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# Antiperspirant efficacy

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**Synopsis**

ANTIPERSPIRANT EFFICACY of ALUMINUM CHLOROHYDRATE "TYPE" INGREDIENTS is discussed. The optimal efficacy for aluminum chlorohydrate and aluminum bromohydrate in aqueous solution occurs at concentrations of 15 per cent (3.75 per cent Al) and 24 per cent (5.0 per cent Al), respectively. No difference in efficacy between aluminum chlorohydrate-$AlCl_3$ combinations and aluminum chlorohydrate alone, is found. Efficacy differences are observed as a function of vehicle. For example, aqueous formulations appear to be more efficacious than anhydrous formulations. Efficacy of aluminum-zirconium compounds is discussed in terms of variation of Al:Zr ratio. No differences are found.

## INTRODUCTION

Antiperspirants as topical drugs have come under the scrutiny of FDA-OTC panels. Because of this interest and since the definition of antiperspirants is based on their efficacy, a study of the effectiveness of commonly used active ingredients would be useful. Unfortunately, there is a paucity of published information in this area. Recent papers have dealt with experimental designs and statistical interpretation of data (1,2, 3), mostly on formulated products. Since efficacy can be influenced by adjuvants in formulations, we believed an investigation of active ingredients in simple aqueous and nonaqueous vehicles worthwhile. In recognition of this information gap, we have studied the relationship between active ingredient efficacy with both concentration and solvent variations. We hope that this data will enlarge the cosmetic chemist's horizons, in developing new and improved vehicles for the application of a chosen antiperspirant.

To render this study both feasible and meaningful, we limited our investigational efforts to aluminum chlorohydrate "types" as well as aluminum-zirconium complexes.

Aluminum chlorhydrate, a 5/6 basic aluminum "salt," $Al_2(OH)_5Cl$, has been used as an antiperspirant for over 30 years (4). Other aluminum salts, such as aluminum chloride, were available as antiperspirants in the early part of the twentieth century, primarily for use by actors and models. The drawback of this product is its high acidity resulting in fabric damage and skin irritation. To circumvent this problem, buffers such as urea were used. Then in the early 1940s an internally buffered product, aluminum chlorohydrate, became available. In recent years, however, aluminum chloride has regained popularity, primarily when used in conjunction with basic aluminum "salts." In a twist of fate, aluminum chlorohydrate, which originally replaced buffered aluminum chloride systems, is now being used to buffer aluminum chloride, the dif-



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ference being that, in the latter case, 2 active ingredients are used rather than one. Some products which use 2 active ingredients also use a buffer such as urea, amino acid, or an inorganic salt to decrease acidity. Other multi-active systems consisting of aluminum and zirconium salts have also received considerable attention in recent years. The effectiveness of all these products is of critical importance to cosmetic chemists.

We will discuss the efficacy of many of these systems and some of their isologs in relation to the effects of concentration and vehicle. For example, one may reasonably ask, "Is the efficacy of aluminum chlorohydrate in aqueous formulations as effective as hydroalcoholic or anhydrous formulations?" We will try to answer questions of this type, but first, a brief review of the clinical procedure will be described.

## EXPERIMENTAL

### DATA COLLECTION*

The efficacy data were obtained using 0.5 ml applications. A gravimetric method was employed to obtain these data (1). Panelists were required to abstain from the use of all antiperspirant materials from enrollment until completion of test.

Sweating of test panelists is induced by having the panelists sit in a room maintained at 100 ± 2°F and at a relative humidity of 35 per cent. Before collection of perspiration, there is an appropriate warmup period. All data were obtained 22 h after final application of product.

### DATA TREATMENT

The geometric mean was used to calculate efficacy (2,3). In the statistical analysis, we use logarithmically transformed milligram weights. The per cent reduction is calculated as follows:

$$\text{Per cent Sweat Reduction} = [1\text{-antilog}(T' - C')] \times 100$$

where $T'$ and $C'$ are the average values of the logarithmically transformed milligram weights for the test (treated) and control (untreated) axillae.

## RESULTS AND DISCUSSIONS

### ONE-INGREDIENT FORMULATIONS

Dose response curves are normally available for drugs. Little information is available, however, on the variation of efficacy (response) with concentration (dose) for antiperspirants, when employed as topical drugs. Efficacy data for one of the more popular

*Efficacy data obtained from Hill Top Research, Inc., Miamiville, OH. For a detailed account of their method, see (1).

