

Figure 4—Comparative permeability of aspirin (curve 3), methylthiomethyl 2-acetoxybenzoate (III) (curve 1), and methylsulfinylmethyl 2-acetoxybenzoate (IV) (curve 2) through hairless mice skin.

while the major part, ~70% of the dose penetrating the skin, is hydrolyzed in the skin to salicylic acid during absorption (Fig. 1).

The hydrolysis half-life of the methylthiomethyl derivative (III) to aspirin was ~10 min and that of VI to salicylic acid, at 30° and pH 5.4, was ~9 min. If any significant amounts of aspirin are formed during passage through the skin or if III penetrates the skin without being metabolized, aspirin would be detected in the receptor phase. On the other hand, only salicylic acid was found when III was applied to the skin, which means that III is metabolized in the skin to VI or salicylic acid or both (Fig. 2).

The hydrolysis half-life of the methylsulfinylmethyl derivative (IV) to aspirin was ~10 days and that of VII to salicylic acid, at 30° and pH 5.4, was ~6 days. Thus, very little hydrolysis should occur in the receptor phase and almost all metabolites of IV detected in the receptor phase must be formed in the enzymatic cleavage in the skin. No aspirin was detected in the receptor phase after application of IV to the skin; only large amounts of VII and salicylic acid were found (Fig. 3). These results indicate that ~57% of IV penetrating the skin is metabolized to VII and that ~43% of IV is metabolized to salicylic acid.

The comparative cumulative penetration profiles for aspirin, III, and

IV are shown in Fig. 4. The methylthiomethyl derivative (III) of aspirin is absorbed at a rate about two times faster than that of aspirin, while the methylsulfinylmethyl derivative (IV) is absorbed at the same rate as aspirin within experimental error.

It is clear that significant metabolism of all salicylic acid derivatives, including aspirin and its prodrugs, occur in the fresh mouse skin. The various ester functions hydrolyze with different rates and in a different order than what was shown to be their chemical hydrolysis or enzymatic cleavage in plasma or after the intravenous *in vivo* administration. The amounts penetrating the skin, however, are significant. It is possible to achieve therapeutic levels either as keratolytic or anti-inflammatory or analgesic agents. Further *in vivo* studies should be performed to answer these questions.

REFERENCES

- (1) D. E. Duggan, K. F. Hooke, R. M. Noll, H. B. Hucker, and C. G. Van Arman, *Biochem. Pharmacol.*, **27**, 2311 (1978).
- (2) J. R. DeBaun and J. J. Menn, *Science*, **191**, 187 (1976).
- (3) H. P. Baden, in "Recent Advances in Dermatopharmacology," P. Frost, E. C. Gomez, and N. Zaias, Eds., Spectrum New York, N.Y., 1977, p. 2.9.
- (4) J. R. Vane, *J. Allergy Clin. Immunol.*, **58**, 691 (1976).
- (5) E. Aron, B. Delbarre, and J. C. Besnard, *Therapie*, **31**, 247 (1976).
- (6) E. G. Weirich, J. K. Longauer, and A. K. Kirkwood, *Dermatologica*, **152**, 87 (1976).
- (7) A. Rannatier, P. Jenner, B. Testa, and J. C. Etter, *Drug Metab. Rev.*, **8**, 319 (1978).
- (8) W. C. Schneider, *J. Biol. Chem.*, **176**, 259 (1948).
- (9) T. Loftsson and N. Bodor, *J. Pharm. Sci.*, **70**, 750 (1981).
- (10) M. Katz and B. J. Poulsen, in "Handbook of Experimental Pharmacology," B. B. Brodie and J. Gillett, Eds., Springer-Verlag, Berlin, Germany, 1971, chap. 7.
- (11) T. Higuchi, *J. Soc. Cosmet. Chem.*, **11**, 85 (1960).
- (12) R. J. Scheuplein, I. H. Blank, G. J. Brauner, and D. J. MacFarlane, *J. Invest. Dermatol.*, **52**, 63 (1969).
- (13) T. Nakagawa, M. Takehara, and H. Oishi, *Chem. Pharm. Bull.*, **24**, 1774 (1976).
- (14) J. L. Fox, C. D. Yu, W. I. Higuchi, and N. F. H. Ho, *Int. J. Pharm. Sci.*, **2**, 41 (1979).
- (15) J. Albery and J. Hadraft, *J. Pharm. Pharmacol.*, **31**, 129 (1979).
- (16) W. Meyer and N. Neurand, *Lab. Animals*, **10**, 237 (1976).

