DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 18(3), 345-353 (1992)

KINETICS AND EFFECTIVENESS OF ALUMINIUM HYDROXIDE GELS: 1.- SYNTHESIZED AT DIFFERENT VALUES OF pH.

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ABSTRACT

The antacid effectiveness and kinetic behaviour of three aluminium hydroxide gels, synthesized at different values of pH of precipitation, have been studied with the pH-Stat technique. Results indicate that these properties improve with increasing pH of precipitation and are structure related.

INTRODUCTION

Two properties primarily define an antacid's effectiveness:

a) The amount of acid which it can neutralize.
b) The rate at which the neutralization reaction occurs.

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The methods used, which can be described as static or dynamic, should measure these properties as faithfully as possible, and furthermore, correlate well with acid neutralization *in vivo*.

Dynamic methods either measure pH, giving its profile, during the neutralization reaction, or else, the reaction rate at constant pH. The modified Rosset-Rice method, which tries to simulate the behaviour of the stomach, can be put in the first group; the methods in the second group are more sensitive and are called pH-Stat.

With pH-Stat, different variables, such as pH, temperature and stirring rate, can be assessed in their effect on the acid reactivity of aluminium hydroxide gels. Information on changes in gel structure is provided too and it is possible to test "slightly" reactive gels.

From pH-Stat neutralization curves, the values T_{25}, T_{50} and T_{90} can be defined as the time taken to consume 25, 50 and 90%, respectively, of the amount of 1N HCl necessary to completely neutralize the aluminium hydroxide gel (2).

FIG. 1 shows a pH-Stat neutralization curve for a completely reactive aluminium hydroxide gel, containing carbonate ions. There are three steps in the reaction: an initial fast step (I), a slow, zero-order step (II) and a faster, also zero-order, terminal step (III) (2).

The neutralization rate for step I is very large and the autoburette's delivery rate for the quantity of acid necessary for neutralization is exceeded, hence only the total volume of acid neutralized can be known, kinetic measurements not being possible.

The neutralization rate for steps II and III can be calculated using the zero-order rate constants K_{II} and K_{III}, linear correlation coefficients and the time for the start of step III, calculating the latter from the intersection of the lines defined by K_{II} and K_{III}, using simultaneous equations of linear regression.

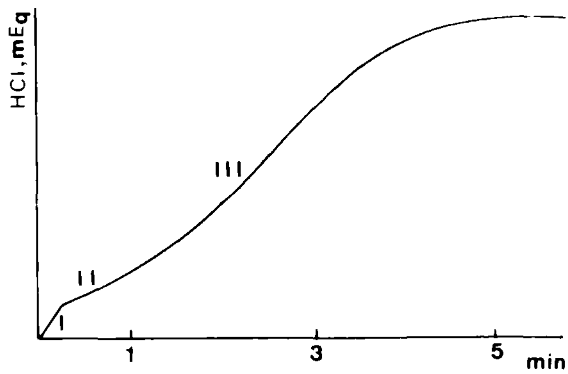


FIGURE 1: Characteristic pH Stat titrigram of carbonate containing aluminum hydroxide gel showing phases I,II and III.

The pH-Stat technique is useful since, through the parameter T_{50}, the structure of the gel, which is directly related to how the gel ages, can be explored, whereas other tests such as acid-consuming capacity or the Rosset-Rice time are practically insensitive to changes in gel structure (2).

MATERIALS AND METHODS

Synthesis.-

Three gels were synthesized at pH 4.5, 7.2 and 9.0 and called, respectively, SULCAA 4, SULCAA 7 and SULCAA 9 (TABLE 1), the reaction between 0.6 M aluminium sulphate and 1 M ammonium carbonate being used:

$$Al_2(SO_4).18H_2O + 3(NH_4)_2CO_3 \dashrightarrow$$
$$\dashrightarrow 2Al(OH)_3 + 3(NH_4)_2SO_4 + 15H_2O$$

Methods.-

X-ray diffraction (XRD) was performed twice on each gel to identify possible crystalline phases, each gel being washed centrifugally in order to remove the salts, formed as reaction by-products, for the second XRD run.

TABLE 1.- Precipitation parameters of synthesized gels.

GEL	Concent. $Al_2(SO_4)_3$	Concent. $(NH_4)_2CO_3$	pH Precip.	Structure	% Al_2O_3 (W/V)
SULCAA 4	0.6 M	1 M	4.5	Amorphe	1.56
SULCAA 7	O.6 M	1 M	7.2	Amorphe	2.48
SULCAA 9	0.6 M	1 M	9.0	Cristalline	2.97

Antacid capacity and reaction rate were studied, and the pH-Stat technique applied for the three gels.

