Effects of Some Lignosulfonates on Sweat Gland Activity

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Abstract □ The antihidrotic activity of several lignosulfonates on pilocarpine-induced sweating in anesthetized cats has been investigated. Two lignosulfonates produced significant inhibition of sweating when applied topically on the foot pads of the cat. The most effective material was comparable to $Al(OH)_2Cl$. Preliminary experiments indicated that this lignosulfonate was also effective in reducing emotionally induced finger sweating in human volunteers.

Keyphrases □ Lignosulfonates—antihidrotic activity □ Pilocarpine-induced sweating—lignosulfonates effect □ Antihidrotic activity—screening

The antiperspirants in general use today usually contain salts of metals such as aluminum. When and how these salts came to be recognized as antiperspirants is not known. An effort to find other substances effective in reducing eccrine sweat gland activity has focused attention on macroanions. The macroanions investigated were crude and purified lignosulfonates and are considered to be composed mainly of the following monomeric units: [4-hydroxy-3-methoxyphenylpropane)$_N$ and [4-hydroxy-3,5-dimethoxyphenylpropane]$_N$, Pearl, 1967 (1). The purpose of the studies reported here was to evaluate the antihidrotic effects of these substances on pilocarpine-induced sweating in the anesthetized cat. In addition, it seemed desirable to determine, in preliminary experiments, if antihidrotic effects could be demonstrated in the human subject.

EXPERIMENTAL

The method of Alphin *et al.* (2) was used for determining the antihidrotic effects of aqueous solutions of the lignosulfonates. Various concentrations were applied directly (0.1–0.2 ml.) to a front foot pad of a cat anesthetized with sodium phenobarbital (125 mg./kg., i.p.). After application of test substance, the foot pad was allowed to dry before sweating determinations were made. The other front paw, enclosed in an identical chamber, served as a control. Sweating was elicited by the administration of pilocarpine hydrochloride (0.1 mg./kg.) *via* a jugular vein previously cannulated with P.E. 50 tubing. The sweating response was determined by measuring the maximum height (cm.) of the sweating curve for both control and treated paws. The differences between means (in cm.) of control and treated sweating curve heights were tested for significant differences by the Student *t* test (3).

Effects in human volunteers were measured by the apparatus employed in the cat experiments. Kuno (4) and others have shown that sweat responses to mental stimulation occur on the plantar and palmar surfaces as well as in the axillae. It is well recognized that human emotions are a common physiological cause of increased sweating and appear to be under the control of a center in the cerebral cortex. In preliminary experiments involving emotionally induced sweating, primary considerations were given to the duration as well as the type of stimulus used with each subject, insofar as possible under the present experimental conditions. The lignosulfonate was dissolved in a commercial lotion to a final concentration of 20% (w/v, pH 4.9) and applied with a standard roll-on bottle. After recording control responses to emotional stimuli (such as answering questions or asked to recall events) the lotion was applied to the entire surface area of the middle (third) finger of either the right or left hand. The same lotion, without compound, was applied to the corresponding finger of the other hand which served as a control. Both fingers were allowed to dry before being placed into the recording chambers. After a constant sweating rate had been established for both fingers, the emotional stimuli were repeated to determine the change in sweating responses.

The authors gratefully acknowledge the generous samples of lignosulfonates from the various manufacturers.[1]

A commercial aluminum chlorhydroxide preparation was used as a reference standard.

