A NOTE ON SODIUM PROPIONATE

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It is known that the normal skin can combat pathogens such as streptococci and staphylococci and an interesting account of its autosterilising action is provided by Bigger,[1] who states that few bacteria are able to survive on the human skin owing to the presence of bactericidal substances. The antibacterial and antifungal properties of sodium propionate have been discussed in a previous communication[2] and it is evident that the compound is effective against a wide range of pathogens, although its activity against viruses is doubtful. Peck and Rosenfeld[3] were apparently the first workers to show that the human perspiration is fungistatic owing to its content of fatty acids, although the literature contains earlier references to the inhibitory action of these acids against micro-organisms. The normal sweat exuded from the glands exhibits the slight alkalinity of plasma, but the reaction becomes acid after admixture with sebum and substances excreted by the epidermis. Propionic acid, a constituent of human body fluids, is probably produced chiefly by the breakdown of higher fatty acids; it is found in the sweat as free acid or as salts. These substances are metabolised in the body and Lorber and his associates[4] gave isotopic sodium propionate to fasted rats, isolated the resulting liver glycogen and hydrolysed the latter to glucose. Their results indicate that propionate may give rise to pyruvate by a process involving loss of orientation of the α- and β-carbon atoms of the propionate, the pyruvate acting as intermediate in glucose and glycogen formation. Unlike acetates, propionates are not used by the body in synthesising cholesterol.[5]

Since glycogen is present in the sweat glands, it may be suggested that a portion of the propionate in perspiration could be formed locally by the reverse of the process proposed by Lorber *et al.*, the mechanism thus resembling that whereby glycogen is converted into lactic acid. Further quantities, produced in the liver during the metabolism of fat, may escape oxidation in the extra-hepatic tissues and pass into the sweat.

Some Pharmacological Properties

Sodium propionate is a white solid, soluble in about two parts of water. Specimens of the substance available commercially were found to have a variable, alkaline reaction, but neutral products can be prepared for pharmaceutical use.

The acute toxicity is apparently so low that it was considered neither practicable nor necessary to determine it in terms of LD50. Daily oral doses of 6 g. administered to an adult male rendered the urine faintly alkaline but caused no appreciable diuresis, catharsis or other effects. It would seem that sodium propionate is absorbed fairly readily, so producing insignificant osmotic effect in the bowel, and the greater part of a dose is probably oxidised in the tissues with the formation of carbonate.

Theodore[6] reported that 20 per cent. solutions caused no deleterious effects when instilled into the eyes of rabbits and that 10 per cent. solutions appeared to facilitate the healing of experimental lesions. This investigator employed sodium propionate in the treatment of about 1200 cases of ocular diseases and concluded that the drug is particularly suitable for ophthalmic use. Application of a 10 per cent. solution of *p*H 7·2 to the conjunctiva and nasal mucosa of human subjects has been found to cause only slight, transient stinging and no appreciable irritation of the intact skin was produced by 20 per cent. solutions with *p*H values of 7 to 8·5. Alkaline preparations appeared to irritate the skins of dogs and cats, but this effect was probably due solely to the *p*H factor, since similar irritation was caused by sodium bicarbonate solutions of *p*H 8·4 and since a neutral propionate preparation was well tolerated by these animals. Chronic topical use did not result in sensitisation in any member of a group of subjects and extensive clinical trials have proved sodium propionate to be hypoallergenic. It has no apparent anticoagulating effect and this observation is supported by Hecht's report[7] that fatty acids have no action on the coagulation of chicken plasma. A 10 per cent. solution of *p*H 7·2 was diluted to provide a range of concentrations and the osmotic pressures were determined by the freezing-point technique and by means of a semi-permeable membrane/manometer apparatus. The results indicate that the concentration of sodium propionate which is isotonic with serum and lachrymal fluid is approximately 2·4 per cent.

Antihistaminic Activity. One drop of a 0·1 per cent. sterile solution of histamine acid phosphate was allowed to remain in contact with uniformly scarified areas on the left arms of male and female volunteers for a period of 5 minutes. After removing the histamine, one weal was left untreated as control and the others were treated respectively with 2 per cent. diphenhydramine hydrochloride, 2 per cent. antazoline hydrochloride and 15 per cent. sodium propionate. Measurement of the weals after a further interval of 10 minutes demonstrated the following order of decreasing antihistaminic activity in each case:—

Subject	*Order of increasing weal-size*
F. 1	Diphenhydramine, Antazoline, Propionate, Control.
F. 2	(Propionate, Diphenhydramine), Antazoline, Control.
M. 1	Propionate, Diphenhydramine, Antazoline, Control.
M. 2	Diphenhydramine, Propionate, Antazoline, Control.

Uniformly scarified areas on the right arms of the same subjects were then treated with (*a*) 0·05 per cent. histamine acid phosphate, (*b*) 0·05 per cent. histamine acid phosphate plus 1 per cent. diphenhydramine hydrochloride, (*c*) 0·05 per cent. histamine acid phosphate plus 1 per cent. antazoline hydrochloride, (*d*) 0·05 per cent. histamine acid phosphate plus 7·5 per cent. sodium propionate. The weals were then measured after an interval of 15 minutes.

Subject	*Order of increasing weal-size*
F. 1	(Diphenhydramine, Antazoline, Propionate), Control.
F. 2	Propionate, Diphenhydramine, Antazoline, Control.

Subject	*Order of increasing weal-size*
M. 1	Propionate, Diphenhydramine, Antazoline, Control.
M. 2	Diphenhydramine (Antazoline, Propionate), Control.

Note.—Brackets indicate only slight differences in weal-size.

These results demonstrate the variation of activity of antihistaminic drugs in different persons which has been observed by a number of investigators, but it is apparent that sodium propionate exhibits some local antihistaminic effect. Although its potency is less than that of similar concentrations of recognised histamine antagonists, this property is likely to be of practical advantage when sodium propionate is used as an antiseptic in the treatment of burns and certain diseases of the skin and mucous membranes. The value of this effect, moreover, may be particularly apparent when the compound is substituted for penicillin, sulphonamides or other drugs in patients who have become sensitised to these agents.

SUMMARY

1. Sodium propionate has a low systemic and local toxicity.
2. It is hypoallergenic and virtually non-irritant in appropriate therapeutic concentrations.
3. The concentration of sodium propionate isotonic with serum and lachrymal fluid is approximately 2·4 per cent.
4. The drug has some local antihistaminic activity.

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