

## Potentiometric/turbidometric titration of antiperspirant actives

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### Synopsis

A titration procedure that simultaneously monitors the pH and turbidity of an antiperspirant solution during neutralization with sodium hydroxide was developed to characterize antiperspirant actives. Aluminum chloride, aluminum chlorohydrate (ACH), and aluminum zirconium glycine complex (AZG) gave distinctive pH/turbidity profiles. The activated forms of aluminum chlorohydrate (ACH') and aluminum zirconium glycine complex (AZG') produced more turbidity than the non-activated forms. On an equimolar basis, AZG' produced more turbidity than any of the antiperspirant actives tested.

### INTRODUCTION

Antiperspirants are water-soluble compounds that diffuse into the sweat duct and produce an insoluble phase when exposed to sweat. The precipitate physically plugs the sweat duct (1). This mechanism was first proposed by Reller and Luedders (2) and was supported by other investigators (3–7). The major antiperspirant actives currently in use are ACH and AZG. Teagarden *et al.* (8) demonstrated that ACH solutions become turbid when diluted with deionized water. The insoluble material was identified by infrared spectroscopy as gibbsite, a polymorph of aluminum hydroxide.

Standards for ACH and related compounds, as well as complexes related to AZG, are given in *The United States Pharmacopoeia* (9). Tests to characterize ACH (10) or AZG (11) have been recently described. However, none of the standards or tests are related to the ability to precipitate in the sweat duct. Thus, a study that combined potentiometric and turbidometric titration was undertaken in an attempt to characterize the precipitation behavior of antiperspirant actives. This approach expands on the standard potentiometric

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titration of aluminum chloride (12) and provides an optical method to determine the onset and extent of precipitation.

## MATERIALS AND METHODS

The antiperspirant actives studied were ACH (Chlorhydrol PDR, Reheis, Berkeley Heights, NJ), ACH' (Reach-101, Microdry, Reheis), AZG (Westchlor ZR 30B, Westwood, Middletown, NY), and AZG' (Westchlor ZR 30B DM XF, Westwood).

The apparatus used for the potentiometric/turbidometric titration is shown in Figure 1. Twenty-five milliliters of antiperspirant solution, adjusted to 0.1 M in metal ion (either Al or Al plus Zr) with double distilled water, was placed in the reaction vessel. An automatic titrator (Radiometer) added 0.5 N NaOH to the reaction vessel and recorded the pH. The contents of the reaction vessel were circulated through a 1-cm pathlength flow-through optical transmission cell using a peristaltic pump. The flow rate was 100 ml/min. The volume of the flow-through cell and lines was 10 ml. The absorbance was recorded at 600 nm using a  $\lambda 19$  UV-visible spectrometer (Perkin Elmer).

## RESULTS AND DISCUSSION

The potentiometric/turbidometric titrigrath of 0.1 M  $\text{AlCl}_3$  is shown in Figure 2. Both the pH and turbidity increased slowly until approximately 12 ml of 0.5 N NaOH was added. Both the pH and turbidity increased rapidly at this point. The maximum turbidity occurred when 13.2 ml of base was added. The pH was 7.4 at this point. The

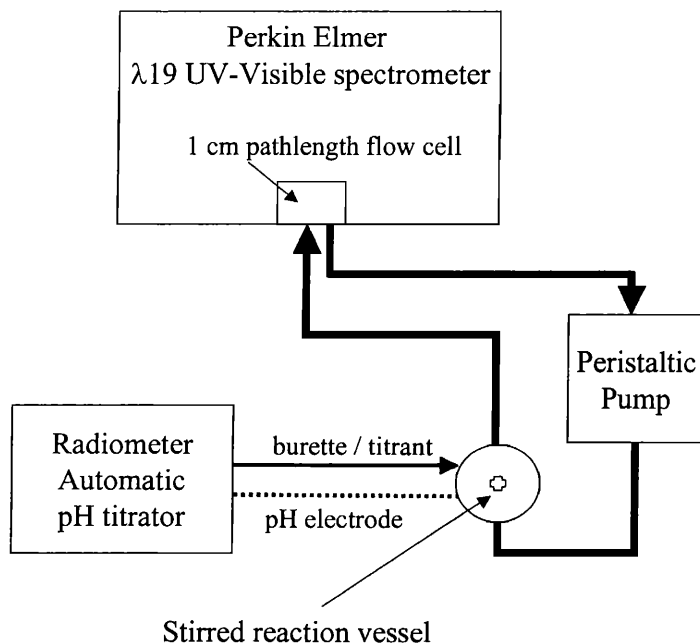


Figure 1. Schematic of the potentiometric/turbidometric titration apparatus.