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antiperspirant ingredients, aluminum chlorohydrate,* at 3 different concentrations, 10, 15, and 20 per cent w/w, are summarized in Table I. These efficacy values were obtained from different test panels. Average point estimates were obtained by taking antilogarithms of the average of the logarithms at each concentration. Analysis of variance on logarithmically transformed data, in conjunction with a Neuman–Keuls range test, shows the following order of effectiveness at 95 per cent confidence limits: 15 per cent > 20 per cent, and 10 per cent. No significant statistical difference in efficacy is observed between 10 and 20 per cent concentrations. Surprisingly, the efficacy reaches a maximum, rather than a plateau. Reasons for this occurrence are unknown. We have, however, observed similar trends with other basic aluminum "salts."

Table I
Per Cent Sweat Reduction for Aluminum Chlorohydrate[a]

| | Concentration<br>10 Per Cent w/w | 15 Per Cent w/w | 20 Per Cent w/w |
|---|---|---|---|
| | 25[b] | 63 | 38 |
| | (11–38)[c] | (57–68) | (30–47) |
| | 38 | 56 | 35 |
| | (27–48) | (43–69) | (23–46) |
| | 36 | 58 | 50 |
| | (26–47) | (50–67) | (39–60) |
| | 43 | | 44 |
| | (30–55) | | (38–51) |
| | 40 | | 37 |
| | (30–49) | | (26–47) |
| | 51 | | |
| | (35–56) | | |
| | 46 | | |
| | (39–53) | | |
| Average | 39[d] | 59 | 40 |

[a]Chlorhydrol.®
[b]Point estimate per cent sweat inhibition.
[c]Per cent confidence limits.
[d]Antilogarithm of average logarithms at each concentration.

Table II
Per Cent Sweat Reduction for Aluminum Bromohydrate[a]

| Concentration Per Cent w/w | Per Cent Sweat Reduction | 95 Per Cent Confidence Limits |
|---|---|---|
| 10 | 52 | 43–61 |
| 24 | 63 | 60–66 |
| 28 | 51 | 46–56 |
| 36 | 46 | 38–54 |
| 43 | 46 | 39–53 |

[a]B.A.B.®

*In our studies, we used Chlorhydrol®, a product of Reheis Chemical Company, Division of Armour Pharmaceutical Company, Berkeley Heights, NJ 07922.

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For example, an isolog of aluminum chlorohydrate is aluminum bromohydrate.* Efficacy data for this product are shown in Table II. Again, we observe a peaking effect. In this case, however, the maximum efficacy occurs at 24 per cent (5 per cent Al), whereas for aluminum chlorohydrate the maximum efficacy occurs at 15 per cent (3.75 per cent Al).

While the analysis shows a maximum for dose-response data, we are not totally convinced that this peaking effect is real. To help resolve this problem, we plan to run multiple crossover studies with aluminum chlorohydrate at several different concentrations.

### ALCOHOL SOLUBLE ANTIPERSPIRANTS

Since many new products on the market use anhydrous or hydroalcoholic vehicles rather than predominantly aqueous ones, we explored the effect of solvent on antiperspirant activity.

Most nonaqueous formulations use an aluminum chlorohydrate "type" complex alone or in conjunction with $AlCl_3$. Since we already know the efficacy of aluminum chlorohydrate in aqueous systems at different concentrations (Table I), it would be instructive to compare the effectiveness of one of these systems with an analogous hydroalcoholic formulation. Table III shows the per cent sweat inhibition for a 50 per cent ethanol solution of aluminum chlorohydrate at 20 per cent to be 41 per cent. The alcohol has not attenuated the activity of this product, as can be seen by comparing the above efficacy with that in Table I (39 per cent) for the same product at an identical concentration. We have observed similar results for Al-Zr combinations. While hydroalcoholic systems are as efficacious as aqueous systems in the formulations studied, some reduction in activity for anhydrous systems has been noted.

Table III
Per Cent Sweat Reduction for Alcohol Soluble Antiperspirants

| Antiperspirant[a] | Per Cent Sweat Reduction | 95 Per Cent Confidence Limits |
|---|---|---|
| Aluminum chlorohydrate[b] propylene glycol complex | 21 | 9-31 |
| Alcohol soluble[c] aluminum chlorohydrate | 47 | 40-55 |
| Aluminum chlorohydrate[d] | 41 | 31-52 |

[a]All solutions made up to 5 per cent Al in SDA-39C.
[b]Rehydrol®, Reheis Chemical Company, Division of Armour Pharmaceutical Company, Berkeley Heights, N.J. 07922.
[c]A.S.C.®, Reheis Chemical Company, Division of Armour Pharmaceutical Company, Berkeley Heights, N.J. 07922.
[d]50 per cent hydroalcoholic solution.

