Effect of Benzanthrone on the Urinary Bladder of Guinea-Pig

In dyestuff industries it has been observed that workmen who come in contact with the dye benzanthrone (an anthraquinone derivative) during its manufacture, pulverization, and storage develop itching, burning sensation, erythema and skin pigmentation[1-4]. Anthraquinone derivatives are known to have some toxic effect on the urinary bladder mucosa[5]. In the present preliminary investigation, therefore, an attempt has been made to study the effect of benzanthrone on the urinary bladder of guinea-pig.

Materials and methods. I.T.R.C. Colony bred guinea-pigs (body weight 350–400 g) were used in this investigation. The animals were divided into 3 groups of 40 each. 20 animals of each group were administered benzanthrone daily by local application, oral and i.p. routes respectively.

Group I (topical application). The skin of 20 animals was painted with a 2% benzanthrone suspension in isotonic saline by the method of SINGH et al[1]. The 20 control animals were painted with isotonic saline only.

Group II (oral administration). 20 animals were fed by stomach tube with the dye (25 mg/kg of body-weight) suspended in 2 ml isotonic saline. 20 controls received only 2 ml of isotonic saline.

Group III (i.p. injection). 20 animals were injected with the dye (25 mg/kg body weight) suspended in 2 ml sterile isotonic saline. 20 control animals were injected only 2 ml of sterile isotonic saline.

All animals were fed routine laboratory diet (Hind Lever Ltd., India) and kept under uniform husbandry conditions throughout the experimental period. In each group, 10 from benzanthrone administered animals and 10 controls, were sacrificed at the interval of 7 and 15 days.

Routine autopsy was performed on all animals. Abdominal viscera were inspected for any gross lesions. Urinary bladder from each animal was removed and fixed in freshly prepared 10% neutral formalin. Serial paraffin sections of 5 μm thickness were stained with haematoxylin and eosin.

Gross examination of visceral organs showed normal appearance in animals of all the groups at 7 and 15 days. A few small light brown particles, which appeared to be benzanthrone, were seen entangled in the omentum and diaphragmatic surface of benzanthrone injected animals at 7 and 15 days.

Microscopic examination of urinary bladder epithelium of all animals in groups I, II and control of group III at 7 and 15 days showed normal appearance (Figure 1). All benzanthrone injected guinea-pigs of group III showed mild vascular congestion in the lamina propria and submucosa at 7 days (Figure 2). Epithelium and muscular layers showed normal appearance. At 15 days 6 animals showed marked vascular congestion in lamina propria and submucosa. 4 animals showed evidence of mucosal lesion

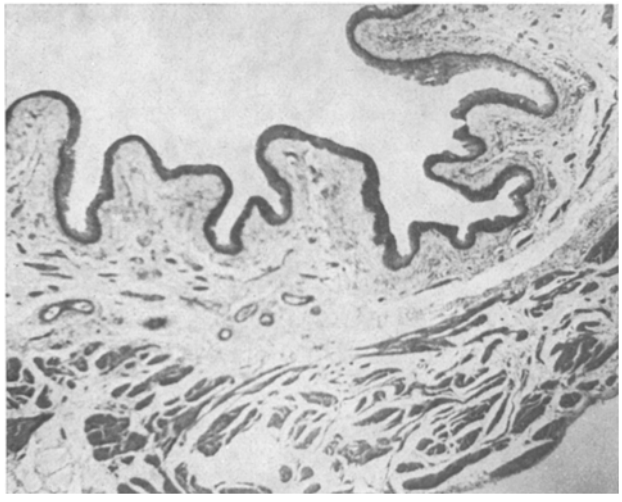

Fig. 1. Normal appearance of the urinary bladder wall. HE, × 28.

[1] G. B. SINGH, S. N. SHARMA and S. H. ZAIDI. Indian J. med. Sci. *21*, 727 (1967).
[2] D. H. TRIVEDI and A. K. NIYOGI, Indian J. ind. Med. *14*, 13 (1968).
[3] G. B. SINGH and S. H. ZAIDI, J. Indian med. Ass. *52*, 558 (1969).
[4] G. B. SINGH, Indian J. ind. Med. *16*, 122 (1970).
[5] D. HUNTER, *The disease of occupations*, 5th edn. (The English Universities Press Ltd., London 1969), p. 827.

