Role of Carbonate in Aluminum Hydroxide Gel Established by Raman and IR Analyses

Keyphrases □ Carbonate—role in aluminum hydroxide gel, Raman and IR analyses □ Aluminum hydroxide gel—role of carbonate, Raman and IR analyses □ Raman spectroscopy—association of carbonate and aluminum in aluminum hydroxide gel □ IR spectroscopy—association of carbonate and aluminum in aluminum hydroxide gel

To the Editor:

Aluminum hydroxide gel has been recognized as an effective antacid by the Food and Drug Administration (FDA) (1) and is included in USP XVIII (2). However, FDA makes no attempt to describe the structure of aluminum hydroxide gel. The USP states that aluminum hydroxide gel contains the equivalent of 3.6–4.4% of aluminum oxide in the form of aluminum hydroxide and hydrated oxide. This statement does not fully describe aluminum hydroxide gel, since a number of reports (3–6) have concluded that anions present during precipitation are incorporated in the gel structure and act to stabilize the gel. Carbonate ion is the most effective in stabilizing the gel (3). For this reason, reactive aluminum hydroxide gels usually contain carbonate. In this communication, we report that Raman and IR spectroscopy clearly demonstrate that an association exists between carbonate and aluminum in aluminum hydroxide gel. Thus, carbonate is an integral part of reactive aluminum hydroxide gel and is not simply present in solution or as a void-filling occluded ion.

The Raman spectrum of carbonate ion in solution was compared to the Raman spectrum[1] of aluminum hydroxide gel and to a crystalline sodium aluminum hydroxy carbonate gel. The aluminum hydroxide gel was prepared, following a previously described procedure (3), by the addition of a solution of aluminum chloride to a solution of sodium carbonate and sodium bicarbonate until pH 6.5 was reached. The aluminum hydroxide gel was amorphous by X-ray diffraction, contained the equivalent of 3.2% Al_2O_3, and was fully reactive as measured by the acid-consuming capacity test (2). The amount of carbonate in the gel was determined by the gasometric determination of carbon dioxide (7). The gel evolved 1.4% CO_2.

A crystalline sodium aluminum hydroxy carbonate gel containing 6.9% $NaAl(OH)_2CO_3$, which is equivalent to 2.4% Al_2O_3, was evaluated by Raman and IR spectroscopy. The crystalline gel contained the equivalent of 2.8% CO_2 and possessed X-ray diffraction bands at 5.67, 3.38, 2.784, 2.601, 2.151, 1.988, and 1.728 Å, which identify the gel as dawsonite (8).

The Raman spectrum of carbonate ion in solution (9) has a very strong band at 1063 cm^{-1}, weak bands at 1415 and 680 cm^{-1}, and an inactive band at 880 cm^{-1}. The Raman spectrum of the amorphous aluminum hydroxide gel has a broad band ranging from 1060 to 1174 cm^{-1} with the maximum at 1120 cm^{-1}. The crystalline sodium aluminum hydroxy carbonate has a sharp band at 1090 cm^{-1}.

The change in the band at 1063 cm^{-1} from a sharp peak for carbonate ion in solution to a broad band centered at 1120 cm^{-1} in the amorphous gel indicates that varying degrees of interaction are occurring between the oxygens of the carbonate ion and aluminum in the gel. These interactions destroy the symmetry possessed by the carbonate ion in solution, and the loss of symmetry causes a shift in the peak position. In aluminum hydroxide gel, numerous degrees of association are possible due to the amorphous nature of the gel. Therefore, the carbonate peak appears as a broad band reflecting the varying degrees of association of carbonate with aluminum.

In crystalline sodium aluminum hydroxy carbonate, a sharp peak appears at 1090 cm^{-1}. This shift indicates that the symmetry of carbonate ion is destroyed due to the association of carbonate with aluminum. However, the carbonate is associated with the aluminum in only one environment, as indicated by the sharp peak.

The IR spectra also indicate that definite association exists between carbonate and aluminum in aluminum hydroxide gel. Because of interference by strong water bands in the 1400–1700-cm^{-1} region, the IR spectra[2] were run as air-dried films of the gels on a zinc sulfide[3] window.

The IR spectrum of sodium carbonate has bands at 1450, 880, and 720 cm^{-1} (10). In aluminum hydroxide gel, bands associated with carbonate occur at 1525, 1415, 1100, and 850 cm^{-1}. The band at 1450 cm^{-1} for sodium carbonate has split into two bands, 1525 and 1415 cm^{-1}, in aluminum hydroxide gel. Nakamoto (10) and Healy and White (11, 12) showed that when carbonate ion coordinates to a metal, the ν_3 vibration splits into two bands. The magnitude of the splitting has been shown to be dependent on whether a uni- or a bidentate complex forms.

Carbonate bands occur at 1580, 1390, 1080, and 840 cm^{-1} in the crystalline sodium aluminum hydroxy carbonate. The carbonate band occurring at 1450 cm^{-1} for sodium carbonate has again split, but the magnitude of the split is 190 cm^{-1} for the crystalline gel in comparison to 110 cm^{-1} for the amorphous gel (Fig. 1). The magnitude of the split of this carbonate band may be useful in predicting the acid reactivity of aluminum hydroxide gel.

