Research Article

Effect of Low Dose of Butylparaben on Liver Weight of Ovariectomised C3H Albino Mice

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ABSTRACT

Butylparaben is widely used in man's daily used products like pharmaceuticals, cosmetics and foodstuff as a preservative for having good anti microbial activity. In many in vivo experimental studies in CD1 and CF1 mice, butylparaben elicit toxic effect in various organs including liver, thyroid, kidney, spleen, reproductive organs. However, the effects of butylparaben on organs showed strain differences in sensitivity. In this experiment, effect of low dose of butylparaben on weight of liver was studied in C3H albino mice. For the experiment three doses of butylparaben of 10 mg/Kg body weight/day, 50 mg/Kg body weight/day and 100 mg/Kg body weight/day was considered. The ovariectomised C3H albino mice were grouped as vehicle control (olive oil), positive control (estradiol) and the above three doses of butylparaben and were administered with the doses for seven consecutive days through subcutaneous route of administration. After the short-term exposure of seven consecutive days, butylparaben was found to exert a dose dependent change in liver weight of ovariectomised C3H albino mice. Positive control (estradiol) showed a significant increase in liver weight ($p<0.01$) compared to as vehicle control (olive oil).10 mg/Kg body weight/day and 100 mg/Kg body weight/day showed a significant increase in liver weight ($p<0.01$) compared to as vehicle control (olive oil). However, 50 mg/Kg body weight/day showed a non-significant decrease in liver weight compared to as vehicle control (olive oil).

Keywords: Anti microbial, Butylparaben, estradiol, liver weight

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INTRODUCTION

Estrogen contributes to the development of secondary sex characteristics, which are the defining differences between men and women that do not relate to the reproductive system. Environmental estrogens are natural or synthetic chemicals that mimic enhance or inhibit endogenous hormones [1, 3]. There has been increasing concern over the widespread exposure of human to many natural and synthetic chemicals having potential to disrupt endocrine system in man by acting estrogenic or androgenic [1, 4]. Of all the parabens, butylparaben shows stronger estrogenic response but its potency is 10,000 fold times less potent than 17β estradiol, a natural estrogen produced in the body. However, this wide use of the compound has been of concern to the scientific community as many experimental studies involving both in vivo and in vitro studies have shown that these compounds are estrogenic [2, 5] . The alkyl esters of p-hydoxybenzoic acid known as parabens includes a group of compounds of which methylparaben, ethylparaben, propylparaben and butylparaben are widely used as preservative in many daily used products of human including pharmaceuticals and personal care products, food stuffs and in products for children [2, 6]. This compound enters into human body through inhalation, ingestion and dermal absorption. Butylparaben has been of concern as its presence has been found in breast tumour tissue. Even though butylparaben is found to be weakly estrogenic (10,000 fold times less potent

than 17β estradiol) but long term human exposure to this compound is a matter of concern [7, 8].

Materials and methods:

Animals and Housing:

For the experiment female albino mice of C3H strain were selected from Animal house facility of department of zoology, Gauhati University (Animal ethical clearance number: 902/AC/05/CPCSEA). 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 consider 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, and 100 mg/Kg body weight. Due to solubility constraint, butylparaben was first dissolved in ethanol and than in olive oil.

Preparation of 17β estradiol:

Due to solubility constraint, 500 ng of estradiol was prepared by dissolving estradiol first in ethanol than in olive oil.

Experiment design:

The mice were subjected to complete bilateral ovariectomy following the method used by Kalita et al., (1998). Ovariectomy leads to removal of the major source of estrogen hormone in the blood and thus the estrogen sensitive tissue in the body remains in there basal state. After bilateral ovariectomy the mice are allowed to recover for 12 days.

Administration of dose: Female mice of 8 weeks of age group and of average body weight 25 ± 2 g were selected for the experiment.

The ovariectomised mice were grouped into three groups (n=6) and were administered with 20 µl olive oil (vehicle control group), 500ng estradiol (positive control group) and 3 doses of butylparaben of 10 mg/Kg body weight, 50 mg/Kg body weight, 100 mg/Kg body weight daily.

