90 Day Dermal Toxicity of DDVP in Male Rats

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DDVP (O,O-dimethyl 2,2-dichlorovinyl phosphate) has been known as a versatile insecticide. It is being used as a contact and systemic insecticide due to its penetrant and volatile properties (ANONYMOUS, 1968). It has been used against a variety of pests in agriculture, in household and public health programmes and also in the disinfestation of aircrafts (WITTER, 1960; RASMUSSEN et al.,1963; STEIN et al. 1966; DURHAM et al., 1959). The most common and important route of exposure during spray operation and in accidental spillage of pesticides is skin. DDVP is quickly absorbed by the skin and also by other routes. The rate of absorption by skin is greatly influenced by hot and humid weather as in the tropical countries. Since skin irritations are rare, cases of accidental poisoning by percutaneous absorption frequently remain unnoticed.

Extensive studies have been made by GILLETT et al., (1972) to evaluate the possible human health hazards by DDVP resin strips. They observed that DDVP did not induce developmental effects, mutagenicity, teratogenicity and carcinogenicity, at sublethal dosages. In contrast, reports of LOFROTH (1970) and KRAUSE and HOMOLA (1974) have shown that DDVP induces cellular changes. The rationale for the present study is, therefore, to inquire whether prolonged percutaneous absorption of DDVP has any effect on the male gonadal system, besides skin. Male gonad in mammals is a complex system having both endocrine and exocrine functions (a source for both testosterone and gamete formation). Since testis has a variety of cells which are extremely sensitive to changes in its environment, we considered it interesting to report here our findings on the action of DDVP on the skin and testis of rat.

EXPERIMENTAL

Material: DDVP (96.3% purity) was obtained from M/s CIBA (India).

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Animals and treatment

Sixty colony bred male albino rats of Industrial Toxicology Research Centre's colony (150 ± 10 g) were used. The animals were housed under conventional conditions and were maintained on ad libitum pellet diet and water during the present studies. The animals were divided into two groups of 48 (Group I-experimental) and 12 (Group II-control) respectively. The hair on the lateroabdominal area of approximately 4 x 4 cm of all animals were clipped off by animal grooming clipper ("OSTER" model 5) and cleaned with ethanol-acetone(1:1) mixture.

DDVP (21.4 mg/kg) in 0.5 ml ethanol (50%)or 0.5 ml ethanol alone was later applied slowly on the specified area by means of 1 ml graduated pipette fitted to a vaqu-pette. Animals of group I and group II were treated daily, 5 days a week, for 13 weeks. 48 animals of group I were killed (8 each) at intervals of 7, 15, 30, 45, 60 and 90 days; two animals each were similarly killed from group II. Skin and testes were fixed in Bouin's fluid. After routine processing the tissues were embeded in paraffin. Sections were cut at 6 μ thickness and stained in haematoxylin and eosin for histopathological examination.

RESULTS

Gross pathology

During autopsy gross pathological examination was carried out on all animals. Except for the spontaneous death of 4 animals on day 5 of the serial painting, none of the animals showed symptoms of insecticide poisoning nor died. Macroscopic examination of skin throughout the 90 day study did not show anysign of dermatitis or other skin lesions.

Microscopic study

Microscopic examination of DDVP treated rat skin, did not show any pathological changes. However, certain cellular changes were more marked in the epidermis of the DDVP treated rat skin in comparison to those of control animals after 90 days. But for the vacuolization of epidermal cells and thinning of the epidermis there were no noticeable histopathological damage due to DDVP in any of the animals (Figs. 1,2).