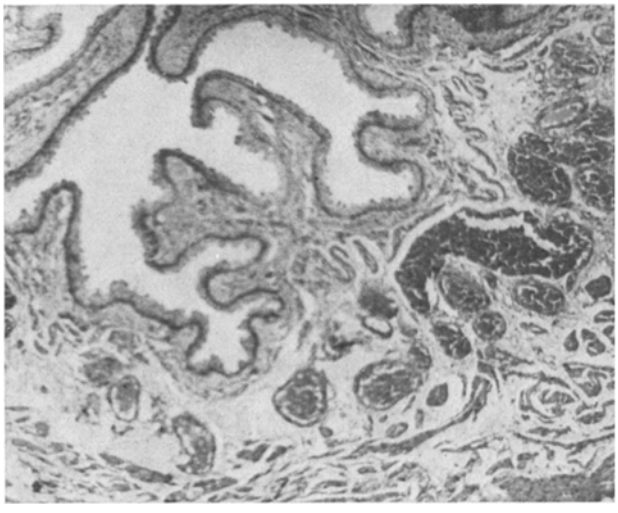

Fig. 2. Vascular congestion more marked in the submucosal layer. HE, × 28.

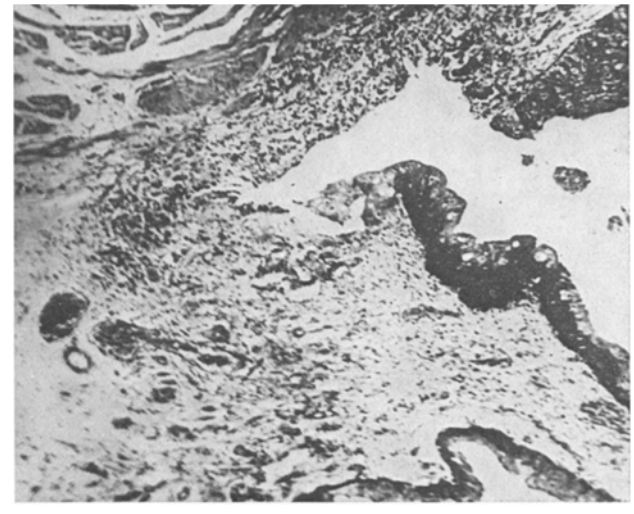

Fig. 3. Localised damage of the epithelial layer. HE, × 40.

(Figure 3). Large number of acute inflammatory cells were present in the lamina propria and submucosa. Muscular layers presented normal appearance. Vascular congestion was severe. No proliferative activity of the epithelial mucosa was observed.

Benzanthrone caused significant decrease of ascorbic acid level in blood and other body organs[6]. PANDYA[7] noted the presence of benzanthrone or its possible metabolites in guinea-pig urine after i.p. administration of benzanthrone. Lowered body ascorbic acid level combined with the effect of benzanthrone or its possible metabolites excreted in the urine may be responsible for epithelial damage. Mucosal lesion was not discernible on dermal application or oral administration of benzanthrone[8].

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Lucknow (India), 19 April 1972.

[6] K. P. PANDYA, G. B. SINGH and N. C. JOSHI, Acta pharmac. tox. *28*, 499 (1970).
[7] K. P. PANDYA, under communication (1972).
[8] Authors are grateful to Dr. S. H. ZAIDI, Director of the Centre for his keen interest in the work. Technical assistance of Messrs. MULKRAJ and V. G. MISRA is highly appreciated. Mr. M. AHMAD is responsible for the prepararion of photomicrographs.
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Effect of Lindane[1] on the Skin of Albino Rats

Lindane is being used extensively as dusts, emulsions and vapours to control insects under different conditions[2,3] Occupational poisoning among workers engaged in the synthesis, formulation and application of lindane is also reported by different workers[4–6]. Literature on the histopathological changes in the skin of individuals repeatedly exposed to lindane is not adequate. Physicochemical factors such as particle size, the period of exposure and the vehicles are known to influence the degree of toxicity. In the light of such variations, dermal application of lindane under tropical conditions, as in this country, merits further study. This report, which is the continuation of our earlier observations[7,8], deals with the histopathological changes in the skin of albino rats after they are exposed directly to the action of lindane.

