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# The mechanism of antiperspirant action by aluminum salts. I. The effect of cellophane tape stripping on aluminum salt-inhibited eccrine sweat glands

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**Synopsis**

Studies were performed to determine the relative site of inhibition in the sweat gland caused by the three antiperspirants, aluminum chlorohydrate (ACH), aluminum zirconium chlorohydrate glycine complex (AZAP) and aluminum chloride ($AlCl_3$). For these studies, human forearm sweat glands were examined using the Scotch tape stripping procedure, a technique which removes the stratum corneum layer of skin and exposes the stratum granulosum layer of the viable epidermis. As judged by the degree to which sweat glands inhibited by overnight occlusive application of these antiperspirants could be restored to firing after Scotch tape stripping, ACH and AZAP acted most superficially, whereas $AlCl_3$ functioned at a level below the stratum corneum.

## INTRODUCTION

To understand the mechanism of action by which aluminum-based antiperspirant salts inhibit eccrine sweat gland function, it is useful to know the site within the gland at which those salts function. Several regions of the gland which are potential targets for inhibition by these salts can be delineated. First, there is the neuroglandular junction. If it is impeded from releasing acetylcholine, for example by the use of an anticholinergic such as scopolamine, then sweat gland secretion itself does not occur (1). A second challenge point is the secretory coil in the dermal layer of skin. If an agent can affect or inhibit the active transport processes which are intricately involved in the secretion of salt and water, then no sweat will appear at the skin surface (2,3). The third potential site of activity is the resorptive duct portion of the gland, also in the dermis. Disruption of the integrity of this area of the sweat gland, for example, might cause extensive reabsorption of secreted sweat back into the interstitial space [the "leaky hose" hypothesis as proposed by Papa and Kligman (4)]. Finally, an aluminum salt might function by blocking the flow of sweat to the skin surface through the

formation of an obstructive mass or plug at some point in the gland's duct as proposed by Reller and Leudders for $AlCl_3$ and an aluminum zirconium solution (5). This ductal blockage could occur anywhere ranging from its deepest region all the way up to its outermost poral opening in the stratum corneum.

To determine at which level of the sweat gland an antiperspirant is functioning, specific experiments, both histological and physiological, can be designed and performed. For the most part, however, such studies are extensive and involved despite their high value. Alternatively, a first step in the approach to the problem is to identify the antiperspirant's site of action without prior regard to any proposed mechanism. The sweat gland secretory coil is located in the dermal layer of the integument, but its duct passes through the viable epidermis and then the outermost stratum corneum. Techniques are available to remove those latter two layers. Blistering the skin, by occlusively patching with cantharidin, separates the dermal and epidermal layers (6). Removing the blister cap exposes the dermis. Alternatively, Scotch® tape stripping is a technique that has been widely used to remove the stratum corneum layer, thereby exposing the stratum granulosum layer of the viable epidermis. In so removing one or both of the layers, one can determine whether a given sweat gland, previously inhibited by an antiperspirant, now resumes normal firing. If firing is restored, then the site of action within the gland is at the level within the layer which had been removed. In this fashion, one at least approximates the depth in the sweat gland to which the inhibition is occurring.

The technique of Scotch® tape stripping has been used previously to determine the site of action of several antiperspirants. Papa and Kligman first demonstrated that human forearm sites, made anhidrotic by the overnight occlusive application of 20% aluminum chloride, still failed to sweat after the stratum corneum layer had been removed by stripping. They concluded that the site of action was deeper than within that layer (4). Their findings were subsequently confirmed by Gordon and Maibach (7). The findings of a later report by Zahejsky and Rovensky on aluminum chloride's site of action were somewhat inconsistent with the previous investigations. Their results indicated that anhidrosis is much more readily removable by stripping (8). However, the authors used a less agressive method of application of the test agent.

The purpose of the studies in this communication was to determine at which skin layer sweat glands had been inhibited following treatment with the marketed conventional antiperspirant salts, aluminum chlorohydrate (ACH) and aluminum zirconium chlorohydrate glycine complex (AZAP), as well as to repeat the observations by others for aluminum chloride ($AlCl_3$).

## MATERIALS AND METHODS

Both male and female adults participated in these studies. Four sites, two on the volar surface of each forearm, were selected. The sites, measuring ½-in. square, were marked with indelible ink. A template was used in order to ensure subsequent precise relocation of the sites. The subjects then entered an environmental chamber set at 100°F and 30–35% RH for thermal stress. A mixture of starch, castor oil and 2% iodine in ethanol, a modification of the original method described by Wada and Takajaki (9), was applied to the forearm sites to visualize the sweat droplets. At 20, 40 and 60 min

after the appearance of the first sweat droplets, photographs of each of the sites were taken. The subjects then left the environmental chamber and the starch mixture was removed.

