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EFFECT OF PRECIPITATION TEMPERATURE, pH AND AGITATION ON THE ACID REACTIVITY OF ALUMINUM HYDROXYCARBONATE GEL

Edward A. Lipka[x], Ming K. Wang[o], Joe L. White[o] and Stanley L. Hem[x]
[x]Department of Industrial and Physical Pharmacy and [o]Department
of Agronomy
Purdue University
West Lafayette, Indiana 47907

ABSTRACT

A completely randomized 2^3-factorial design study of the precipitation of aluminum hydroxycarbonate gel by the reaction of aluminum chloride with sodium carbonate and sodium bicarbonate showed that the precipitation temperature and end-point pH were significant in terms of the rate of acid neutralization at the 0.01 level and that stirring speed was significant at the 0.05 level. No significant interactions occurred between the parameters. The most reactive gels were precipitated at 25°, pH 6.5 and either 15 or 500 rpm. After aging for 105 days at 25° these gels exhibited a twelvefold greater rate of acid neutralization than the least reactive gel which was precipitated at 4°, pH 5.8 and 15 rpm. The results are analyzed in terms of the effect of each parameter on the particle size and structure of aluminum hydroxycarbonate gel.

INTRODUCTION

Recent advances in ulcer therapy including high intensity antacid therapy [1-3] and the report of the OTC Panel on Antacids[4] suggest that antacids must be able to neutralize acid rapidly in order to be effective. Thus precipitation conditions must be controlled to produce an aluminum hydroxycarbonate gel which exhibits a rapid rate of acid neutralization.

The influence of precipitation factors on the properties of aluminum hydroxide gel has been noted in reports over the past thirty years[5-12], although the complex structure of aluminum hydroxycarbonate gel has only recently been described[13-15]. When the literature relating to the precipitation of aluminum hydroxide gel or aluminum hydroxycarbonate gel is reviewed, it is apparent that temperature, pH and agitation are the most frequently cited factors. However, the major problems apparent in the literature are the difficulty in designing experiments which isolate the effect of a single precipitation parameter and the incomplete understanding of the structure of aluminum hydroxycarbonate gel. Thus a factorial design study was undertaken to investigate the effect of precipitation temperature, end-point pH and agitation on the acid reactivity of aluminum hydroxycarbonate gel and to determine if any interactions occur between these factors. In addition, the results of the factorial study were interpreted in light of the currently understood structure of aluminum hydroxycarbonate gel.

MATERIALS

One liter batches of aluminum hydroxycarbonate gel were prepared by adding a solution made by dissolving 181 g of aluminum chloride hexahydrate in 1600 ml of double distilled water at a rate of 15 ml/min (Varistaltic Pump, Fisher) to a solution prepared by dissolving 60.4 g of sodium carbonate monohydrate and 112.2 g of sodium bicarbonate in 2500 ml of double distilled water. The aluminum chloride solution was added until the end-point pH was reached. The reaction mixture was then maintained at this pH for 1 hour by carefully controlling the rate of addition of the aluminum chloride solution. The aluminum hydroxycarbonate gel was then washed with three liters of double distilled water and the final volume was adjusted to yield a gel equivalent to 3% Al_2O_3.

The temperature was controlled at either 4° or 25°, the end-point pH was either 5.8 or 6.5 and the stirring speed (Stedi-Speed Stirrer, Fisher) was either 15 or 500 rpm.

METHODS

The equivalent aluminum oxide content was determined by chelatometric titration[16].

The rate of acid neutralization was determined in duplicate by automated pH-stat titration[17] at pH 3.0, 25° and expressed as T_{50}, the time required to add 50% of the total 1.0 N HCl needed to neutralize the gel. The standard deviation observed was less than 0.1 min.

The carbonate content, determined by gasometric displacement using the Chittick apparatus[18] (Sargent-Welch) was expressed as the molar ratio of carbonate to aluminum.

All gels were examined by X-ray diffraction[19].

Eight aluminum hydroxycarbonate gels were precipitated in random order using one of the combinations of temperature, end-point pH and stirring speed.

The rate of acid neutralization was analyzed by the split-plot design[20] (Table 1) where the blocks are the different ages of the gels (2, 21 or 105 days). The estimated mean square was obtained by the pooling technique[20] using all block interactions with other sources in the analysis of variance.

