostly been studied in CD1 and CF1 mice. It is found in many experimental studies that there are strain differences in sensitivity of rodents to different endocrine disrupting substances including butylparaben. In this experiment sensitivity of butylparaben exposure on ovary of C3H albino mice was studied considering change in ovarian weight of C3H albino mice taking 5 different doses of Butylparaben of 10 mg/Kg body weight/day, 50 mg/Kg body weight/day, 100 mg/Kg body weight/day, 500 mg/Kg body weight/day, 1000 mg/Kg body weight/day. The C3H albino mice were grouped as vehicle control (olive oil), positive control (estradiol) and the above five different doses of Butylparaben and were administered the doses for 7 consecutive days through subcutaneous route of administration. After the short term exposure of 7 days, butylparaben was found to exert a dose dependent change on ovarian weight of C3H albino mice.

Keywords: Butylparaben, estrogenic activity, pharmaceuticals and personal care products, ovarian weight

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INTRODUCTION

Environment is found to contain wide variety of both naturally occurring and synthetic chemicals which shows estrogenic activity. Butylparaben has been widely used as a preservative in many PPCP for a long time for its good antimicrobial activity, good pH and heat stability [1- 3]. It is regulated by the U.S. FDA as a synthetic flavouring and adjuvant [6]. Butylparaben is present in widely used cosmetics like various facial products because of which its dermal absorption into the human body occurs and also in various medications which leads to its entry into the human body through inhalation and ingestion [2, 5]. However in recent years there has been increasing concern over the wide use of butylparaben as it is found to exhibit estrogenic activity in many experimental systems including both in *in vivo* and *in vitro* system along with

reproductive toxicity [4, 7, 8, 10]. It is found to influence growth, differentiation and function of reproductive system [4].

The two ovaries are the major reproductive organs of the female body and concerned not only with production of female gamete but also serves the function of production of reproductive hormones like estrogen, progesterone which affect many other organs like mammary gland, uterus. Exposure to endocrine disruptors like butylparaben is found to show adverse effect on ovary and other related organs which are under the influence of ovarian hormones [3-4].

MATERIALS AND METHODS**Animals and Housing:**

Female albino mice of C3H strain were selected from Animal house facility of department of zoology, Gauhati University

and the animals were housed in wire mesh plastic cages with solid bottom containing saw dust and maintained under uniform condition of natural photoperiod (12 hr light/dark cycle), relative humidity(75%-87%) and temperature (30±2°C). The mice had free access to water and commercially available animal diet, vitamins and mineral supplement (purchased from Agrivet Farm Care Division, Glaxo Smithkline, Chennai, India) and were fed ad libitum.

Estrous cycle was observed everyday by microscopic examination of vaginal smear. Only mice showing four consecutive cycles were considered for the experiment.

Preparation of doses of Butylparaben:

Butylparaben (Sigma Aldrich) was prepared in doses of 10 mg/Kg body weight, 50 mg/Kg body weight, 100 mg/Kg body weight, 500 mg/Kg body weight, 1000 mg/Kg body weight. Due to solubility constraint

butylparaben was first dissolved in ethanol and then in olive oil. 500ng of estradiol was prepared by dissolving estradiol first in ethanol than in olive oil.

Experiment design:

Female albino mice of 8 weeks of age group and of average body weight 25±2g were selected for the experiment. The mice were divided into 7 groups (n=6) and were administered with 20µl olive oil (vehicle control group), 500ng estradiol (positive control group) and 5 doses of butylparaben of 10 mg/Kg body weight, 50 mg/Kg body weight, 100 mg/Kg body weight, 500 mg/Kg body weight, 1000 mg/Kg body weight daily through subcutaneous route of administration.

After 24 hrs of last dose the mice were weighed and sacrificed by cervical dislocation under mild anaesthesia (diethyl ether).

RESULTS

Table 1: Showing effect of butylparaben on ovarian weight of C3H MICE (P<0.001).

Sc = subcutaneous.

