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**Short Communication**

# Foetotoxic effect of potassium chromate ($K_2CrO_4$) in Swiss albino mice

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**Abstract**

The embryotoxic and teratogenic potential of potassium chromate was evaluated by the teratological analysis of mouse foetuses. The test chemical was administered intraperitoneally to laboratory-bred Swiss albino mice of both sexes for 30 days. Teratological scanning of the foetuses born to treated animals revealed a reduction in the number of live implants and litter size. Higher incidence of resorption and dead litter indicated the embryotoxic effect of the test chemical. Malformations, both skeletal and morphological, suggest the possibility of potassium chromate($K_2CrO_4$) being foetotoxic.

**Keywords:** Carcinogen, embryocidal, ossified foetuses, prenatal death.

## 1. Introduction

The growing awareness that chemicals existing in human environment cause deleterious heritable changes has provided an impetus to explore the impact of environmental chemicals on human health, especially with respect to genetic and foetal damage. The use of chromium and its compounds in tanning industry has for many years raised questions about their impact on foetal development and infant health. Changes in the birth weight, sex and death ratio, infertility rates, morphological and skeletal abnormalities may be the indirect indications of the adverse effects of these compounds.

Epidemiological studies have implicated potassium chromate as an important inorganic environmental carcinogen (PSRMC[1]). Hexavalent chromium salts were reported to induce mutations and cancer in man[2]. Because of the importance of potassium chromate as an important industrial chemical, extensive studies have been carried out to explore the genetic toxicity induced by this chemical in various *in vivo* and *in vitro* test systems[3].

These salts are reported to be more effective in inhibiting hatching of the blastocyst from the zona pellucida and formation of the inner cell mass[4]. Preimplantation of embryos represents a suitable system to test the toxicity of these chemicals. The metabolic capability of embryo changes considerably during the differentiation process before implantation and its sensitivity may thus vary at different morphological stages[5]. However,

the possibility that potassium chromate is foetotoxic is by no means clear and hence the present research was undertaken with a view to understand and unravel the embryotoxic effect of potassium chromate on mice (*Mus musculus*).

## 2. Materials and methods

Potassium chromate (AR–99.5% pure with very minimum ash content–mol.wt 194.20), obtained from S.D. Fine Chemicals Ltd was used as the test chemical. The chemical solution for exposure was prepared by dissolving 1.25 $\mu$g of the compound in 1 ml of distilled water for a single dose per animal (.0064 $\mu$mol).

### 2.1. *Experimental design*

Thirty 2–3 month-old virgin Swiss albino mice (15 males and 15 females), weighing 25 ± 5 g, were injected intraperitoneally for 30 days with 1 ml of the test chemical at a dose of 50 $\mu$g /kg body weight. The experiments were carried out at controlled temperature (25° C) under hygienic conditions. Pelleted diet was obtained from M/s Lipton India Ltd, Calcutta, and water was provided *ad libidum*. The experiments were designed to treat the male mice and mate them with untreated female animals. One set of female mice were treated and mated with untreated male mice. Another set of treated males were mated with treated female mice. A parallel set of animals were maintained as distilled water controls. The day of observation of vaginal plug was designated as day one