Next, 0.35 ml of the antiperspirant solution was used to saturate the cotton pad portion of an impermeable mylar-backed bandage (10). The occlusive patches were applied to the skin sites and remained in place overnight. The patches were removed at not less than 3 h prior to the subjects' re-entry into the environmental chamber on the following day.

The antiperspirant test solutions were 20% aqueous ACH and 10% aqueous AZAP (each obtained as the dry powder from Wickhen Products, Inc., Hugeuenot, N.Y.), and 8% aqueous aluminum chloride (obtained as the hexahydrate salt from Fisher Scientific Co.). In each instance, the choice of concentration was based on the desire to use that concentration which could be expected to inhibit virtually all sweat glands in the test site, but which would not be so high as to irritate the skin and thus interfere with the determination of the agent's site of action. All four test sites on a subject were treated with the same solution.

At the conclusion of the treatment regimen, the subjects were again thermally stressed and photographic records of the sites were taken as described above. They then returned to ambient temperature and the starch mixture was removed. Each site was stripped to the "glistening" layer (i.e., the entire stratum corneum layer was removed, exposing the stratum granulosum layer of the epidermis) using Scotch® brand high tack tape (11). After the stripping procedure, the subjects were immediately thermally stressed again and, as before, photographic records of the sites were made.

As indicated above, at each of the three thermal stress periods, three photographs (20, 40 and 60 min after sweating had begun) were taken. The 20- and 60-min photographs, however, were principally precautionary only (i.e., to safeguard against the possibility that either coalescence of individual sweat droplets or an inadequate sweating pattern would be manifest at the 40-min interval). In the overwhelming number of instances, the evaluations discussed below were made using the 40-min photographs. For the most part, however, it was observed that the 20- and 60-min gland counts closely agreed with those seen for the 40-min period. Using these photographs, the number of actively firing sweat glands, each indicated by the black dot resulting from the starch/iodine—sweat reaction, was counted for each site before treatment, after treatment, and after stripping. With this approach, the number of sweat glands which had been inhibited by the given antiperspirant, but then had been restored to active function because of the Scotch tape stripping procedure, could be determined. A representative series of photographs is presented in Figure 1.

The data are expressed as the percentage of inhibited glands which have been restored to firing after stripping. These values are calculated as follows:

A = Number of glands observed before treatment minus the number of glands observed after treatment.

B = Number of glands observed after stripping minus the number of glands observed after treatment but before stripping.

$\frac{B}{A} \times 100$ = Percent of those inhibited glands which were restored to firing.

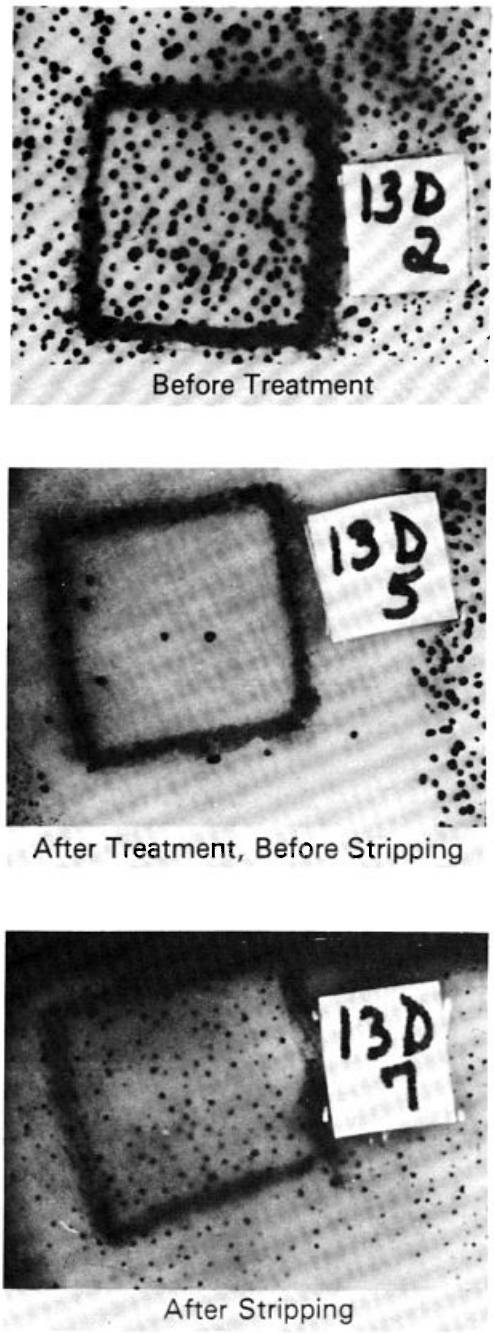


**Figure 1.** The effect of cellophane tape stripping on sweat gland function following occlusive application of 10% aqueous AZAP.