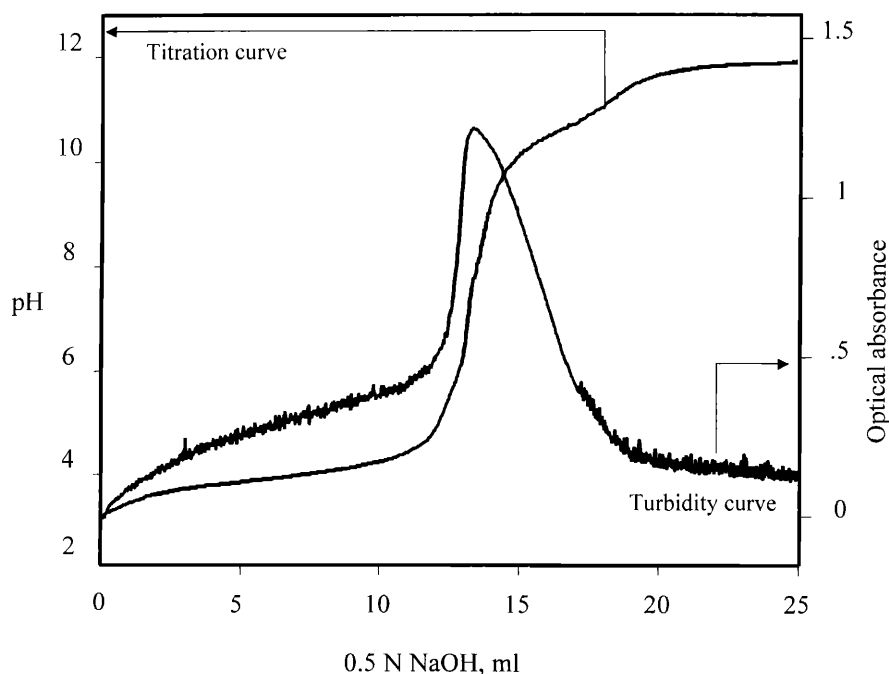


Figure 2. Potentiometric/turbidometric titrighraph of 25 ml of 0.1 M  $\text{AlCl}_3$  titrated against 0.5 N NaOH.

turbidity decreased as more base was added. The precipitate had dissolved when 19.2 ml of the base (pH 11.6) was added.

The potentiometric/turbidometric titrighraph is consistent with the properties of aluminum chloride and the pH-solubility profile of aluminum hydroxide. The relatively constant pH observed until approximately 12 ml of base had been added indicates that the added hydroxyls were coordinated to aluminum ions and thus did not significantly raise the pH. Polymerization of the hydroxy-aluminum species began at this point, and the turbidity increased sharply. The pH also increased sharply at this point, as the added hydroxyls were not completely coordinated to aluminum (13). The dissolution of the precipitate as the titration proceeded above pH 7.4 is believed to be due to the amphoteric nature of aluminum. The minimum solubility of aluminum hydroxide occurs at pH 5.8 (14). Thus, the dissolution of the precipitate when the pH was above 7.4 reflects the conversion of  $\text{Al}(\text{OH})_3$  to soluble aluminate anion ( $\text{Al}(\text{OH})_4^-$ ). Based on the turbidity curve, the precipitate dissolved after 19.2 ml of base was added.

The potentiometric/turbidometric titrighraph of ACH is shown in Figure 3. Formation of a precipitate required much less base than was required for aluminum chloride. The pH increased sharply from the beginning of the titration. The turbidity increased after the addition of approximately 1 ml of 0.5 N NaOH. The maximum turbidity occurred when 4.0 ml of 0.5 N NaOH was added. At this point, the pH was 11.7. The precipitate completely dissolved after 6.3 ml of 0.5 N NaOH was added. This point corresponds to a pH of 12.0.