Aluminum Chlorohydrate I: Structure Studies

DIRK L. TEAGARDEN*, JOHN F. KOZLOWSKI‡, JOE L. WHITE§, and STANLEY L. HEM*^x

Received October 3, 1980, from the *Department of Industrial and Physical Pharmacy, the †Department of Medicinal Chemistry and Pharmacognosy, and the §Department of Agronomy, Purdue University, West Lafayette, IN 47907. Accepted for publication December 8, 1980.

Abstract □ X-ray diffraction and IR and ²⁷Al-NMR spectroscopy indicate that aluminum chlorohydrate is composed of a central aluminum in a tetrahedral configuration surrounded by 12 aluminum atoms in octahedral configuration. The complex, Al₁₃O₄(OH)₂₄(H₂O)₁₂⁷⁺, is essentially spherical, with the +7 charge equally distributed on the surface. Seven chloride ions are associated with the complex as counterions. This structure is consistent with both the method of synthesis and the proposed mechanisms of antiperspirant activity.

Keyphrases □ Aluminum chlorohydrate—structure proposed by X-ray diffraction and IR and ²⁷Al-NMR spectroscopy □ X-ray diffraction—aluminum chlorohydrate, structure proposed □ Spectroscopy, IR—aluminum chlorohydrate, structure proposed □ ²⁷Al-NMR spectroscopy—aluminum chlorohydrate, structure proposed □ Antiperspirant activity—aluminum chlorohydrate, structure proposed based on X-ray diffraction and IR and ²⁷Al-NMR spectroscopic studies

Aluminum chlorohydrate, a basic aluminum complex, is widely used for its antiperspirant activity, for sealing porous strata in oil drilling operations, and to control the viscosity of kaolinite clays. It is known as aluminum

chlorohydrate, aluminum hydroxychloride, basic aluminum chloride, or chlorhydrol. The empirical formula, Al₂(OH)₅Cl·2H₂O, is known (1), but the structure has not been characterized. The chemistry of partially hydrolyzed

aluminum solutions has been studied extensively, and various aluminum species have been proposed. At high degrees of hydrolysis, which is suggested by the hydroxyl to aluminum ratio of 2.5 in the empirical formula, the proposed aluminum species include: $\text{Al}_6(\text{OH})_{12}(\text{H}_2\text{O})_{12}^{6+}$ (2), $\text{Al}_8(\text{OH})_{20}^{8+}$ (3, 4), $\text{Al}_{13}\text{O}_4(\text{OH})_{24}(\text{H}_2\text{O})_{12}^{7+}$ (5-10), $\text{Al}_{14}(\text{OH})_{34}^{8+}$ (11, 12), $\text{Al}_{10}(\text{OH})_{22}(\text{H}_2\text{O})_{16}^{8+}$ to $\text{Al}_{54}(\text{OH})_{144}(\text{H}_2\text{O})_{38}^{18+}$ (13), $\text{Al}_6(\text{OH})_{16}(\text{H}_2\text{O})_{4-5}^{2+}$ (14), $\text{Al}_6(\text{OH})_{15}\text{O}^{1+}$ (14), and $\text{Al}_{20}\text{-Al}_{200}$ (15).

This study investigated the structure of aluminum chlorohydrate using X-ray diffraction and IR and ^{27}Al -NMR spectroscopy.

EXPERIMENTAL

X-Ray Diffraction—Commercial aluminum chlorohydrate¹ solutions [50% (w/w)] were air dried, and a powder was prepared by trituration in an agate mortar and pestle. Randomly oriented powder samples were prepared in McCreery mounts. Diffractograms were recorded² from 4 to 60° 2θ under the following conditions: CuK_α radiation, 30 kv, 28 mamp, 1000 cps, and 2°/min.