**Table I**
The Effect of Scotch® tape Stripping on Sweat Gland Function
Following Occlusive Treatment with 20% ACH[1]

| | $\bar{x}$ + S.E. | Median |
|---|---|---|
| Percentage of glands inhibited | 95 ± 2 | 98 |
| Percentage of inhibited glands restored to firing | 51 ± 6 | 50 |

[1]N = 25 subjects

For example, if the pre-treatment, post-treatment, and post-stripping values were 100, 20 and 40 respectively, then

$$\frac{40 - 20}{100 - 20} = \frac{20}{80} \times 100 = 25\% \text{ of the inhibited glands were restored to firing.}$$

## RESULTS

For the subjects studied, the number of sweat gland droplets in an experimental site prior to treatment ranged from about 100 in the less dense proximal areas to as many as 500-600 in the heavily populated distal areas. Most subjects, however, had an average of 200-300 sweat glands per site. The effect of Scotch® tape stripping on these sites subsequent to their overnight occlusive treatment with either 20% ACH, 10% AZAP or 8% $AlCl_3$ was as follows.

### ACH

The occlusive application of 20% ACH resulted in virtually total inhibition of sweat gland function, with only 5% of the treated glands able to fire under thermal stress (Table I). After Scotch tape stripping away the stratum corneum layer of the skin, however, half the number of those glands which had been inhibited were now restored to normal firing.

### AZAP

As had been seen for ACH, the overnight occlusive application of AZAP also resulted in nearly total inhibition of sweat gland function. The effect of stripping on these glands resulted in restoration, on average, of two-thirds of them to function (Table II).

**Table II**
The Effect of Scotch® tape Stripping on Sweat Gland Function
Following Occlusive Treatment with 10% AZAP[1]

| | $\bar{x}$ + S.E. | Median |
|---|---|---|
| Percentage of glands inhibited | 93 ± 2 | 97 |
| Percentage of inhibited glands restored to firing | 67 ± 9 | 66 |

[1]N = 25 subjects

**Table III**
The Effect of Scotch® tape Stripping on Sweat Gland Function Following Occlusive Treatment with 8% $AlCl_3$[1]

| | $\bar{x}$ + S.E. | Median |
|---|---|---|
| Percentage of glands inhibited | 92 ± 3 | 97 |
| Percentage of inhibited glands restored to firing | 11 ± 3 | 2 |

[1]N = 33 subjects

$AlCl_3$

Once again, 18 h of occlusive treatment nearly completely abolished sweating. However, in distinct contrast to the observations described above for ACH and AZAP, removal of the stratum corneum had little effect on restoring gland function. In fact, for 13 of the 33 subjects studied, no restoration of function whatsoever in the population of inhibited sweat glands was observed, that situation explaining the relatively large discrepancy between the average and median values for the percentage of restoration of inhibited glands (Table III).

## DISCUSSION

Not unexpectedly, the overnight occlusive application of each of the three aluminum-based antiperspirant solutions resulted in virtually complete inhibition of sweat gland function. For ACH, however, despite the high level of effectiveness, the penetration of the polymer into the sweat gland duct is not extensive, as evidenced by the finding that half the inhibited glands are restored to normal function when the 25–35 $\mu$m thick stratum corneum layer is removed.

Similarly, AZAP's site of action is also quite superficial, with two-thirds of the inhibited glands being restored to firing following the stripping away of the horny layer. Statistical evaluation of the data demonstrated that the difference between the percentage of restored AZAP-inhibited glands (67%) and ACH-inhibited glands (51%) is significant ($p < .01$). For both ACH and AZAP, the two most widely used commercial antiperspirant agents, the location of the inhibition of eccrine sweat gland function in the duct is relatively near the skin surface.

On the other hand, in stark contrast to the observations made for ACH and AZAP, removal of the stratum corneum had little effect on attempts to restore the function of those sweat glands inhibited by $AlCl_3$, indicating that the primary site of action in the sweat duct for $AlCl_3$ is deeper than the level of the stratum corneum in nearly all instances. The difference in restoration between $AlCl_3$-inhibited glands (11%) and ACH- or AZAP-inhibited glands is significant ($p < .001$). Similar findings for $AlCl_3$, although less precisely determined, have been reported by others (4,7). One possible reason for this difference in the primary sites of action between $AlCl_3$ and ACH or AZAP is that the aluminum species of $AlCl_3$, being smaller, are able to diffuse down the sweat duct more rapidly than the larger polycationic species of ACH and AZAP.

## CONCLUSIONS

The relative site of action within the sweat gland was determined for three antiperspirant agents, ACH, AZAP and $AlCl_3$ using the Scotch® tape stripping procedure. It was found that the primary site of action of ACH and AZAP was at the level of the stratum corneum layer, whereas $AlCl_3$'s site was deeper.

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