RESULTS

The effects of a number of lignosulfonates on pilocarpine-induced sweating in the anesthetized cat are shown in Table I. Under the authors' experimental conditions, only Substance 13 (65%; $p < 0.05$) and Substance 12 (53%; $p < 0.05$) produced significant inhibition of sweating. Substance 13 considered to be a purified lignosulfonate (average mol. wt. approximately 5,000), was prepared by a modified protein precipitation method of Jantzen (1958) (5). Substance 1 (+26%) and Substance 2 (+21%) appeared to enhance the flow of sweat; however, further studies must be done to confirm these observations. The antihidrotic effects appeared to

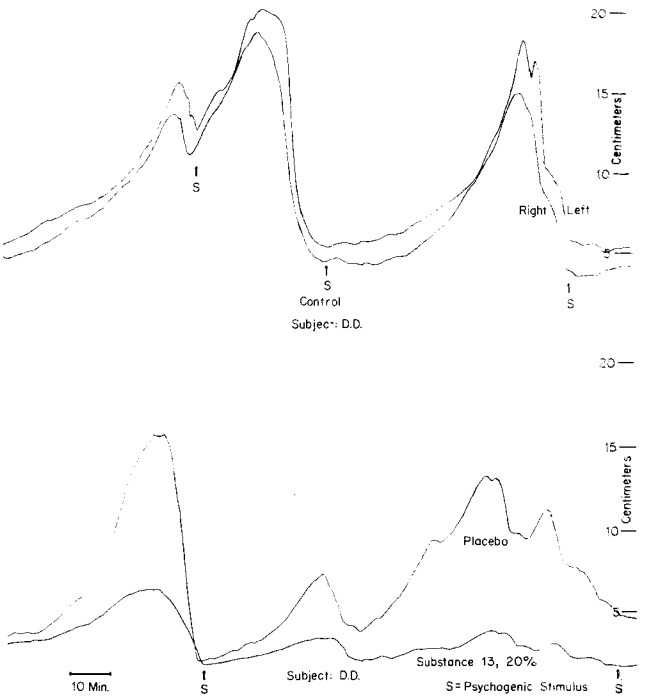

Figure 1—*Typical effects of a lignosulfonate (20% w/v) on finger sweating in a human subject. Nontreated response in upper tracing; treated response in lower. Respective fingers are designated by right and left.*

[1] Arthur C. Trask Co., Chicago, Ill. (Trastan SL, Trastan AL, Peritan); American Can Company, Neenah, Wisc. (Norlig 11, Maratan 24, Marasperse CB); Crown Zellerbach, Camas, Wash. (Orzan G); West Virginia Pulp and Paper, North Charleston, S.C. (Polyfon H, Reax 80A, Polyfon O, Polyfon T, Reax 85A); Lake States Division St. Regis, Rheinlander, Wis. (Toranil B). See Table I for identification of substances as discussed in text.

Table I—Effect of Various Lignosulfonates on Pilocarpine-Induced Sweating in the Anesthetized Cat

Lignosulfonates Substance[a]	Total Sulfur,[a] %	Cation	Sulfur–Methoxy Ratio[a]	Reducing Sugar as Glucose,[a] %	pH of Applied Solutions[b]	% Change[c] in Sweating Response	p Value
1[d]	6.2	Na, NH_3	0.72	27.0	6.8	+26	>0.5
2	6.0	Ca	0.70	18.5	4.2	+21	>0.5
3	6.4	NH_3	[e]	[e]	4.8	+6	>0.5
4	5.2	Na	0.44	None	8.3	−13	>0.5
5	6.8	Ca	0.77	5.0	4.6	−20	>0.2
6	7.4	Na	0.81	None	10.7	−25	>0.2
7	6.6	NH_3	0.77	28.0	3.9	−25	>0.2
8	[e]	[e]	[e]	[e]	3.6	−30	<0.1
9	1.6	Na	0.13	None	8.6	−32	>0.4
10	7.7	Na	0.73	None	9.3	−42	<0.1
11	11.3	Na	1.33	None	9.5	−43	>0.4
12	4.4	Na	0.38	None	9.8	−53	<0.05
13	6.6	Na	0.60	0.14	8.4	−65	<0.05