The molecular dimension of aluminum chlorohydrate was determined by examining the increase in the interlayer spacing of montmorillonite as a result of intercalation of aluminum chlorohydrate. Approximately 50 ml of a 0.69% suspension of sodium-saturated montmorillonite was centrifuged at 5000 rpm for 5 min. The supernate was discarded, and the clay was resuspended in 50 ml of a 25% (w/w) aluminum chlorohydrate solution. The suspension was centrifuged as described, and the clay was resuspended in a second portion of aluminum chlorohydrate solution.

The process was repeated a total of four times to ensure complete saturation of the clay by aluminum chlorohydrate. The aluminum chlorohydrate-saturated montmorillonite was washed four times with double-distilled water by following the described procedure and then was air dried and stored in a vacuum desiccator. X-ray diffractograms were recorded while using special precautions to avoid the adsorption of water by the clay (16).

IR Spectroscopy—Air-dried aluminum chlorohydrate was incorporated into potassium bromide pellets, and the IR spectrum was recorded³.

NMR Spectroscopy—Aluminum chlorohydrate solutions were diluted with deuterium oxide to produce solutions that were 1 M in aluminum. The ^{27}Al -NMR spectrum was obtained at 20.723 MHz and 18.7 kg⁴. Potassium aluminum sulfate (0.1 M) in acidified deuterium oxide at pH 1 was the reference. The chemical shift of tetrahedral aluminum in aluminate, $\text{Al}(\text{OH})_4^-$, was determined from a solution of aluminum chloride titrated with sodium deuteroxide to the soluble region above pH 10.

RESULTS AND DISCUSSION

An X-ray diffractogram of aluminum chlorohydrate characteristic of all of the commercial samples is shown in Fig. 1. A broad peak occurred in the range of 4–10° 2θ, indicating a *d*-spacing of 11.8 Å. The X-ray diffractogram indicated a poorly ordered material. The line broadening at 11.8 Å suggested a crystallite dimension that is normal to the reflecting planes *hkl* of ~50 Å. No well-crystallized forms of aluminum hydroxide such as gibbsite or bayerite were seen.

To estimate the size of the aluminum chlorohydrate complex, montmorillonite was used as a molecular caliper (17, 18). The X-ray diffractograms indicated that the interlayer spacing of montmorillonite increased by 8.9 Å as a result of aluminum chlorohydrate intercalation. Thus, the minimum dimension of aluminum chlorohydrate is believed to be 8.9 Å.

The proposed structures of highly hydrolyzed aluminum species were

¹ Lot 8473, Wicken Products, Huguenot, N.Y.; Chlorhydrol, lots 6178 and 5880, Reheis Chemical Co., Berkeley Heights, N.J.; Astringen, lot 4445, Robinson Wagner, Mamaroneck, N.Y.; lot 6138, Delmar, Elk Grove Village, N.Y.; and lot 735, Summit Research Laboratories, Somerset, N.J. All commercial samples gave similar X-ray diffractograms and IR and ^{27}Al -NMR spectra. All data in this report were obtained using lot 8473, Wicken Products, Huguenot, N.Y.

² Siemens AG Kristalloflex 4 generator, type F diffractometer, Karlsruhe, West Germany.

³ Model 180, Perkin-Elmer Corp., Norwalk, Conn.

⁴ FT-80, Varian Associates, Palo Alto, Calif.

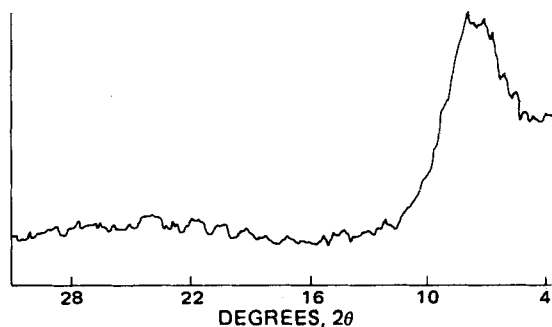


Figure 1—X-ray diffractogram of aluminum chlorohydrate.

examined to determine if any species has a dimension of ~8.9 Å. The $\text{Al}_{13}\text{O}_4(\text{OH})_{24}(\text{H}_2\text{O})_{12}^{7+}$ complex is essentially spherical and is closest in size, 9 Å (6), to the experimentally determined size of aluminum chlorohydrate.