**Table I**

**Teratological assessment of litter born to treated and untreated animals with a single dose of $K_2CrO_4$**

| *Mode of treatment*[pf] | *Dose* $\mu$g/kg (b.w.) | *No. of litter examined* | *Sex ratio (F/100 M)* | *Body weight (g) ($\bar{X}$ ± SD)* | *Head length (cm) ($\bar{X}$ ± SD)* | *Head width (cm) ($\bar{X}$ ± SD)* | *Body length (cm) ($\bar{X}$ ± SD)* | *Tail length (cm) ($\bar{X}$ ± SD)* | *Hind limb length (cm) ($\bar{X}$ ± SD)* | *Fore limb length (cm) ($\bar{X}$ ± SD)* |
|---|---|---|---|---|---|---|---|---|---|---|
| Control d.w. (30 nos) | — | 51 | 95.83 | 1.76 ± 0.06 | 1.30 ± 0.13 | 1.07 ± 0.09 | 2.76 ± 0.28 | 1.58 ± 0.20 | 1.21 ± 0.15 | 1.30 ± 0.21 |
| Males treated (15 nos) | 50 | 32 | 88.23* | 1.36 ± 1.02* | 1.21 ± 0.12* | 1.00 ± 0.03* | 2.42 ± 0.25* | 0.97 ± 0.05* | 0.99 ± 0.06* | 0.99 ± 0.07* |
| Females treated (15 nos) | 50 | 54 | 52.94* | 1.31 ± 0.05* | 1.13 ± 0.10* | 1.06 ± 0.13* | 2.36 ± 0.19* | 1.09 ± 0.12* | 0.92 ± 0.16* | 0.93 ± 0.12* |
| Males & Females treated (30 nos) | 50 | 49 | 73.07* | 1.23 ± 0.55* | 1.03 ± 0.15* | 0.85 ± 0.10* | 2.23 ± 0.21* | 0.94 ± 0.12* | 0.97 ± 0.11* | 0.97 ± 0.10* |

Period of treatment: 30 days, d.w.: distilled water, b.w.: body weight.

pf: pre-fertilization, sd: standard deviation, $\bar{X}$: Mean.

Statistically significant from the control * $P < 0.01$.

of pregnancy. These animals were sacrificed on the 20th day of pregnancy and about 50% of the foetuses were teratologically analyzed as per the procedures of Wilson *et al.*[6], and Gupta *et al.*[7] Parameters like the number of offsprings per pregnant animal, number of resorbed sites and dead implants, sex ratio of the offspring, birth weight, morphological measurements of the foetuses, skeletal abnormalities like fusion of ribs, stunted ribs, overlapping of rib bones, and forked ribs were analyzed. Morphological malformations like ossified foetuses, absence of digits in the limbs, and stunted limbs were also screened. The skeletal abnormalities were scanned following the modified Alizarin Red Stain technique[8]. Statistical significance was evaluated by using students' t-test[9].

## 3. Results

The results on the foetotoxic effect of potassium chromate are summarized in Tables I and II. There was a significant departure from 1:1 sex ratio among the foetuses born to treated animals ($P < 0.01$). The reduction in the foetal weight and morphological measurements revealed growth retardation *in utero* (Table II). The length of the head in litter was reduced significantly in all foetuses born to treated animals as compared to control group ($P < 0.01$). Also, it was observed that the head width reduced significantly in foetuses born to treated males mated with untreated female mice($1.00 \pm 0$ .003 cm). The mean values on the body length of the litter was observed to be significantly reduced in the litter born to treated and untreated group of animals. The tail length of the litter born to untreated females mated with treated males showed a significant reduction ($0.97 \pm 0.05$) ($P < 0.01$). However, a similar trend of results was observed in all treated groups. A statistical significance in the mean values of the length of hind and fore limbs ($P < 0.01$) was observed in the litter born to treated group of animals.

A high resorption rate was found in the untreated female mice mated with male mice (16.25%). Incidence of skeletal abnormalities like missing, stunted, fused, widely spaced, and fractured ribs was observed in the foetus born to treated animals (Fig.1). However, the morphological abnormalities were observed again in the litter born to treated female mice mated with untreated males (Table II).

**Table II**
**Details of physical and skeletal abnormalities observed in litter born to $K_2CrO_4$-treated animals**

| *Parameters* | | *Pre-fertilization treatment (30 days)* | | |
|---|---|---|---|---|
| | *Control d.w.* | *Males treated* | *Females treated* | *Males and females* |
| Total litter examined | 51 | 32 | 54 | 49 |
| Resorption (%) | — | 16.25 | 3.70 | 3.92 |
| Dead litter (%) | — | — | 14.28 | 8.16 |
| Skeletal abnormalities (%) | — | 15.62 | 16.66 | 8.16 |
| Physical abnormalities (%) | — | — | 3.70* | — |

Skeletal abnormalities observed : Fusion and overlapping of ribs, and forked ribs.