[a] Analytical data supplied by the respective suppliers. [b] All compounds applied locally on foot pads as 20% (w/v) aqueous solutions. [c] A minimum of two cats and four pilocarpine injections were used to test each compound. (+) = sweating increase from control, (−) = sweating decrease from control. [d] Substance 1, Trastan-SL; 2, Norlig 11; 3, Orzan G; 4, Polyfon H; 5, Toranil B; 6, Reax 80A; 7, Trastan AL; 8, Maratan 24; 9, Marasperse CB; 10, Polyfon O; 11, Polyfon T; 12, Reax 85A; 13, Peritan. [e] Not determined.

be unrelated to the total sulfur content. Various salts (sodium, ammonium, and calcium) of the lignosulfonic acid were used, and did not seem to influence sweat gland activity. Neither the sulfur–methoxy ratio nor the pH of the applied solutions appeared to have a relationship to the rate of sweating.

The effects of Substance 13 and $Al(OH)_2Cl$ on pilocarpine-induced sweating in the anesthetized cat are compared in Table II. A dose-response relationship was obtained with both substances. $Al(OH)_2Cl$ appeared to be slightly more effective; however, the difference was not statistically significant.

Typical results obtained with Substance 13 in the human subject are shown in Fig. 1. It is evident from control tracings (upper half of Fig. 1) that the emotionally induced sweating response is quite similar in both fingers. The lower half shows that after application of 20% Substance 13, the sweating response is considerably less than that of the corresponding control finger under the same experimental conditions. This is supportive evidence that Substance 13 has antiperspirant properties.

DISCUSSION

A search of the literature did not disclose previous reports concerning the effects of lignosulfonates on sweat gland activity. Studies with various lignosulfonates failed to show a relationship between antiperspirant effect and total sulfur content, sulfur–methoxy ratio, reducing sugar content, or pH of the applied solution. The viscosity of the applied lignosulfonates also appeared to have little, if any, effect on the antiperspirant action.

Even though many of the lignosulfonates are known to be protein-precipitating agents (1), this action may, or may not, partially account for their antiperspirant effect. In this regard, other studies with chemical fractions of Substance 13 were conducted, and there was no suggestion of any correlation between antiperspirant effects and gelatin-precipitating properties.

Many hypotheses have been proposed to explain the mechanism by which aluminum salts produce antiperspirant effects. One of the most recent theories suggests that they increase the permeability of the sweat gland duct, resulting in complete dermal resorption of the sweat (6). As in the case of the aluminum salts, the mechanism(s) of the antiperspirant action of lignosulfonates is not understood. The antihidrotic effects appear to be reversible, as thorough washing of the treated area eliminated the inhibition of sweating.

It is interesting to note that two of the lignosulfonates not only failed to produce inhibition of sweating but appeared to increase the flow of sweat. Thus far, the authors have been unable to adequately explain the different effects observed. It should be pointed out, however, that the lignosulfonates tested were produced by several manufacturers using, in many cases, different processes and sources of original starting materials. In this regard, different samples of Substance 13 (obtained from production runs in 1966 and 1968) have been tested and found to provide reproducible antihidrotic effects. This is not surprising since the material is produced under controlled conditions. Only one batch of each of the other lignosulfonates was investigated and therefore the reproducibility of these remains to be determined.

The true significance of the antihidrotic effects of the lignosulfonates reported in these studies will have to await more extensive investigations.

Table II—Comparative Effects of Substance 13 and $Al(OH)_2Cl$ on Pilocarpine-Induced Sweating in the Anesthetized Cat

Compound	Percent[a]	No. Cats	No. Responses[b]	% Inhibition Sweating
Substance 13	0.1	5	10	21
	1.0	4	6	41[c]
	10.0	4	8	56[c]
	20.0	7	13	65[c]
$Al(OH)_2Cl$	0.1	2	4	13
	1.0	5	8	44[c]
	10.0	4	7	73[c]
	20.0	5	9	81[c]

[a] Percent refers to concentration of substance applied on cat paw. [b] Pilocarpine (0.1 mg./kg. i.v.). [c] $p < 0.05$.

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