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HISTOCHEMICAL STUDY OF THE PILOTROPIC ACTION OF 1-(CHLOROMETHYL)-SILATRANE ON GUINEA PIG SKIN

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Much interest has recently been shown by research workers in a new class of organosilicon compounds — the silatranes; this is due, in particular, to the broad spectrum of their biological activity.

It has been shown that silatranes stimulate growth of the hair in laboratory animals. Microscopic and macroscopic investigations of the pilotropic action of 1-substituted silatranes with the general formula $XSi(OCH_2CH_2)_3N$ have shown that the most active of them is 1-(chloromethyl)silatrane ($X = ClCH_2$) [1, 3, 5].

To shed light on some aspects of the mechanism of the pilotropic action of this silatrane a histochemical study of the skin of experimental animals was undertaken after its application: The effect of 1-(chloromethyl)silatrane was studied on the principal components of connective tissue, namely glycogen, mucopolysaccharides, and nucleic acids.

EXPERIMENTAL METHOD

The hair was removed from an area of skin of guinea pigs by means of 2% Epilin ointment. For the next 3 months, 5% 1-(chloromethyl)silatrane ointment was rubbed into the epilated areas of skin. At the end of the experiment the animals were killed and the skin subjected to histochemical analysis. The material was processed by the usual methods. The distribution of polysaccharides was revealed by the PAS reaction (with amylase control), mucopolysaccharides by alcian blue at different pH values (with hyaluronidase control), and RNA by Einarson's method (with ribonuclease control). These substances were determined quantitatively microspectrophotometrically [3, 4].

EXPERIMENTAL RESULTS

Under the influence of 1-(chloromethyl)silatrane the content and concentration of glycogen was increased both in the basement membrane and in the outer epithelial sheath of the hair follicle (Table 1).

It can be postulated that this compound has a beneficial effect on a certain stage in carbohydrate metabolism, acting as a stimulator intensifying this process. An increase in the glycogen content can also be explained on the grounds that the structure of the synthesized glycogen becomes "cross-linked," evidently on account of silicon "bridge" atoms.

Of all the mucopolysaccharides in the guinea pig skin, heparin was chosen for demonstration (Table 2).

It will be clear from Table 2 that the heparin content in the skin of the experimental animals was sharply reduced. There are several possible reasons for this: 1) Heparin is neu-

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TABLE 1. Changes in Glycogen Content in Basement Membrane and Outer Epithelial Sheath of Hair Follicles as a Result of Application of 5% 1-(Chloromethyl)silatrane Ointment for 3 Months

Group of animals	Thickness of layer, μ		Glycogen content in layer, conventional units	
	basement membrane	outer epithelial sheath	basement membrane	outer epithelial sheath
Control	10,0±0,4	8,6±0,2	382,6±0,9	304,9±0,7
Experimental	8,8±0,1	7,2±0,5	417,3±0,2 (9,09)	358,2±1,6 (17,5)

Legend. Increase in glycogen content (in %) shown in parentheses; $P < 0.1$.

TABLE 2. Changes in Concentration of Mucopolysaccharides in Connective Tissue of Guinea Pig Skin after External Application of 5% 1-(Chloromethyl)silatrane Ointment

Test object	Content of mucopolysaccharides, conventional units		P
	control	experiment	
Stratum papillare of dermis	17,2±1,0	11,2±0,9 (34,9)	<0,01
Reticular layer of dermis	7,8±1,0	3,1±0,8 (60,2)	<0,01
Outer epithelial sheath of hair follicle	16,7±0,9	11,5±0,7 (31,1)	<0,01

Legend. Decrease in mucopolysaccharide content (in %) shown in parentheses.

tralized by the reaction with triethanolamine, formed during hydrolysis of silatranes; 2) functional groups of heparin, containing an active hydrogen atom (—SO_3H, —COOH, —OH), react with organosilicon products of silatrane metabolism with the formation of Si—O—S and Si—O—C groups. As a result, the reactive groups of heparin are blocked and, consequently, its physiological activity is reduced; 3) delay of heparin synthesis from glucuronic acid and glucosamine because of blocking of the functional groups of these reagents by products of silatrane metabolism (hydrolysis).

The fall in heparin concentration weakens its inhibitory action on hyaluronidase, the main function of which is depolymerization of hyaluronic acid and chondroitin sulfates.

The fall in heparin concentration thus leads to increased hyaluronidase activity and this, in turn, stimulates polymerization of hyaluronic acid and increases connective tissue permeability.

Considering the important role of protein biosynthesis in hair growth, it was decided to study the state of RNA in cells of the outer epithelial sheath and the epidermis (Table 3).

The results in Table 3 show that the RNA concentration rose sharply both in the epidermis and in the outer epithelial sheath after application of 5% 1-(chloromethyl)silatrane ointment. The results of these experiments agree with those obtained previously by a different method [6] and they indicate that 1-(chloromethyl)silatrane stimulates RNA synthesis.

It can accordingly be concluded from the results of the present investigation that 1-(chloromethyl)silatrane activates both carbohydrate and protein metabolism. By stimulating

TABLE 3. Changes in RNA Concentration in Epidermis and Outer Sheath of Hair Follicle on Guinea Pig Skin after Application of 5% 1-(Chloromethyl)silatrane Ointment

Test object	RNA concentration		P
	control	experiment	
Epidermis	0,258±0,05	0,593±0,03 (129,8)	<0,01
Outer epithelial sheath of hair follicle	0,195±0,03	0,461±0,04 (136,4)	<0,01

Legend. Change in RNA concentration (in %) shown in parentheses.

vitally important metabolic processes (RNA and glycogen synthesis), by reducing the number of reactive groups of heparin, and by intensifying vascularization of the skin, 1-(chloromethyl)-silatrane, like certain other silatranes, has a pilotropic effect.

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