In addition to the splitting of the degenerate vibration, the appearance of the inactive band at 1100 cm^{-1} in the amorphous gel and 1080 cm^{-1} in the crystalline gel is also typical of a substantial lowering of symmetry due to association between carbonate and aluminum (12).

Thus, it is concluded that Raman and IR spectroscopy are useful tools for studying the role of anions in stabilizing aluminum hydroxide gel. Raman spectroscopy is especially useful because water does not interfere and the gels can be run in their natural condi-

[1] Raman spectra were run on a Spex RAMALOG 4, courtesy of Spex Industries, Metuchen, N.J.

[2] Model 421, Perkin-Elmer Corp., Norwalk, Conn.

[3] Irtran 2, Eastman Kodak, Rochester, N.Y.

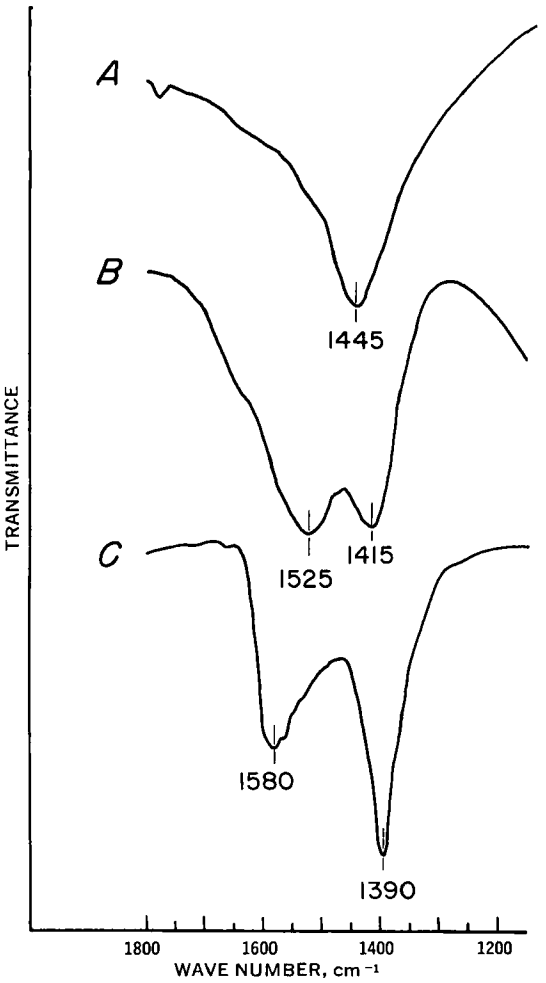

Figure 1—*IR spectra of 1200–1800-cm^{-1} region. Key: A, sodium carbonate; B, aluminum hydroxide gel; and C, sodium aluminum hydroxy carbonate.*

tion. Both methods clearly indicate that carbonate is associated with aluminum in aluminum hydroxide gel and should be recognized as an integral part of the structure of reactive aluminum hydroxide gel.

A report on the role of carbonate in aluminum hydroxide-type antacids is in preparation.

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Joe L. White

Department of Agronomy
Purdue University
West Lafayette, IN 47907

Stanley L. Hem ˣ

Department of Industrial and Physical Pharmacy
Purdue University
West Lafayette, IN 47907

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ˣ To whom inquiries should be directed.

Cytolytic Effects of Bromoacetylcholine on Neuroblastoma *In Vitro*

Keyphrases □ Bromoacetylcholine—cytolytic effects on neuroblastoma *in vitro* □ Neuroblastoma—cytolytic effects of bromoacetylcholine *in vitro* □ Cancer chemotherapeutic agents—cytolytic effects of bromoacetylcholine on neuroblastoma *in vitro* □ Cytolytic activity—bromoacetylcholine on neuroblastoma *in vitro*

To the Editor:

Neuroblastoma, probably the most common solid cancer in children (1), is treated with vincristine and cyclophosphamide. However, the remission rate in neuroblastoma patients is quite low and the duration of drug effectiveness is fairly short (2–4). Thus, new chemotherapeutic agents are needed to cope with this highly malignant tumor.

Recent studies revealed that the nature of neuroblastoma cells can be cholinergic, adrenergic, or inactive (5–8). It is also known that acetylcholinesterase is present in all cases and that these cells possess membranes that respond to acetylcholine and are electrically excitable, indicating the existence of cholinergic receptors at the membrane site (7, 9). Attempts made to destroy these tumor cells with an irreversible adrenolytic agent, 6-hydroxydopamine (10), have met with only partial success, possibly due to the inhibition of adrenergic components without an affect on the cholinergic parts of these tumor cells. Therefore, we proposed to kill these tumor cells with irreversible cholinolytics or with cholinergics such as bromoacetylcholine perchlorate, $BrCH_2COOCH_2CH_2{}^+N(CH_3)_3{\cdot}ClO_4{}^-$.

Bromoacetylcholine is a cholinergic agonist which stimulates both nicotinic and muscarinic receptors directly (11–13). However, when it is incubated with cell membranes for 15 min or longer, it binds irreversibly and specifically to the cholinergic receptor at the nicotinic site but not at the muscarinic site (11, 14). Therefore, it was thought that this compound might inhibit the growth of neuroblastoma cells. In this investigation, bromoacetylcholine inhibited the growth of neuroblastoma effectively at concentrations of 10^{-6}–10^{-5} *M*. Therefore, it is hoped that bromoacetylcholine can be used to treat the malignant tumor.