RESULTS AND DISCUSSION

The before washing XRD results for the three gels show the presence of $(NH_4)_2SO_4$ as a reaction by-product. For the washed gels, amorphous structures were observed in those synthesized at acid or neutral precipitation pH. At pH 9, however, the gel is crystalline, forming as a hydroxycarbonate of aluminium and ammonium (FIGS. 2a and 2b).

In neutralization capacity, the three gels show similar values (TABLE 2) which in each case are greater than the theoretical (4). The neutralization profiles (FIG. 3) show that the slowest gel is that precipitated at acid pH.

The same graph reveals, moreover, that the gels buffer the pH of the medium between 3 and 4, even after addition of 2 ml/min of artificial gastric juice for more than one hour (FIG. 3).

The pH-Stat curves (FIG.4) show that in antacid capacity and rate of neutralization the gels obtained at neutral or basic pH perform better, the SULCAA 4 gel performing far worse than the other gels.

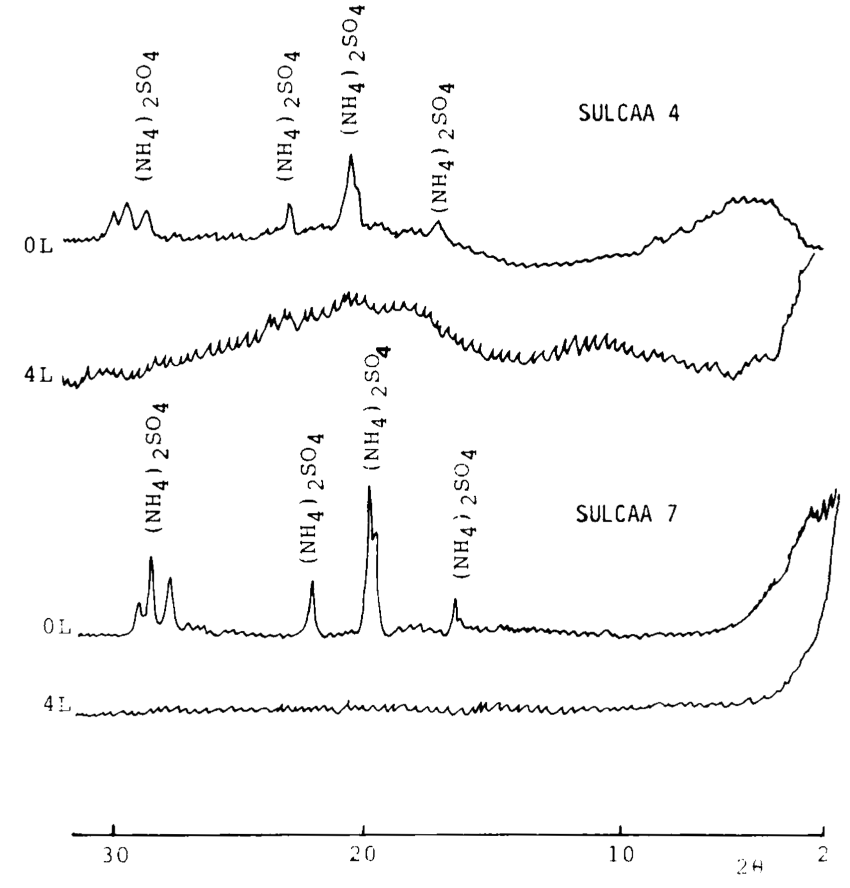
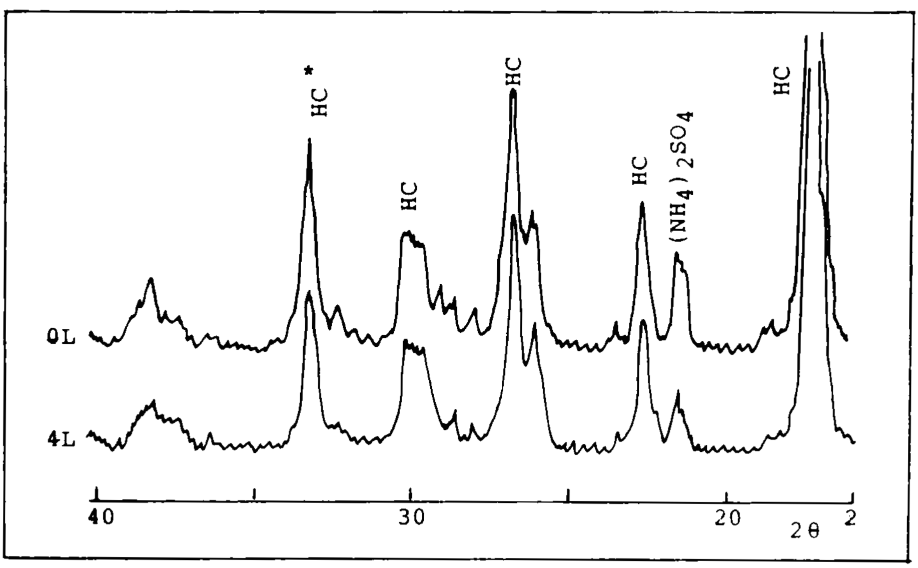