ACH required much less base to initiate precipitation than aluminum chloride because it is partially neutralized (10). Consequently, the starting pH of 0.1 M ACH solution

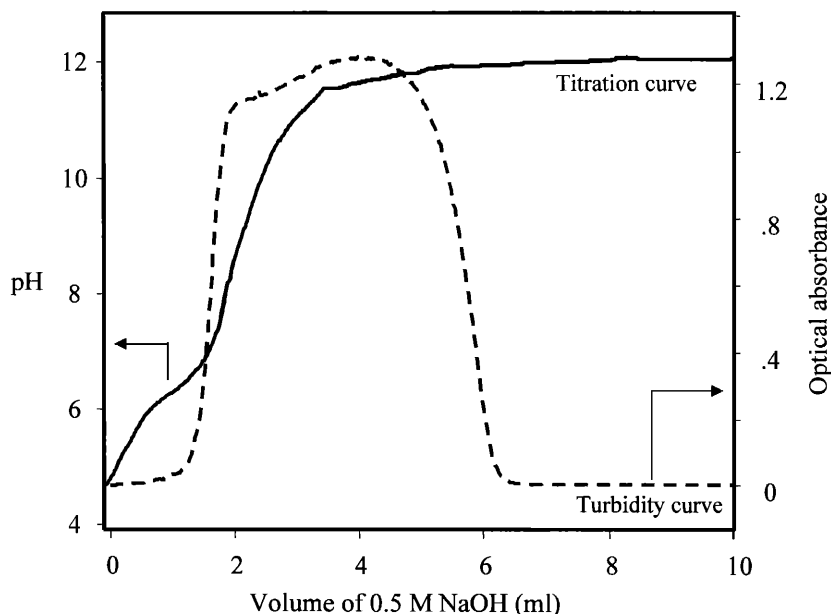


Figure 3. Potentiometric/turbidometric titrigrath of 25 ml of 0.1 M ACH titrated against 0.5 N NaOH.

was 4.5 (Figure 3) compared to a starting pH of approximately 3.0 for 0.1 M  $\text{AlCl}_3$  (Figure 2). A practical consequence of this higher initial pH is that ACH produces less skin irritation and less damage to clothing than aluminum chloride (15).

The potentiometric/turbidometric titrigrath of AZG is shown in Figure 4. The turbid-

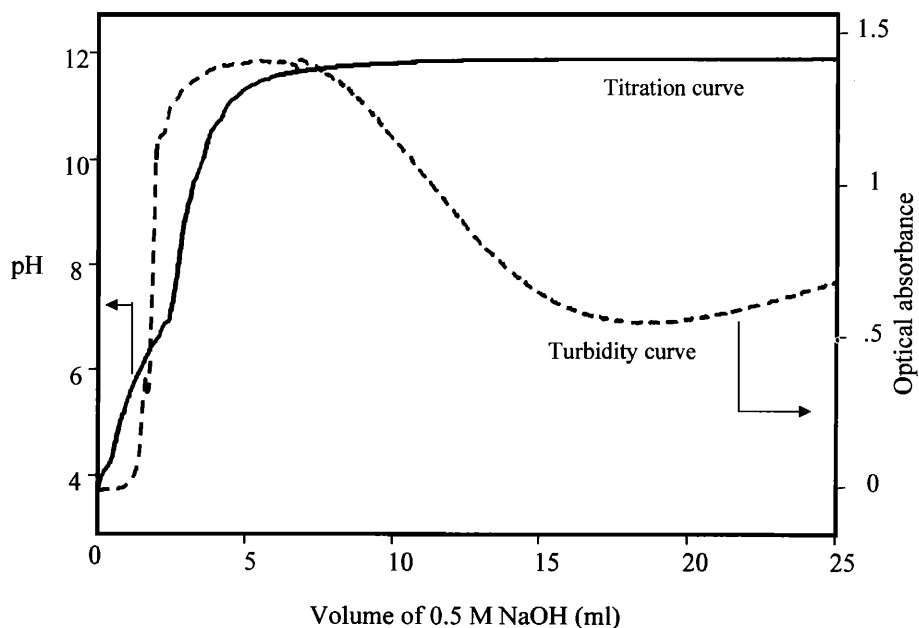


Figure 4. Potentiometric/turbidometric titrigrath of 25 ml of 0.1 M AZG titrated against 0.5 N NaOH.

