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The site of antiperspirant action by aluminum salts in the eccrine sweat glands of the axilla

RICHARD P. QUATRALE, EILEEN L. THOMAS, and
JAY E. BIRNBAUM, *American Cyanamid Company, Shulton Skin Care Research Center, 697 Route 46, Clifton, NJ 07015.*

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Synopsis

The relative sites of antiperspirant activity within human axillary eccrine sweat glands of aluminum chlorohydrate (ACH), aluminum zirconium chlorohydrate glycine complex (AZAP), and aluminum chloride ($AlCl_3$) were determined by the cellophane tape stripping procedure. Using the starch/iodine method, individual functioning sweat glands were identified prior to antiperspirant treatment, after treatment, and after tape stripping. As had been found earlier in studies of the eccrine sweat glands in the human forearm, $AlCl_3$ acted most deeply within the duct, whereas the sites of action for ACH and, particularly, AZAP were closer to the skin surface. On average, however, both ACH and AZAP appeared to inhibit perspiration outflow at a deeper level in more individual axillary sweat ducts than they did in forearm ducts.

INTRODUCTION

In an earlier study, the sites of antiperspirant action within human forearm eccrine sweat glands which had been inhibited by aluminum chlorohydrate (ACH), aluminum zirconium chlorohydrate glycine complex (AZAP), or aluminum chloride hexahydrate ($AlCl_3$) were demonstrated. Comparison of starch/iodine-generated sweating patterns obtained before and after antiperspirant treatment and then after removal of the intracorneal sweat ducts by the cellophane tape stripping procedure indicated that ACH, and particularly AZAP, functioned relatively superficially. Removal of the horny layer led to restoration of activity of most of the sweat glands previously inhibited by either of these two aluminum salts. In contrast, $AlCl_3$'s site of activity was shown to be deeper within the duct in that stripping caused virtually no restoration of sweat gland function (1).

The means by which aluminum antiperspirant salts, particularly the polymeric forms, inhibit sweating is believed to be by their forming a physical blockage within the ducts, as suggested by Reller and Luedders (2). Presumably, when this blockage is relatively superficial, tape stripping removes it and permits the restoration of the excretory process. For $AlCl_3$, antiperspirant activity is also held to be based on the intraductal formation of these occlusive casts, as further described by Holzle and Kligman

(3). However, inasmuch as $AlCl_3$-caused blockage of the sweat duct is more deeply located in most sweat glands, it is much less readily removed.

Subsequent histological studies using both transmission electron microscopy and fluorescence microscopy confirmed the relative location of each of the three antiperspirants in inhibited forearm sweat glands. ACH was found within the sweat duct at the level of the stratum corneum and in a number of instances at the level of the granular layer of the viable epidermis (4). AZAP was found predominantly in the distal-most region of the duct as it passed through the horny layer (5). In confirmation of previous studies (2,3), $AlCl_3$ has been located within the sweat duct at a depth well below the stratum corneum layer (6).

The use of the human forearm or the back to study eccrine sweat gland function, particularly to assess the effects of prototype antiperspirants on that function, is time-honored. However, despite the practical value that these sites offer, caution needs to be exercised in extrapolating the findings to eccrine sweat gland function in the human axilla. The purpose of the studies reported here is to establish the relative intraductal sites of antiperspirant activity of the three aluminum-based salts in the eccrine sweat glands of the axilla as a first step in elucidating the means by which antiperspirants function in the human underarm.

MATERIALS AND METHODS

The technical approaches used in these studies were virtually identical to those described previously for the forearm studies. Minor variations in the experimental protocol were introduced principally to adjust for the more profuse and rapidly progressing sweating usually encountered in the axilla compared to that found on the forearm.