FIGURE 2a: DRX of synthesized gels.



* Hydroxicarbonate

FIGURE 2b: XRD of synthesized gel SULCAA 9.

TABLE 2.- Effect of pH on Acid-Consuming Capacity.

G E L	pH_p[a]	0.1N HCl consumed per gr of Al_2O_3 ml	Theoretical Acid-Consuming Capacity %
SULCAA 4	4.50	616.2	104.8
SULCAA 7	7.20	593.9	101.0
SULCAA 9	9.00	638.6	108.6

[a] pH of precipitation of gel.

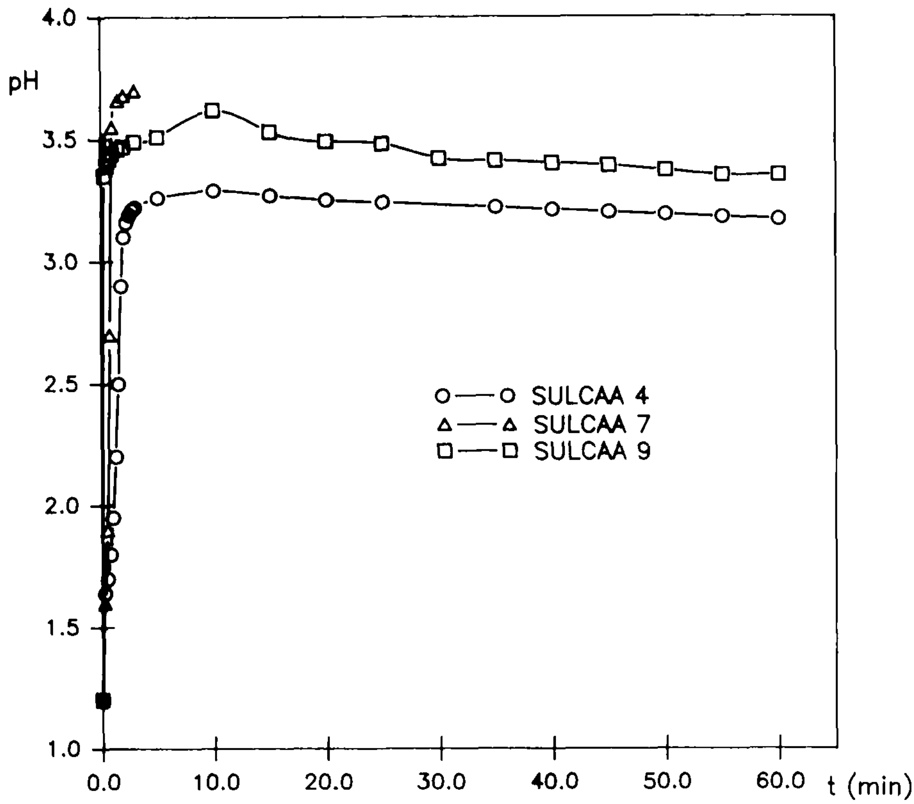


FIGURE 3.– Neutralization profile of synthesized gels.