Materials and Methods. 50 female albino rats of I.T.R.C. stock with an average body weight of 80 g were used in the experiment. The lateroabdominal area measuring approximately 4×4 cm was previously made ready by hair clipping for lindane painting. Lindane (98% purity) was used with propylene glycol (BDH Analar) as the vehicle. 1 ml of the solution which contained 14.4 mg of lindane (this dose is 5 times less than the acute dermal LD_{50} values for the female rats; dermal LD_{50} of lindane for female rats is 900 mg/kg)[9] was slowly transferred on the specified area of the skin with the help of a graduated pipette attached to a vaqupette. 30 animals were treated with lindane daily for a period of 25 days (total number of skin paintings 25). 20 animals of the control group were similarly treated with 1 ml of propylene glycol alone. The animals were killed at intervals of 24 h, 5, 10, 15, 20 and 25 days after treatment. The skin tissue was fixed in Bouin's fluid and paraffin cut sections were stained with haematoxylin and eosin for histopathological observations.

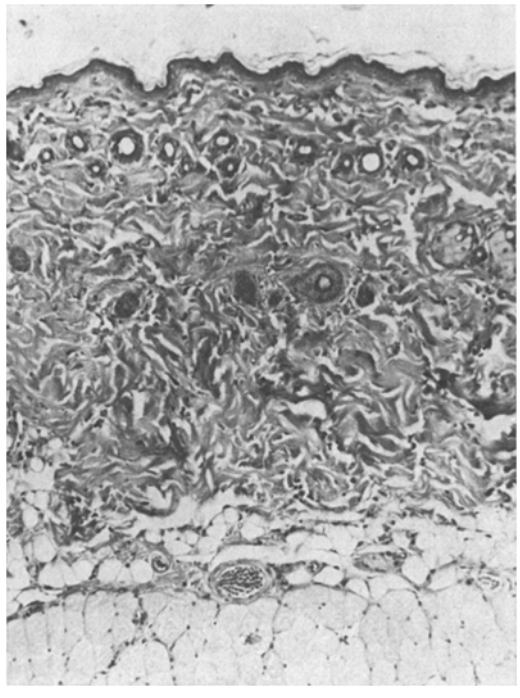

Fig. 1. Normal picture of the skin. Control (25 paintings). ×100.

Results and Discussions. Macroscopic examinations of the skin of experimental animals showed mild dermatitis in 3 animals after 15 paintings. This condition continued up to 25 paintings. In comparison, the skin of control animals did not show any such change.

The normal structure of the skin of the control rat is given in Figure 1. In contrast, microscopic study of the lindane-painted skin revealed various pathological changes. Hyperkeratinization and the migration of inflammatory cells through epidermis was observed in the animals painted for 20 days. Further application of lindane caused formation of abscess, filled in with polymorphonuclear cells. Mild acanthosis was seen with elongated rete ridges and cells of epidermis at some places appeared necrosed (Figure 2). Another skin area of the same animal showed both hyperkeratinization and abscess formation. Exposure of the skin to lindane for a period of 10, 15, 20 and

[1] Pure γ-isomer of 1,2,3,4,5,6-hexachlorocyclohexane.
[2] B. E. CONLEY. J. Am. med. Ass. *147*, 571 (1951).
[3] W. J. HAYES JR., *Clinical Hand Book on Economic Poisons* (U.S. PHS Publication No. 476, 1971), p. 53.
[4] M. P. FRANCONE and W. CHENA, Semana méd. B. Aires *55*, 573 (1949).
[5] M. P. FRANCONE and W. CHENA, Revta assoc. méd. argent. *64*, 187 (1950).
[6] L. SIELICKA and J. WALICHIEWICZ, Polski Tygod. lek. *13*, 795 (1958).
[7] P. P. KAR and T. S. S. DIKSHITH, Experientia *26*, 634 (1970).
[8] T. S. S. DIKSHITH and K. K. DATTA, Experientia *28*, 169 (1972).
[9] T. B. GAINES, Toxic. appl. Pharmac. *2*, 88 (1960).