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Two different type alcohol soluble products, which are applicable for anhydrous systems, are aluminum chlorohydrate-propylene glycol complex (A) and alcohol soluble aluminum chlorohydrate (B). Table III shows per cent sweat reduction values for these 2 materials at identical aluminum concentrations. The efficacy of B is greater than A. The difference in results may be a function of the water content of the active ingredient and, hence, the ethanol-water balance of the formulation. For example, the 20 per cent alcoholic aluminum chlorohydrate system contains *ca.* 4 per cent water, whereas the 25 per cent aluminum chlorohydrate-propylene glycol complex system contains a maximum 1 per cent water. It is possible that small amounts of water are necessary to catalyze antiperspirant activity of the metal salt. We plan to study thoroughly the relationship, if any, that exists between ethanol:water ratios and efficacy for a variety of alcohol soluble antiperspirants.

### MULTI-INGREDIENT FORMULATIONS

In the evolution of antiperspirant formulation technology, combination systems of 2 or more active ingredients have recently generated much interest.

Today, many cosmetic chemists prefer 2 active ingredients in their formulation instead of one component systems. For example, many formulators use aluminum chlorohydrate-$AlCl_3$ combinations. One reason for interest in these systems is the belief that more acidic products (e.g., aluminum chlorohydrate + $AlCl_3$) have superior efficacy. There are hypotheses which correlate efficacy with pH. For example, the interaction of aluminum salts with skin protein is a function of pH (5). This type of reaction has been proposed as a possible mechanism for antiperspirant activity.

Table IV.
Per Cent Sweat Reduction for Aluminum Chloro- and Bromohydrate-$AlC_3$ Combinations

| Concentration Per Cent w/w | Al:Cl Ratio 1:1 | Al:Cl Ratio 2:1 | Al:Br Ratio 1:1 | Al:Br Ratio 2:1 |
|---|---|---|---|---|
| 10 | 35[a] (23–48)[b] | 44 (33–56) | 52 (41–62) | 52 (53–63) |
| 20 | 49 (38–59) | 38 (27–48) | — | — |

[a]Point estimate per cent sweat inhibition.
[b]95 per cent confidence limits.

Table V
Per Cent Sweat Reduction for Al-Zr Complexes at Different Ratios

| Al:Zr Ratio[a] | Per Cent Sweat Reduction[b] |
|---|---|
| 0.5:1 | 45–<u>54</u>–66 |
| 2.0:1 | 50–<u>58</u>–68 |
| 4.0:1 | 48–<u>59</u>–70 |
| 6.0:1 | 50–<u>60</u>–69 |

[a]All at 10 per cent w/w.
[b]Point estimate underlined. Outer points at 95 per cent confidence limits.

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For example, the maximum reaction of aluminum chloride with skin protein occurs at a pH of 3.51, with the binding of aluminum falling off sharply on either side of the pH. At low pH levels, skin protein exhibits a decreased activity for aluminum ions due to the existence of its carboxyl groups predominantly as the undissociated —COOH species. At high pH levels, the carboxyl groups are ionized to the $—COO^{-}$ state. Consequently, their interaction with aluminum would be expected to be enhanced. In light of the foregoing, it seems reasonable that sweat reduction mediated via the use of antiperspirants could be a function of pH, assuming that the mechanism of such activity is controlled by the precipitation of skin protein with the basic aluminum species.

Table IV compares efficacy results for aluminum chloro- and bromohydrate "types" with Al:halide ratios of 2:1 and 1:1. No significant difference between these lower and higher ratio products is evident for these aqueous formulations. It is, of course, possible that the more acidic species are skin irritants and, therefore, act antagonistically (i.e., as "properspirants"), thereby attenuating the properties of the aluminum complex.

In the search for new and effective antiperspirants, aluminum-zirconium combinations have aroused interest. We will only be concerned with nonaerosol aqueous formulations. Table V lists the efficacy for Al-Zr products, with Al:Zr ratios varying from 0.5:1 to 6:1. No significant differences in efficacy from product to product are evident. In general, it appears as if the effectiveness of these systems is comparable with 15 per cent aluminum chlorohydrate. It is believed, however, that these Al-Zr systems, once formulated, retain a higher proportion of their activity than aluminum systems; that is to say, their effectiveness appears less influenced by the chemical environment represented by the formulation medium.

## SUMMARY

To summarize, we believe that, based on our data, the efficacy of some antiperspirant materials peaks at a particular concentration rather than reaching a plateau. Reasons for this effect are unknown. Vehicle also plays a role in controlling efficacy. For example, anhydrous systems have a lower efficacy than aqueous or hydroalcoholic formulations. Our data regarding the relationship between efficacy and vehicle are limited. We plan to fill in this gap, in the near future, by studying the relationship between ingredient efficacy and vehicle as well as variations in Al:Cl ratio and concentration. Finally, we have found that the efficacy of aluminum-zirconium complexes is independent of Al:Zr ratio.

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