The empirical formula for aluminum chlorohydrate, $\text{Al}_2(\text{OH})_5\text{Cl}\cdot 2\text{H}_2\text{O}$ (1), gives an aluminum to chloride ratio of 2:1, an aluminum to water ratio of 1:1, and an hydroxyl to aluminum ratio of 2.5:1 and compares well to the formula for the $\text{Al}_{13}\text{O}_4(\text{OH})_{24}(\text{H}_2\text{O})_{12}^{7+}$ complex if seven chloride anions are assumed to be present to neutralize the charge of the complex. The aluminum to chloride ratio of the proposed complex is 13:7 or ~2:1, and its aluminum to water ratio is 13:12 or approximately equal to the 1:1 ratio of the empirical formula. Its hydroxyl to aluminum ratio is 24:13. However, the four oxygen atoms in the proposed complex would appear as eight hydroxyl anions by the techniques commonly used to establish the stoichiometry of aluminum compounds (19). Therefore, the hydroxyl to aluminum ratio of the proposed complex would appear to be 32:13 or ~2.5:1, as for the empirical formula.

The excellent fit of the stoichiometry of the $\text{Al}_{13}\text{O}_4(\text{OH})_{24}(\text{H}_2\text{O})_{12}^{7+}$ complex to the empirical formula for commercial aluminum chlorohydrate further supports the hypothesis that the $\text{Al}_{13}\text{O}_4(\text{OH})_{24}(\text{H}_2\text{O})_{12}^{7+}$ complex is the structure of aluminum chlorohydrate. The small differences between the generally accepted empirical formula and the hypothesized structure may be due to the minor presence of other aluminum species in aluminum chlorohydrate and to the relatively nonspecific methods used for establishing the empirical formula.

The structure of the $\text{Al}_{13}\text{O}_4(\text{OH})_{24}(\text{H}_2\text{O})_{12}^{7+}$ complex is shown in Fig. 2. This structure is unusual since it contains a central aluminum atom

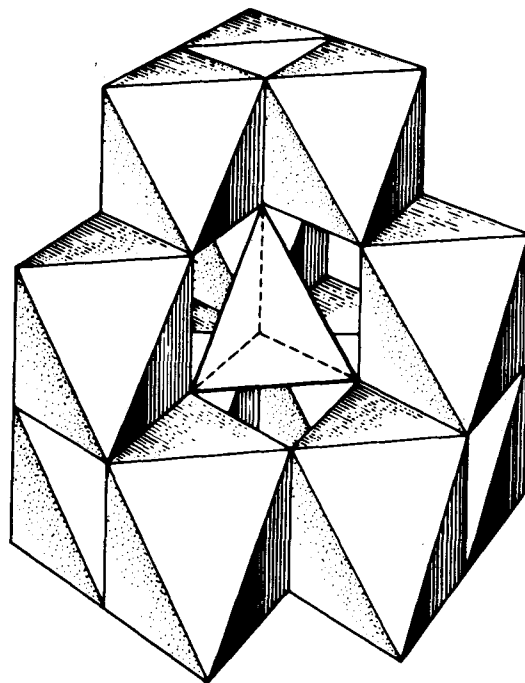


Figure 2—Structure of the $\text{Al}_{13}\text{O}_4(\text{OH})_{24}(\text{H}_2\text{O})_{12}^{7+}$ complex showing the tetrahedral aluminum surrounded by 12 aluminums in octahedral configuration. (Reproduced, with permission, from Ref. 8.)

in a tetrahedral environment surrounded by 12 aluminum atoms in octahedral environments. Aluminum in a tetrahedral environment is characterized by aluminate, $\text{Al}(\text{OH})_4^-$, which only exists at high pH conditions. Aluminum in octahedral configuration occurs at neutral and acidic pH conditions and is the configuration of aluminum in aluminum hydroxide. Thus, aluminum chlorohydrate was examined by IR and ^{27}Al -NMR spectroscopy to determine if aluminum was present in both octahedral and tetrahedral environments.