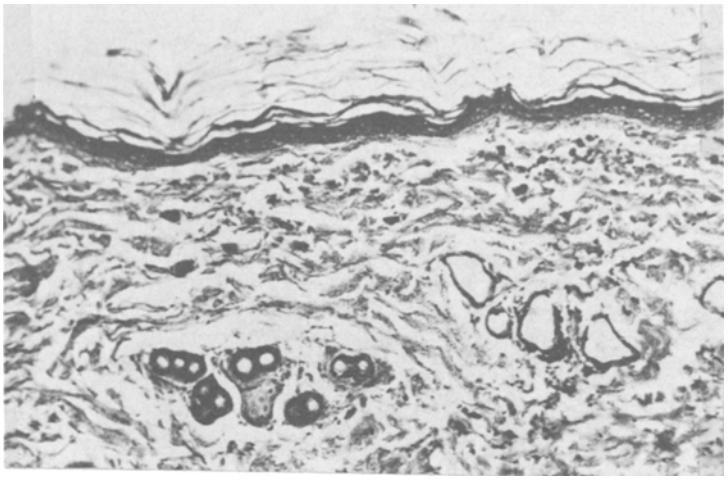

Fig. 1. Section of rat skin (control) showing normal histology. HE X 170.

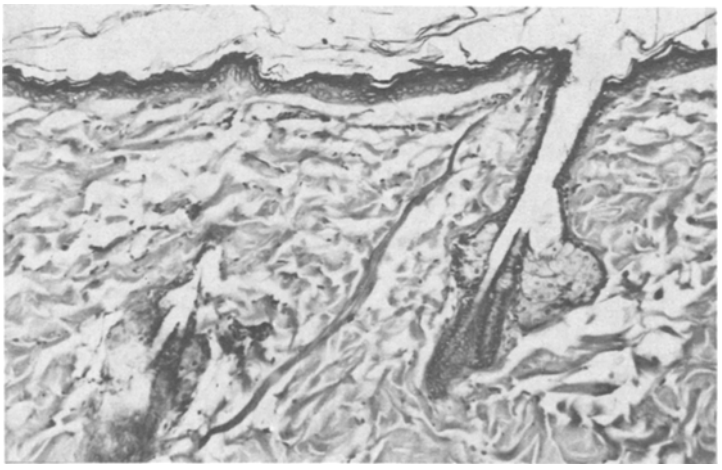

Fig. 2. Section of rat skin after 90 days of dermal painting with DDVP (21.4 mg/kg) HE X 170.

Histological study of the testis did not present any consistent damage. While the testis of two rats which had died after 5 paintings of DDVP showed complete necrosis of the majority of the seminiferous tubules, there was no such testicular damage in the remaining animals or in the subsequent exposures upto 90 days.

Of the 44 animals only 8 rats have shown necrosis (Figs. 3 and 4).

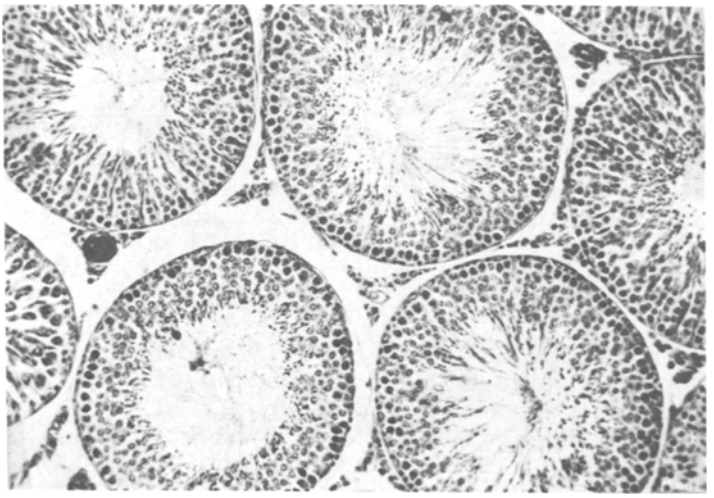

Fig. 3. Section of rat testis (control) showing normal seminiferous tubules. HE X 170.