* Ossified litter, stunted forelimb.

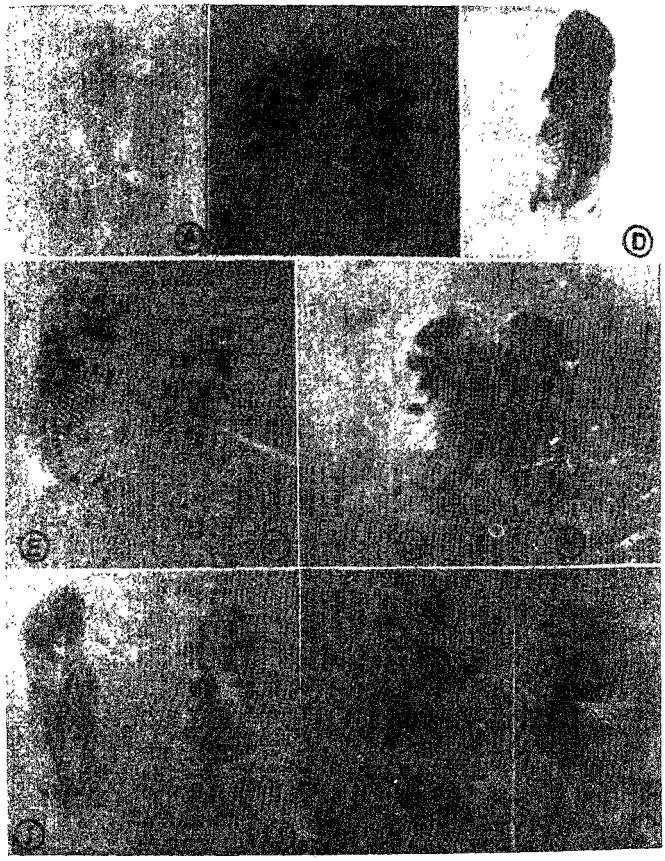

FIG 1 Skeletal abnormalities observed in the foetus born to treated animals. A. Foetus with normal skeletal system ( control ). B Absence of 9th rib—failure of development of rib joint; C A foetus showing widely spaced 7th and 9th ribs (floating ribs); D: Stunted 13th rib on either side of the vertebral column; E: Stunted 13th rib on one side of the vertebral column; F: Foetus showing stunted 13th rib; 8th rib is fractured, absence of 7th rib. failure of development of rib joints; G Foetus showing stunted 13th and bent 10th ribs; H: Foetus showing stunted 1st rib and the presence of fused 12th and 13th ribs; I and J. Foetus with 13th rib missing; K & L: Foetuses showing widely spaced ribs ; (8th to 10th)

## 4. Discussion

The results of the present observation are in agreement with the frequency of cell survival and multiplication affected by the hexavalent chromium salts in cultured mammalian cells[10–11]. The above findings reveal the anti-implantation activity and the embryotoxic potential of potassium chromate. This is similar to the reports of Leonard *et al.*[12] who observed such changes in mice treated with potassium chromate.

Experiments show that metal compounds like nickel chloride are powerfully foetotoxic to chick[13] and rat embryos by inducing prenatal death and foetal abnormalities[14]. Abrin and phytolectin have also been reported to induce teratological effect in mouse foetuses[15]. It has been established that the hexavalent chromium gets transformed into trivalent chromium after entering the cells of cultured mouse embryos and accumulates in the nuclear fractions of the cell where it may inhibit nucleoside uptake[16–19] or other metabolic events. Our results also demonstrate that potassium chromate is teratogenic in mice foetuses. Therefore, it is presumptuous to conclude that the effects observed in this study after pre- and post-fertilization treatment of mice with potassium chromate would be only the consequence of a clastogenic action. The study forms the basis for further research work on the foetotoxic effects of potassium chromate and similar compounds.

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