IR spectra have been published for aluminum chlorohydrate, aluminum hydroxide chloride, aluminum hydroxide, and hydrolyzed alumina (20–24). Based on these reports, the $3700\text{--}3400\text{-cm}^{-1}$ region should show hydroxyl-stretching vibrations for ionic or surface hydroxyl anions. The hydroxyl-stretching vibrations of aluminum in octahedral configuration, $\text{Al}(\text{H}_2\text{O})_6^{3+}$, should occur between 3100 and 2500 cm^{-1} . The region of $1200\text{--}800\text{ cm}^{-1}$ should show absorption bands for the deformation of Al-O-H or Al-OH-Al . Absorption bands for the rocking of coordinated water and the vibrations of AlO_6 octahedra should occur below 800 cm^{-1} . IR absorption bands for aluminum in tetrahedral configuration were assigned as follows based on the IR spectrum of aluminate, $\text{Al}(\text{OH})_4^-$: 725 cm^{-1} , AlO_4 antisymmetric stretching; 625 cm^{-1} , AlO_4 symmetric stretching; and 325 cm^{-1} , AlO_4 antisymmetric bending (25). The 800-cm^{-1} band in synthetic trioctahedral analogs of kaolinite was assigned as Al-O tetrahedral vibrations (26).

Figure 3 shows the hydroxyl-stretching region of the IR spectrum of aluminum chlorohydrate. Riesgraf and May (20) assigned the 3400-cm^{-1} band to the stretching of hydroxyl anions bound to aluminum. Bands between 3000 and 2500 cm^{-1} were attributed to antisymmetric and symmetric stretching of water coordinated to aluminum. No changes were observed in this region of the IR spectrum during aging, as was observed for aluminum hydroxide (22, 23).

Figure 4 shows the IR spectrum of aluminum chlorohydrate for the $1200\text{--}300\text{-cm}^{-1}$ region. The 1080-cm^{-1} band was assigned as Al-O-H bending of bridge hydroxyl anions, and the 970-cm^{-1} band was assigned as Al-OH deformation bending of Al-OH and Al-OH_2 (20). The bands at 780 and 640 cm^{-1} were observed previously but not assigned (20). Based on the assignments of aluminum in a tetrahedral environment (25, 26), the bands at 780 , 640 , and 345 cm^{-1} (Fig. 4) can be assigned as an AlO_4 antisymmetric stretch frequency, an AlO_4 symmetric stretch frequency, and an AlO_4 antisymmetric bending frequency, respectively. Both the AlO_4 antisymmetric stretching and AlO_4 symmetric stretching bands occurred at higher frequencies than were observed in aluminate, $\text{Al}(\text{OH})_4^-$. This finding indicates that a slightly longer Al-O bond is present in the tetrahedral aluminum of aluminum chlorohydrate in comparison to aluminate. Thus, the IR spectrum of aluminum chlorohydrate clearly shows the presence of aluminum in both octahedral and tetrahedral configurations and suggests that the tetrahedral aluminum interacts with the octahedral aluminum atoms.

^{27}Al -NMR spectroscopy has been used to investigate aluminum complexes in solution (9, 25, 27–36). The ^{27}Al -NMR spectrum of aluminum chlorohydrate at pH 4.8 (Fig. 5) consisted of three distinct signals: a sharp peak at 63.5 ppm and two broad peaks at ~ 1.7 and $\sim -0.4\text{ ppm}$. The relative chemical shift differences were referenced to an external standard of $\text{Al}(\text{H}_2\text{O})_6^{3+}$ at pH 1. The peak at 63.5 ppm is indicative of an Al-O bond