The subjects were adult females. One site (total area: 4 cm^2) in the approximate center of the axillary vault was selected and marked. On Day I of the study, the subject was thermally stressed in an environmental chamber (100°F, 30–35% RH) for 40 minutes while resting supine. At the end of this acclimation period, the test site was blotted dry with absorbent tissue and a thin layer of the starch, castor oil, and iodine mixture was applied to it to display the sweating pattern. Within a few minutes virtually all subjects in all instances exhibited a complete punctate pattern of sweat gland activity at which point the first photographic record was made. Subsequent photographs, at 10 and at 20 minutes after the initial photograph, were also taken. The number of sweat glands found at all three time points appeared to be identical. However, at these latter points, the sweating pattern of many subjects had lost its discreteness and coalescence of the individual sweat droplets was frequently observed. Accordingly, evaluation of the sweating patterns for all subjects was made using the first photograph only. After recording the control (pretreatment) sweating pattern, the starch mixture was removed and the subject was dismissed.

The subject returned the following morning (Day II) at which time the axillary test site was relocated using a template. Next, approximately 0.35–0.45 ml of one of the antiperspirant test solutions was used to saturate the cotton pad component of an impermeable mylar-backed bandage (Readi-Band®, Parke-Davis & Co., Detroit, Michigan). The occlusive patch was then affixed to the skin test site and further secured with strips

of Micropore Surgical Tape® (3M Co., St. Paul, Minnesota) to prevent inadvertent loosening. The patch remained in place for 22–24 hours.

The antiperspirant test solutions were 20% aqueous ACH*, 10% aqueous AZAP**, and 8% aqueous $AlCl_3$***. Several additional subjects, serving as controls, were treated with distilled water and processed identically.

The patch was removed in the morning of Day III at not less than four hours prior to further study. Using this treatment regimen, the maximum inhibition by the antiperspirant test solution was insured, while sham inhibition, due to the process of occlusive application of a solution, was afforded time to dissipate.

In the afternoon of Day III, the subject again entered the environmental chamber, and, as described above, photographs of the starch/castor oil/iodine-generated sweat pattern were taken after an initial 40-min period of acclimation to thermal stress. (Photographs were also taken after the subject had been under thermal stress for 50 and 60 minutes as well).

The starch mixture was then removed and the subject returned to ambient temperature. Using cellophane tape, the stratum corneum layer of the antiperspirant-treated axillary test site was quickly stripped away, exposing the granular layer. The subject was then immediately thermally stressed for the third time and a series of post-stripping photographs was taken in the usual manner.

The number of functioning sweat glands, as evidenced by the individual black dots resulting from the reaction between the sweat droplets (water) and the starch mixture, was determined for each of the three periods—pre-treatment, post-treatment and post-stripping.

The percentage of those sweat glands which were inhibited by the antiperspirant treatment but which were restored to function when the intracorneal segment of their ducts had been removed could then be calculated. For example, if the number of sweat glands observed before and after treatment was 100 and 20, respectively, and the number of glands observed after treatment and after stripping was 20 and 60, respectively, then:

$$\frac{60-20}{100-20} = \frac{40 \text{ inhibited glands restored}}{80 \text{ inhibited glands}} \times 100 = 50\% \text{ restoration.}$$

RESULTS

For the participants in this study, the average density of eccrine sweat glands in the axilla was approximately 90/cm^2, but there was a considerable range (50–200 glands/cm^2) among them. The effect of the overnight occlusive application of the three aluminum antiperspirants, ACH, AZAP, and $AlCl_3$, on axillary eccrine sweat gland function was as follows.

* Prepared from a 50% aqueous ACH solution obtained from Wickhen Products, Inc., Huguenot, New York.

** Prepared from the dry powder obtained from Wickhen Products, Inc., Huguenot, New York.

*** Obtained as the reagent grade hexahydrate salt from Fisher Scientific Co.

ACH

When 20% ACH was occlusively applied, approximately 90% of the treated sweat glands, on average, were inhibited. Tape stripping away the stratum corneum resulted in restoring to function an average of slightly more than one quarter of these inhibited sweat glands (Table I).

AZAP

Sweat gland function was again inhibited in 90% of the sweat glands treated with 10% AZAP. Removal of the intracorneal duct segment of these glands resulted in restoring more than 40% of them, on average, to a functional state (Table I).