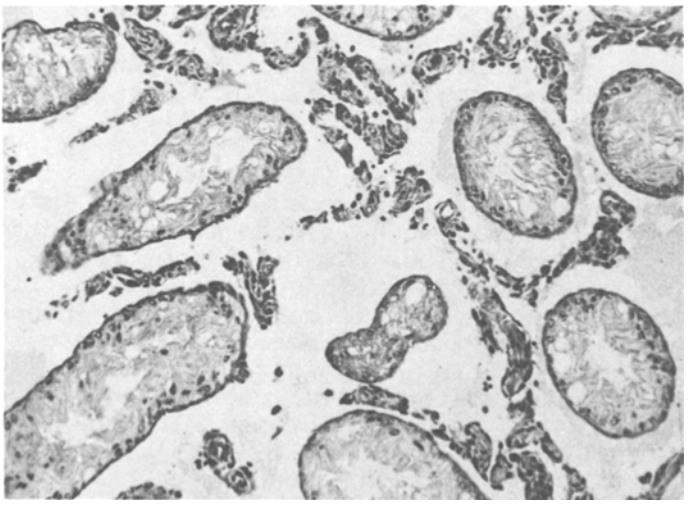

Fig. 4. Section of a rat testis showing tubular degeneration and enlargement of the interstitium. HE X 170

Presence of necrotic seminiferous tubules in one animals of control group, killed on day 45, suggests the intrinsic factor of animal variation in toxicity studies.

Discussion

It has become clear from the present study that DDVP seems to have little effect on skin and testis of the male rats exposed for a period of 90 days through dermal painting. Studies of BLAIR *et al.* (1975) have shown that mice and rats exposed to DDVP through atmospheric inhalation accumulated different concentrations of the insecticide in various organs. While the testis of mice accumulated 0.15 to 0.31 µg/g of DDVP the same in rat testis was much below 0.01 µg/g. Reports on the histopathological changes are, however, not available.

Long term feeding studies of DDVP on breeding rabbits, rats and swine have indicated no effects on reproduction or development (SINGH *et al.*, 1968; JACOBS, 1968; BATTE *et al.*, 1969; WITHERUP *et al.*,1971). KIMBROUGH and GAINES (1968) and VOGIN and CARSON (1971) also reported that DDVP have no teratogenic effect either in rats or rabbits respectively. LOFROTH's (1970) *in vitro* study, however, hinted that DDVP triggers chromosome breaks. KRAUSE and HOMOLA (1974) observed that DDVP besides inhibiting cholinesterase also inhibits nonspecific esterases, which occur abundantly in the Leydig cells. The above workers, however, could not find any synchronization between the occurrence of damage and the spermiogenic cycle. This suggests that DDVP seems to cause no effect on germ cells.

It has been shown by LAWS (1966) that the toxicity of DDVP to rats is markedly lowered when it is infused into the hepatic portal venous system as compared to systemic venous circulation. Oral feeding of DDVP, is routed through the detoxification process of the liver before reaching the systemic circulation. DDVP when applied to skin of rats, as has been studied here, also follows a similar pattern. Significantly, DDVP did not induce any observable pathological changes in skin or testis of rats. This is in conformity with the findings of SLOMKA (1970) and GILLETT *et al.* (1972). Since DDVP undergoes rapid degradation in rats, mice, hamster, pigs and humans (BLAIR *et al.*, 1975) this appears to be the major factor for the absence of any histopathological change in tissues of rat inspite of a 90 day exposure. Since tubular damage and necrosis of the testis was observed in rats of the control group also, any abnormality in DDVP treated rats gains less significance. This suggests that careful scoring is essential before imparting meaningful interpretation or evaluation of a candidate insecticide.

SUMMARY

Exposure of male rats to DDVP (21.4 mg/kg/day) through dermal painting for a period of 90 days did not produce any changes in skin or testis. None of the animals showed any clinical symptoms of DDVP poisoning or mortality during experimentation. Rapid degradation of DDVP and further its detoxification in in liver of rats and other species of mammals seems to be the prime reason for the non-toxic effect of the insecticide.

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