RESULTS AND DISCUSSION

All of the aluminum hydroxycarbonate gels were amorphous to X-rays both initially and after aging at 25° for 105 days. In addition, none of the gels contained any slow-reacting material when examined by pH-stat titration at pH 3.

Analysis of variance for the split-plot design after pooling (Table 2) indicates that temperature and end-point pH are significant at the 0.01 level while the stirring speed is significant at the 0.05 level. None of the possible interactions were significant at the 0.05 level.

TABLE 1

Model for Split-Plot Design Experiment

$$Y_{ijklm} = \mu + A_i + \delta(i) + P_j + AP_{ij} + T_k + AT_{ik} + PT_{jk}$$

$$+ APT_{ijk} + S_l + AS_{il} + APS_{ijl} + TS_{kl} + ATS_{ikl}$$

$$+ PTS_{jkl} + APTS_{ijkl} + \varepsilon_{(ijkl)m}$$

$i = 1,2,3 \quad j = 1,2 \quad k = 1,2 \quad l = 1,2 \quad m = 1,2$

Y_{ijklm} = T_{50} variable analyzed from the i^{th} level of A, j^{th} level of P, k^{th} level of T, l^{th} level of S, m^{th} replicate.

μ = overall mean

A_i = effect of i^{th} level of age

$\delta(i)$ = first restriction error

P_j = effect of j^{th} level of final pH

AP_{ij} = interaction effect of i^{th} level of age with j^{th} level of pH

T_k = effect of k^{th} level of temperature

⋮

S_l = effect of l^{th} level of stir speed

⋮

$\varepsilon_{(ijkl)m}$ = error due to repeating the combination of the i^{th} level of age with the j^{th} level of pH, k^{th} level of temperature, and l^{th} level of stir speed.

Even though all of the gels were amorphous and reacted completely at pH 3, the rate of acid neutralization was strongly affected by the precipitation parameters. As seen in Table 3, the most reactive aluminum hydroxycarbonate gels were precipitated at

TABLE 2

Anova for Split-Plot Design After Pooling

Source	df	MS	F
pH (P)	1	169.5008	33.9422**
Temperature (T)	1	305.0208	61.0799**
P x T	1	6.9008	1.3819
Stir Speed (S)	1	21.0675	4.2187*
P x S	1	0.0008	0.0002
T x S	1	15.6408	3.1321
P x T x S	2	0.0504	0.0101
Pooled error	39	4.9938	

** significant at the 0.01 level

* significant at the 0.05 level

TABLE 3

Rate of Acid Neutralization For Aluminum Hydroxycarbonate Gels Precipitated at Various Combinations of Temperature, End-Point pH, and Agitation After Aging for 2 Days at 25°

	T_{50}, min			
	4°		25°	
pH	15rpm	500rpm	15rpm	500rpm
5.8	6.5	5.4	3.8	3.6
6.5	4.9	3.4	1.0	0.9

25°, pH 6.5 and either 15 or 500 rpm. These gels reacted approximately 7 times faster with acid than the gel precipitated at 4°, pH 5.8 and 15 rmp.

The gels retained the same rank order during aging at 25° although the less reactive gels showed a greater loss of acid reactivity upon agin (Fig. 1). After 105 days, the T_{50} of the