$AlCl_3$

As with 20% ACH or 10% AZAP, the occlusive application of 8% $AlCl_3$ to axillary eccrine sweat glands caused nearly all (92%) of the glands to cease functioning.

However, as had been observed previously in similar forearm studies, the number of sweat glands whose impaired excretory capability was restored upon removal of their intracorneal duct segment constituted a very small percentage of the total (Table I).

For the subjects who served as controls, the number of active sweat glands observed in the test site before and after the occlusive application of distilled water, as well as after tape stripping, was essentially identical.

Table I
The Effect of Cellophane Tape Stripping on Axillary Eccrine Sweat Gland Function Following Occlusive Treatment with Aluminum Antiperspirants

Treatment	$\bar{x} \pm$ S.E.	Median (Range)
20% ACH (N = 10 Subjects)		
Percentage of glands inhibited	91 ± 3	95 (84–100)
Percentage of inhibited glands restored to firing	28 ± 8	24 (4–85)
10% AZAP (N = 9 Subjects)		
Percentage of glands inhibited	90 ± 3	93 (72–100)
Percentage of inhibited glands restored to firing	41 ± 7	36 (12–76)
8% $AlCl_3$ (N = 9 Subjects)		
Percentage of glands inhibited	92 ± 2	91 (84–100)
Percentage of inhibited glands restored to firing	2 ± 1	0.6 (0–9.3)

DISCUSSION

A comparison of the data for axillary eccrine sweat glands reported here to those found previously for similar studies on forearm sweat glands reveals several notable points. First, there was less uniformity in response among individuals in a group. A wider range of values for restoration of sweating after removal of the intracorneal duct by tapestripping was found. There was also some difference in the extent, although not the order, of restoration to function for the inhibited sweat glands following tape stripping.

For ACH-treated eccrine sweat glands on the forearm, sweating had been shown to be blocked at a point in the duct relatively close to the skin surface in a substantial number—about half—of the treated glands. However, for the axilla, we have now demonstrated that the major portion of the population of ACH-inhibited sweat glands —more than two thirds of them—remained non-functional despite removal of the intracorneal duct. In contrast, less than half (41%) of the AZAP-inhibited sweat glands in the axilla were reactivated after stripping, whereas, for the forearm, AZAP's site of action was quite superficial. Two thirds of the sweat glands on the forearm which had been inhibited by AZAP treatment regained their capability to excrete sweat after the stratum corneum had been removed. Restoration of the function of $AlCl_3$-inhibited forearm sweat glands by tape stripping was previously found to be minimal. That finding has now been shown also to hold for the eccrine glands of axilla.

Further definition of the depth within the duct of axillary eccrine glands to which ACH or AZAP penetrated awaits histological studies. However, ACH on average functioned not only more deeply than AZAP did, but its primary site of action was below the level of the stratum corneum in the majority of the sweat glands to which it was applied. At this point in our studies, there is no evidence to support the view that either ACH or AZAP penetrated these glands to the level of the secretory coil.

The extent to which stripping restored the function of $AlCl_3$-treated sweat glands was significantly less than that found for ACH- or AZAP-treated glands ($p < .001$). The difference observed between ACH- and AZAP-treated sweat glands, although directionally similar to that seen in forearm studies, was not statistically significant ($p < .2$). As suggested earlier, $AlCl_3$, a relatively small molecular species, is probably readily able to diffuse down through the distal region of the sweat duct to a point invariably well below the level of the stratum corneum. Histological observations for both the forearm and the axilla confirm this view (3,6,7). On the other hand, ACH and AZAP, which are larger polymeric species, do not penetrate the more proximal region of the sweat glands as readily.

CONCLUSIONS

The relative sites of antiperspirant activity within the eccrine sweat glands of the human axilla were determined for ACH, AZAP and $AlCl_3$. As demonstrated previously for forearm sweat glands, AZAP functioned closest to the surface of the skin, whereas $AlCl_3$ acted most deeply. The site of ACH's activity within the duct was intermediate between the two. Both ACH and AZAP blocked the ducts at a level deeper than they did when they were applied to the sweat glands of the forearm.

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