Compound	Dose (mg/kg bw)	Route of administration	Ovarian weighed (in mg)
Oil	20 µl (per animal)	Sc	16 ± 0.44
E ₂	500 ng	Sc	29.4 ± 1.32
BuPben	10	Sc	10.6 ± 0.927
BuPben	50	Sc	20 ± 1.788
BuPben	100	Sc	11.6 ± 1.63
BuPben	500	Sc	9.4 ± 1.077
BuPben	1000	Sc	21.6 ± 2.15

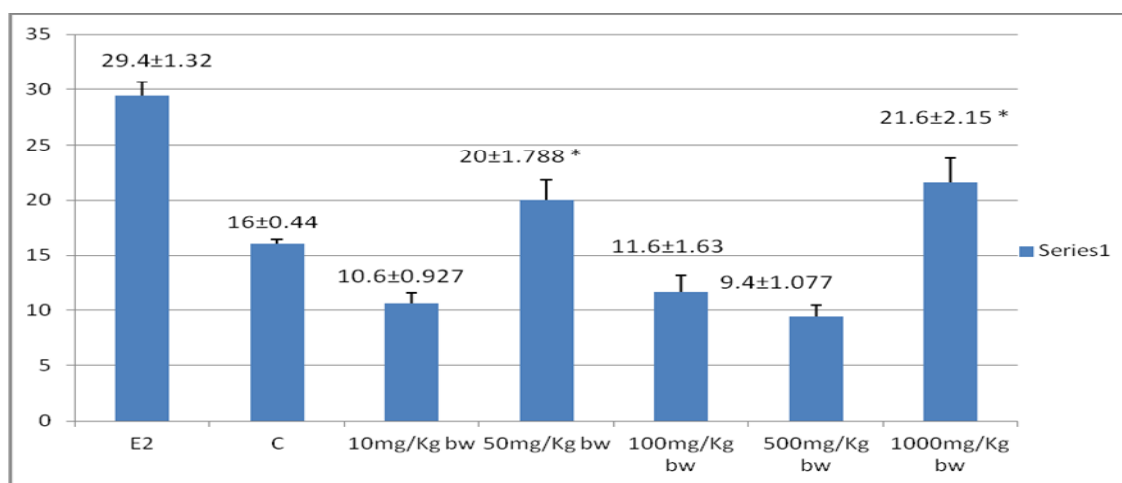


Figure 1: Butylparaben is found to Show Dose Dependent Change in Ovarian Weight of C3H Mice even though Potency lowers than Estradiol (P<0.001%).

The treatment of C3H albino mice with estradiol and five different dose level of butylparaben for 7 consecutive days showed significant change in ovarian weight compared to vehicle control. The estradiol treated group showed significant increase in ovarian (29.4 ± 1.32 mg) (p < 0.001) compared to vehicle control group in which 20µl olive oil was administered per animal per day (16±0.44 mg). However different doses of butylparaben showed a dose dependent effect on ovarian weight. 50 mg/kg body weight and 1000 mg/kg body weight showed a significant increase in ovarian weight (p < 0.1 and p < 0.05 respectively). 10 mg/kg body weight, 100 mg/kg body weight and 500 mg/kg body weight showed a decrease in ovarian weight compared with control. Results are shown in (Table 1 & Figure1).

DISCUSSION

The data obtained shows a significant difference in the sensitivity of ovary of C3H albino mice to butylparaben compared to CD1 and CF1 mice, thus showing a great intra specific variation [1- 4, 9]. Significant increase in ovarian weight of C3H albino mice at doses 50 mg/kg body weight and 1000 mg/kg body weight compared to control explains the effect of butylparaben on ovary. However when all the doses of butylparaben are compared (10 mg/Kg body weight, 50 mg/Kg body weight, 100 mg/Kg body weight, 500 mg/Kg body weight, 1000 mg/Kg body weight) to control it is found that butylparaben shows a dose dependent effect on ovary of C3H albino mice as decrease in ovarian weight is recorded in 10 mg/kg body weight, 100 mg/kg body weight and 500 mg/kg body weight.

Since butylparaben is a widely used compound and is found to affect reproductive organs so wide used of it is a matter of concern.

CONCLUSION

Butylparaben has been reported to have adverse effect in male reproductive system in rodents [2-4]. Adverse effect on the reproductive tract of female in rodents has also been reported but the effects are found to be shown in different doses in different strain of mice showing sensitivity differences [2-4]. However the data here

confirms the adverse effect of butylparaben considering significant ovarian weight gain in C3H mice at different dose level of butylparaben. Many people are still unaware of health and environmental concern that related to the wide use of the compound. Even though this compound is found to show low estrogenic activity but the broad use and long term use of this compound has drawn attention of the scientific community to analyze the effects of the compound.

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