After 24 hrs of last dose the mice were weighed and sacrificed by cervical dislocation under mild anesthesia (di ethylether) and liver was collected, cleared of fats and vascular tissue, if any and weighed.

RESULTS AND DISCUSSION

Table 1: Showing Effect OF Butylparaben on liver weight of C3H Mice

Compound	Dose(mg/kg bw)	Route	Liver weight (in mg)
Oil	20 µl (per animal)	Sc	1.342± 0.0106
E_2	500 ng	Sc	1.781± 0.160*
BuPben	10	Sc	1.536± 0.0391*
BuPben	50	Sc	1.276± 0.067
BuPben	100	Sc	1.526± 0.048*

*** indicates significance at p<0.01 compared to olive oil (vehicle control group). Sc = subcutaneous**

The treatment of ovariectomised adult C3H mice with estradiol and three different dose level of butylparaben for seven consecutive doses showed change in liver weight. The estradiol treated group showed significant increase in liver weight of 1.781±0.160 mg (p<0.01) compared to vehicle control group (olive oil) of 1.342 ± 0.0106 mg. 10 mg/Kg body weight/day and 100 mg/Kg body weight/day showed a significant increase in liver weight (p<0.01) compared to as vehicle control (olive oil) of 1.536 ± 0.0391

mg and 1.526 ± 0.048 mg. However, 50 mg/Kg body weight/day showed a non significant decrease in liver weight compared to as vehicle control (olive oil) of 1.276 ± 0.067 mg.

Results are shown in **Table 1** and **Figure1.**

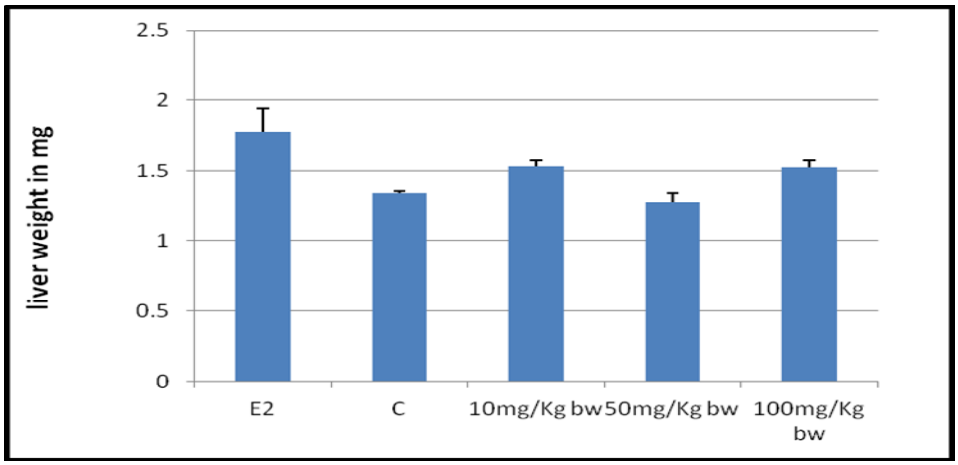

Fig 1: Butylparaben is found to show dose dependent change in liver weight of C3H mice even though potency lowers than estradiol (p<0.01%).

Butylparaben have been of recent concern because of its existence in low concentration in breast tumour [8]. In many experimental studies including both *in vivo* and *in vitro* studies butylparaben is found to mimic estrogen activity, thereby acting as potential xenoestrogen [4, 9]. Studies show that butylparaben exerts reproductive, developmental as well as terratogenic toxicity in experimental animals [4].

CONCLUSION

Increase in liver weight of C3H albino mice at doses 10 mg/kg body weight and 100 mg/kg body weight compared to control explains the effect of butylparaben on liver. However when all the doses of butylparaben are compared (10 mg/Kg body weight, 50 mg/Kg body weight, 100 mg/Kg body weight) to control it is found that butylparaben shows a dose dependent effect in liver weight of C3H albino mice as decrease in liver weight is recorded in 50 mg/kg body weight.

Even though this preservative to which human is widely exposed possess low estrogenic activity, the broad used of it by human is a matter of concern. Thus, the safety of the wide use of chemical should be reassessed.

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