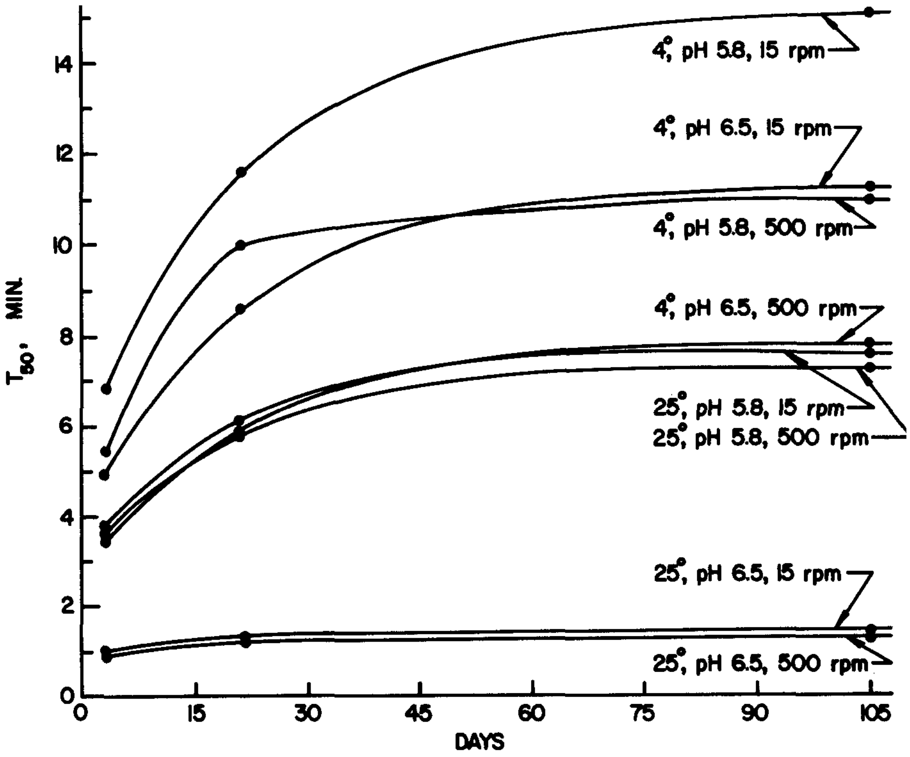

FIGURE 1

Rate of acid neutralization, T_{50}, for aluminum hydroxycarbonate gels precipitated at various combinations of temperature, end-point pH, and stirring speed and aged at 25°.

most reactive gel increased to 1.3 min. In comparison, the T_{50} of the slowest reacting gel increased to 15.1 min. producing a twelve fold difference in rate of acid neutralization of the most reactive and least reactive aluminum hydroxycarbonate gels at 105 days.

Application of the student's t-test ($p \leq 0.05$) to the data in Figure 1 indicates that the difference in the rate of acid neutralization at 2, 21 and 105 days for the aluminum hydroxycarbonate gels precipitated at 25°, pH 6.5, 500 rpm and 25°, pH 6.5, 15 rpm is not statistically significant and that the decrease in rate of acid neutralization during aging is also not statistically significant. Likewise, differences in the rate of acid neutralization are not statistically significiant for the aluminum hydroxycarbonate gels precipitated at 25°, pH 5.8, 500 rpm; 25°, pH 5.8, 15 rpm; and 4°, pH 6.5, 500 rpm. However, the aging effect is statistically significant for these three gels. Differences in all of the other relationships seen in Figure 1 are statistically significant.

The average T_{50} of all of the gels precipitated at 25° was 4.4 min. after 105 days at 25°, while the gels precipitated at 4° had an average T_{50} of 11.3 min. Based upon classical nucleation theory[21], increased temperature will lead to greater concentrations of critical nuclei so that higher precipitation temperatures would be expected to yield smaller particles which should exhibit a rapid rate of acid neutralization. On the other hand, the polymerization of polynuclear aluminum species would tend to be directly related to temperature and larger particles would be expected to result at higher temperatures[14]. The lower T_{50} values which were observed generally in this study at a precipitation temperature of 25° in contrast to 4° suggests the greater importance of the nucleation step in the precipitation of aluminum hydroxycarbonate gel.

The average T_{50} after 105 days at 25° for the gels precipitated at pH 6.5 was 5.5 min. while the average T_{50} for the gels precipitated at pH 5.8 was 10.3 min. This difference appears to be related to the effect of pH on the carbonate to aluminum ratio. The average carbonate to aluminum ratio for the gels precipitated at pH 6.5 was 0.58. In contrast, the average carbonate to aluminum ratio was 0.43 for the gels precipitated at pH 5.8. As pK_{a_1} for carbonic acid is 6.37, it is evident that a greater amount of carbonate was lost from the reaction medium due to the formation of carbon dioxide at pH 5.8. Thus the aluminum hydroxycarbonate gels precipitated at pH 5.8 contained less structural carbonate and as has been previously observed[15], the rate of polymerization is inversely related to the carbonate to aluminum ratio.

The average T_{50} after 105 days at 25° at 15 and 500 rpm was 8.9 and 6.9 min., respectively, reflecting the lower significance level of this parameter. The stirring rate did not produce any significant difference in the rate of acid neutralization when the other precipitation parameters were at optimum levels, i.e., 25° and pH 6.5 (Fig. 1). Stirring speed was a factor when precipitation conditions were not optimum as the slowest reacting gel was precipitated at 4°, pH 5.8 and 15 rpm (Fig. 1). High stirring speeds quickly disperse the reactants and produce more homogeneous conditions in the reaction vessel.

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