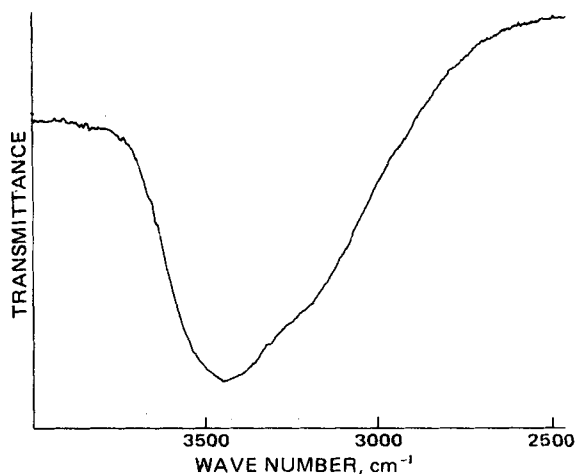


Figure 3—IR spectrum of aluminum chlorohydrate in the $4000\text{--}2000\text{-cm}^{-1}$ region.

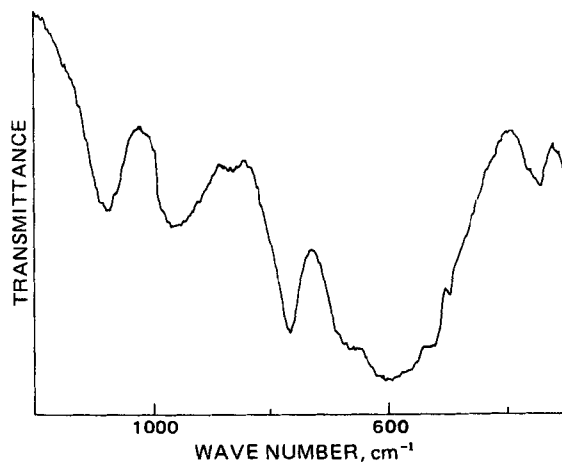


Figure 4—IR spectrum of aluminum chlorohydrate in the $1200\text{--}200\text{-cm}^{-1}$ region.

in an AlO_4 tetrahedral configuration (9). The peak width of $<40\text{ Hz}$ observed for this complex at pH 4.8 suggests that the tetrahedral aluminum is not in equilibrium with the aqueous environment since no line broadening was observed. Consequently, the tetrahedral AlO_4 group is thought to be bonded to other aluminum atoms. The broad resonances, *i.e.*, 150 and 400 Hz at -0.4 and 1.7 ppm , respectively, suggest the presence of aluminum atoms in octahedral environments, which are in rapid equilibrium with the aqueous solution.

The evidence is strong that aluminum chlorohydrate has a structure consisting of a central aluminum atom in a tetrahedral environment surrounded by 12 aluminum atoms in octahedral environments. Usually, tetrahedral aluminum is found only at high pH ($\text{pH} > 10$), but the pH of aluminum chlorohydrate solutions is ~ 4.5 . The question arises as to how this symmetrical complex forms with a tetrahedral aluminum in the center. The major synthetic procedure for preparing aluminum chlorohydrate involves the reaction of 5 moles of metallic aluminum with 1 mole of aluminum chloride (37). The pH of the reaction begins near 3 and ends near 4.5. Since the pH never rises above 4.5, it would be difficult for