ity did not increase until 1.4 ml of 0.5 N NaOH was added. However, the pH increased from the beginning of the titration. The turbidity reached a maximum when approximately 5.0 ml of 0.5 N NaOH was added. The pH was 11.3 at this point. Continued addition of base led to the partial dissolution of the precipitate. No attempt was made to identify the precipitate, but it had different properties from the precipitates produced by aluminum chloride or ACH, as these precipitates were completely soluble at high pH. We propose that the precipitate produced by AZG is a mixture of aluminum hydroxide and zirconium hydroxide. Aluminum hydroxide is soluble in both acid and base while zirconium hydroxide is soluble only in acid (16). Thus, the decrease in turbidity at high pH may be due to the dissolution of the aluminum hydroxide phase but not the zirconium hydroxide phase. Research is needed to characterize the precipitate produced from AZG.

Although ACH and AZG are the most widely used antiperspirants, advances in their preparation have led to activated ACH (10) and activated AZG (11). AZG' is generally recognized as the most effective antiperspirant active currently in wide use (10,11). The potentiometric/turbidometric titrations of aluminum chloride, ACH, ACH', AZG, and AZG' were determined in order to compare their abilities to form precipitates. For clarity, only turbidometric titrations are shown in Figure 5. The aluminum chloride turbidometric titrations suggest a lower plug-forming capability and possibly a lower antiperspirant efficacy. This conclusion is not consistent with reports that aluminum chloride inhibits sweating by 60% to 70% and that ACH- or AZG-containing products inhibit sweating by 30% to 55% (2,17). It was hypothesized that lower-molecular-weight species, such as aluminum chloride, can diffuse more deeply into the sweat ducts because of their small size (2). In addition, it was proposed that precipitation from aluminum chloride, in a sweat duct with limited buffer capacity, would occur at a slower rate and produce an occlusive plug in the sweat duct at a greater depth because of the higher neutralization requirement (2). Other researchers have suggested that aluminum

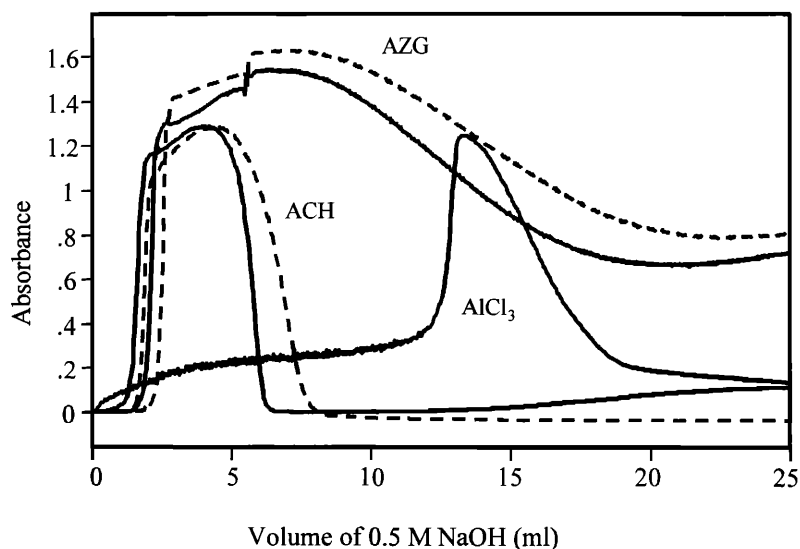


Figure 5. Turbidometric titrations of 0.1 M  $\text{AlCl}_3$ , 0.1 M ACH, 0.1 M ACH', 0.1 M AZG, and 0.1 M AZG' titrated against 0.5 N NaOH. The dashed curves represent ACH' and AZG'.

chloride achieves its antiperspirant effectiveness by destruction of the integrity of the acrosyringium or by a non-specific anti-inflammatory effect (2,18).

The difference between the precipitates formed from ACH and ACH' is seen in the greater volume of base required to completely dissolve the precipitate formed from ACH'. A similar trend is evident in the comparison of AZG' and AZG. Furthermore, on a molar basis, AZG' produced the largest turbidity value of any of the antiperspirant actives tested. This property may be partly responsible for the high degree of efficacy attributed to AZG' (10,11).

The experimental approach used in this study provides new insight into the precipitation behavior of antiperspirant actives. The potentiometric/turbidometric titration technique may prove useful in establishing specifications for antiperspirant actives.

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