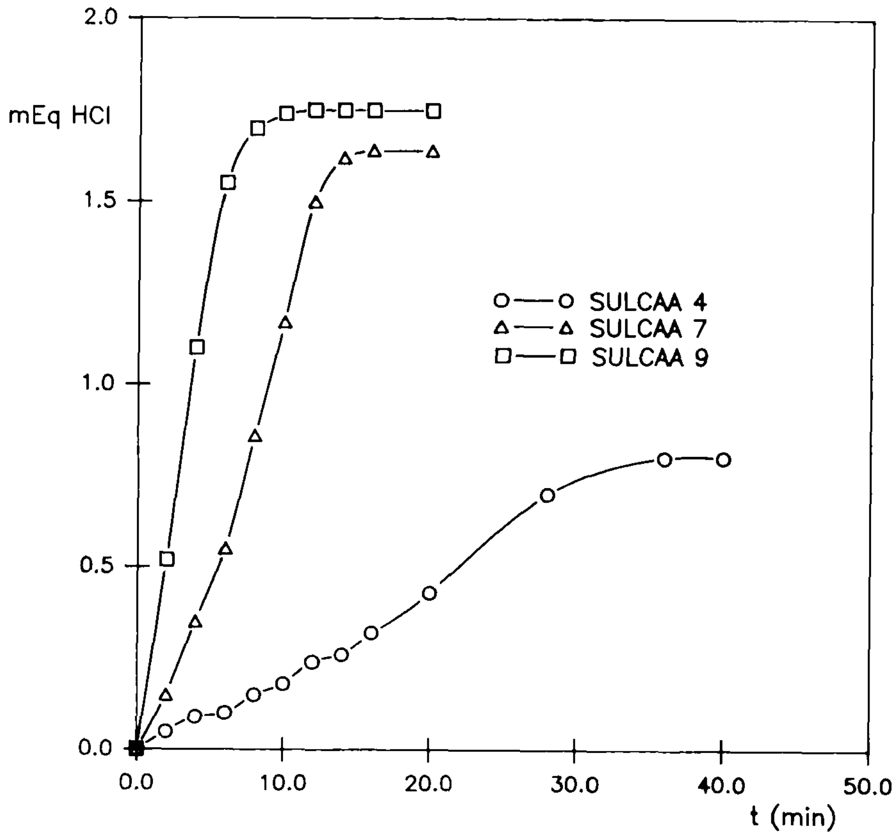


FIGURE 4.– pH–Stat titrigram of synthesized gels.

TABLE 3.- Effect of pH on cinetics parameters of synthesized gels.

GEL	K_{II} mEq/min	K_{III} mEq/min	Initiation of Phase III, min	T_{50} min
SULCAA 4	0.0143	0.0288	14.5	19.0
SULCAA 7	0.0750	0.1560	5.2	7.8
SULCAA 9	0.2000	0.2940	0.6	3.0

TABLE 3 shows the kinetic parameters and times to initiation of step III (see above).

The results indicate decreasing effectiveness of the antacids with decreasing pH of precipitation, the SULCAA 4 gel performing much worse than the other two in this respect. The increase in T_{50}, the fall in the kinetic rate constants K_{II} and K_{III} and the prolongation of the slow reaction step (step II) (as seen by the time for step III to start) show the reactions become progressively slower.

The values of these parameters point to a polymeric structure of chains of aluminium atoms linked by O-H bridges, in which the CO_3^{2-} ion plays an important part too. In terms of this, step I represents the rapid reaction of the acid with the free, hydroxide surface groups that are readily accessible, hence their study is of no consequence.

Step II represents reaction with the bound hydroxide groups, being slower since these groups are less available. An increased reaction rate is observed as the precipitation pH increases.

The coordinated carbonate is effective in increasing the rate of the process at step III, its reaction with the acid breaking the structure to give more reactive surface. This effect is greatest in the case of the crystalline hydroxycarbonate (SULCAA 9), which shows the greatest K_{III} (0.294 mEq/min), it having the highest ratio of CO_3^{2-}/Al. Even K_{II} is only slightly less for this compound (0.200 mEq/min) and the step it governs is completed in a short space of time (FIG. 4). The ion's absence from the SULCAA 4 gel leads to a lower reaction rate.

CONCLUSIONS

- In the gels, XRD reveals amorphous structures for those synthesized at acid and neutral pH, while the gel synthesized at pH 9 is a crystalline product identified as a hydroxycarbonate of aluminium and ammonium.

- The three gels show similar neutralization capacity values, which are greater than the theoretical predictions due to the acid reaction of the carbonate ion in each gel.

- The kinetic parameters obtained with pH-Stat show the effectiveness of the gels increases with pH of precipitation.

- The most reactive gel is that synthesized at pH 9 (SULCAA 9), it possessing a higher CO_3^{2-}/Al ratio. Through breakage of the crystal structure, the presence of the coordinated carbon in step III makes the reaction proceed more quickly.

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