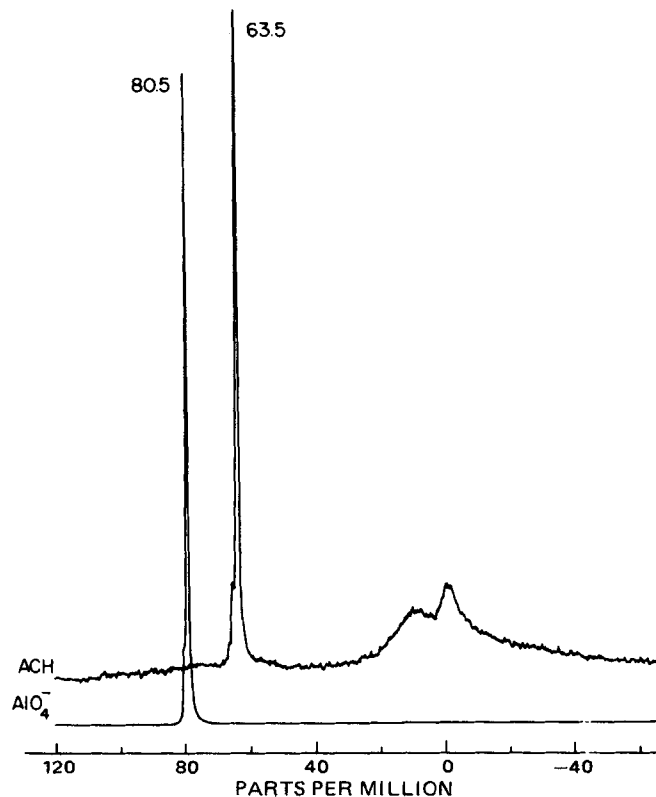


Figure 5— ^{27}Al -NMR spectrum of aluminum chlorohydrate (ACH) and sodium aluminate (AlO_4^-).

a tetrahedral aluminum to form in solution. However, regions of high pH may occur during the reaction even though the bulk solution is at a much lower pH.

The main reactions that occur are the oxidation of metallic aluminum to aluminum ion (Al^{3+}) and the reduction of protons to produce hydrogen gas. These reactions occur only at the surface of metallic aluminum. The protons arise from water dissociation. Since the protons are quickly converted to hydrogen gas, a high hydroxyl concentration may be present at the aluminum surface, resulting in a pH gradient between the surface and the bulk. Therefore, aluminum can exist in a tetrahedral state in the system even though the apparent pH is 3–4.5.

As a cluster of tetrahedral aluminum diffuse away from the metallic aluminum surface, the pH gradient causes the tetrahedral configuration to convert to the octahedral configuration. However, the tetrahedral aluminum in the middle of the cluster is protected from the aqueous pH, and the $\text{Al}_{13}\text{O}_4(\text{OH})_{24}(\text{H}_2\text{O})_{12}^{7+}$ complex forms with a tetrahedral aluminum in the center and surrounded by 12 aluminum atoms in octahedral configuration. Seven chloride anions are associated with the complex as counterions to produce a neutral complex.

The structure of $\text{Al}_{13}\text{O}_4(\text{OH})_{24}(\text{H}_2\text{O})_{12}\text{Cl}_7$ is consistent with the current understanding of antiperspirant activity. Antiperspirant activity has been elicited primarily by the topical application of multivalent metals in ionic form (38). The exact mechanism of antiperspirant activity is controversial; several theories exist. However, most studies indicate that optimum activity is achieved when the metal is presented to the skin in ionic form. Regardless of whether the metal is acting directly as an antiperspirant and/or indirectly as a deodorant, a charged species is necessary. The $\text{Al}_{13}\text{O}_4(\text{OH})_{24}(\text{H}_2\text{O})_{12}^{7+}$ complex is small and compact with the charge well distributed. Therefore, its effective charge to radius ratio is high, and it will act as a highly charged form of aluminum. In addition, the pH of aluminum chlorohydrate solutions is ~ 4.5 , which corresponds to the acid mantle of the skin. The hydroxyl groups present in the complex are responsible for the higher pH in comparison to aluminum chloride solutions. Therefore, little skin irritation is observed, and minimal clothing damage due to acid hydrolysis occurs.

REFERENCES

- (1) "The Merck Index," 9th ed., Merck & Co., Rahway, N.J., 1976, p. 47.
- (2) J. L. Bersillon, D. W. Brown, F. Fiessinger, and J. Hem, *J. Res. U.S. Geol. Surv.*, **6**, 325 (1975).
- (3) E. Matijevic, K. G. Mathai, R. H. Ottewill, and M. Kerker, *J. Phys. Chem.*, **65**, 826 (1961).
- (4) P. Hayden and A. Rubin, *National Technical Information Service*, **PB-241**, 318 (1973).
- (5) G. Johansson, G. Lundgren, L. G. Sillen, and R. Soderquist, *Acta Chem. Scand.*, **14**, 769 (1960).
- (6) W. V. Rausch and H. D. Bale, *J. Chem. Phys.*, **40**, 3391 (1964).
- (7) J. Aveston, *J. Chem. Soc.*, **1965**, 4438.
- (8) R. Mesmer and C. Baes, "The Hydrolysis of Cations," Wiley, New York, N.Y., 1976, chap. 6.
- (9) J. Akitt, N. Greenwood, B. Khandelwal, and G. Lester, *J. Chem.*

Soc. Dalton Trans., **1972**, 604.

- (10) D. N. Waters and M. S. Henty, *ibid.*, **1977**, 243.
- (11) R. E. Mesmer and C. F. Baes, *Inorg. Chem.*, **10**, 2290 (1971).
- (12) D. D. MacDonald, P. Butler, and D. Owen, *J. Phys. Chem.*, **77**, 2474 (1973).
- (13) P. H. Hsu and T. F. Bates, *Soil Sci. Soc. Am. Proc.*, **28**, 763 (1964).
- (14) G. W. Brindley and R. E. Sempels, *Clay Miner.*, **12**, 229 (1977).
- (15) J. D. Hem and C. E. Roberson, *U.S. Geol. Surv. Water-Supply Pap.*, **1967**, 1827-A.
- (16) L. S. Porubcan, C. J. Serna, J. L. White, and S. L. Hem, *J. Pharm. Sci.*, **67**, 1081 (1978).
- (17) R. Green-Kelley, *Trans. Faraday Soc.*, **51**, 412 (1955).
- (18) G. W. Brindley and R. W. Hoffmann, *Clays Clay Miner.*, **9**, 546 (1960).
- (19) P. H. Hsu and T. F. Bates, *Min. Mag.*, **33**, 749 (1964).
- (20) D. A. Riesgraf and M. L. May, *Appl. Spectrosc.*, **32**, 362 (1978).
- (21) J. J. Fripiat, F. Van Cauwelaert, and H. Bowmans, *J. Phys. Chem.*, **69**, 2458 (1965).
- (22) S. L. Nail, J. L. White, and S. L. Hem, *J. Pharm. Sci.*, **65**, 231 (1976).
- (23) H. Elderfield and J. D. Hem, *Min. Mag.*, **39**, 89 (1973).
- (24) A. J. Leonard, F. Van Cauwelaert, and S. S. Fripiat, *J. Phys. Chem.*, **71**, 695 (1967).
- (25) R. J. Moolenaar, J. C. Evans, and L. D. McKeever, *ibid.*, **74**, 3629 (1970).
- (26) C. J. Serna, J. L. White, and B. D. Velde, *Min. Mag.*, **43**, 141 (1979).
- (27) J. W. Akitt, N. N. Greenwood, and G. D. Lester, *J. Chem. Soc. A*, **1969**, 803.
- (28) J. Akitt, N. N. Greenwood, and G. D. Lester, *Chem. Commun.*, **1969**, 988.
- (29) J. W. Akitt, N. N. Greenwood, and G. D. Lester, *J. Chem. Soc. A*, **1971**, 2450.
- (30) E. N. Dicarolo and H. E. Swift, *J. Phys. Chem.*, **68**, 551 (1964).
- (31) J. F. Hon, *Mol. Phys.*, **15**, 57 (1968).
- (32) R. G. Kidd and D. R. Truax, *J. Am. Chem. Soc.*, **90**, 6867 (1968).
- (33) D. E. O'Reilly, *J. Chem. Phys.*, **32**, 1007 (1960).
- (34) C. P. Poole, Jr., H. E. Swift, and J. F. Itzel, Jr., *ibid.*, **42**, 2576 (1965).
- (35) H. E. Swift and J. F. Itzel, Jr., *Inorg. Chem.*, **5**, 2048 (1966).
- (36) H. E. Swift, C. P. Poole, Jr., and J. F. Itzel, Jr., *J. Phys. Chem.*, **68**, 2509 (1964).
- (37) W. Huehn and W. Haufe, U.S. pat. 2,196,016 (Apr. 2, 1940).
- (38) L. Kennon, *J. Pharm. Sci.*, **54**, 813 (1965).

ACKNOWLEDGMENTS

This report is Journal Paper 8254, Purdue University Agricultural Experiment Station, West Lafayette, IN 47907.