Characterization of Antacid Compounds Containing Both Aluminum and Magnesium. II. Codried Powders

Cheryl L. Peterson,[1] Darold L. Perry,[2] Hamid Masood,[1] Joe L. White,[3] Stanley L. Hem,[1,6] Christian Fritsch,[4,5] and Franz Haeusler[4]

Received January 28, 1992; accepted December 21, 1992

The composition and antacid properties of six samples of codried antacids containing both aluminum and magnesium were determined. Aluminum hydroxide–magnesium carbonate codried gel and aluminum hydroxide–magnesium hydroxide codried gel were nonhomogeneous, as the samples contained combinations of hydrotalcite, amorphous aluminum hydroxide, magnesium hydroxide, magnesium hydroxycarbonate, and magnesium carbonate. All samples passed the preliminary antacid test and had high acid neutralizing capacities. However, the rate of acid neutralization varied between samples. In some cases the rate of acid neutralization at a dose of 400 mg was too slow to raise the pH to 3.0 as required by the Rossett–Rice test.

KEY WORDS: codried antacids; aluminum and magnesium antacids.

INTRODUCTION

Amorphous aluminum hydroxycarbonate gel and magnesium hydroxide gel are frequently combined in antacid products. The effectiveness of this mixture has led to the development of several antacid materials which contain both aluminum and magnesium but which are claimed to be unique antacids rather than physical mixtures. These antacid materials include aluminum hydroxide–magnesium carbonate codried gel (1,2), aluminum hydroxide–magnesium hydroxide codried gel (3,4), and crystalline powders such as hydrotalcite and magaldrate, which were studied in Part I in this series (the preceding paper) (4). Although all of these antacid materials are used commercially in antacid products, a survey of the literature revealed little about their composition or antacid properties.

Codried gels are produced by blending suspensions of an aluminum-containing antacid, usually amorphous aluminum hydroxycarbonate, and a magnesium-containing antacid, such as magnesium carbonate or magnesium hydroxide, and then drying the mixture (1,3). The structure of codried gels has not been established, although they are referred to as mixtures rather than new compounds (1,3). Therefore, the composition and properties of these antacids were studied.

EXPERIMENTAL

The six commercial antacid samples studied are identified in Table I. Samples were tested during the summer of 1990 except for samples M, O, and P, which were tested during the summer of 1991. The test procedures utilized are detailed in Part I (4).

RESULTS AND DISCUSSION

Aluminum Hydroxide–Magnesium Carbonate Codried Gel. The aluminum, magnesium, and carbonate contents of three commercial aluminum hydroxide–magnesium carbonate codried gels are presented in Table II. Although the aluminum and carbonate contents varied widely, the magnesium contents of the samples are virtually identical. Since no standard of composition or empirical formula exists for codried gels, there is no reason to expect consistent composition for this type of antacid.

The absence of a well-defined X-ray pattern showed that all three samples were essentially amorphous. However, sample K showed minor diffraction bands at 6.08 and 2.03 A, sample L had minor diffraction bands at 5.85, 2.904, and 2.029 A, and sample M had minor diffraction bands at 9.108, 5.839, 2.909, and 2.030 A. These bands suggest that all the samples contain a minor phase composed of crystalline magnesium hydroxycarbonate and/or magnesium carbonate such as that observed in the almagate and almagcit samples studied in Part I in this series (4).

The infrared spectra of all three samples show hydroxyl stretching bands in the 3416- to 3447-cm^{-1} range which are attributed to structural hydroxyls and hydroxyls from adsorbed water. The water deformation band appears as a shoulder at 1632 cm^{-1}. Bands at 1520 and 1420 cm^{-1} are assigned to carbonate in an unidentate bond typical for amorphous aluminum hydroxycarbonate. Bands at 1095 and 850 cm^{-1} are attributed to carbonate frequencies also.

The morphology of samples K, L, and M was diverse (Table III). Platy particles, aggregates of platy particles and cubic particles were observed. The elemental composition of these samples was also diverse, as only 6 of the 18 particles which were examined exhibited the presence of both aluminum and magnesium. Eleven particles contained only aluminum. One particle contained only magnesium. Thus, the energy dispersive spectrum of individual particles of this group suggests that aluminum hydroxide–magnesium carbonate codried gels are not homogeneous.

The surface areas are also presented in Table III. The surface area of sample K was approximately twice that of samples L and M. The primary crystallite dimension could not be determined because the major phase of the three samples was amorphous.

The antacid properties are summarized in Table IV. All three samples passed the preliminary antacid test and had similar acid neutralizing capacities. The samples gave different results in the Rossett–Rice test. Sample K had a 1-min

---

[1] Department of Industrial and Physical Pharmacy, Purdue University, West Lafayette, Indiana 47907.

[2] School of Materials Engineering, Purdue University, West Lafayette, Indiana 47907.

[3] Department of Agronomy, Purdue University, West Lafayette, Indiana 47907.

[4] Bayer AG, Germany.

[5] Present address: Sandoz AG, Nuernberg, Germany.

[6] To whom correspondence should be addressed at School of Pharmacy, Purdue University, West Lafayette, Indiana 47907.

0724-8741/93/0700-1005$07.00/0

Table I. Antacid Samples Studied

Sample	Description	Manufacturer	Lot No.
K	Aluminum hydroxide–magnesium carbonate codried gel, F-MA11	Reheis Chemical Co.	1457/A
L	Aluminum hydroxide–magnesium carbonate codried gel, C220	Giulini Chemie	88-635-30
M	Aluminum hydroxide–magnesium carbonate codried gel, C225	Giulini Chemie	90-586-30
N	Aluminum hydroxide–magnesium hydroxide codried gel, F-6000M	Reheis Chemical Co.	PD 3-8822-8
O	Aluminum hydroxide–magnesium hydroxide codried gel, C240	Giulini Chemie	90-90931-30
P	Aluminum hydroxide–magnesium hydroxide codried gel, C240	Giulini Chemie	90-90901-30

Table II. The Aluminum, Magnesium, and Carbonate Content

Sample	mmol/100 g		
	Aluminum	Magnesium	Carbonate
Aluminum hydroxide–magnesium carbonate codried gel			
K	820	179	377
L	793	177	325
M	885	179	304
Aluminum hydroxide–magnesium hydroxide codried gel			
N	500	751	200
O	545	998	92
P	600	843	113

lag time and a 10-min Rossett–Rice time for a 400-mg dose. Sample M had a longer lag time and a shorter Rossett–Rice time. Samples K and M both exhibited a buffering pH. Sample L did not react rapidly enough at a dose of 400 mg to raise the pH to 3.0. Thus, the Rossett–Rice test indicates that the rate of acid neutralization follows the order K > M > L. The pH-stat titration ranked the samples in the same order in terms of rate of acid neutralization at pH 3.0, 37°C. The rate of acid neutralization at pH 5.0, 37°C, was very slow as was observed for the hydrotalcite and magaldrate samples in Part I (4).

Aluminum Hydroxide–Magnesium Hydroxide Codried Gel. The aluminum, magnesium, and carbonate contents of three commercial aluminum hydroxide–magnesium hydroxide codried gels varied widely as shown in Table II. There is no accepted empirical formula for this type of antacid.

The X-ray diffractogram of sample N exhibited the characteristic diffraction bands of hydrotalcite at 7.67, 3.80, 2.57, 2.34, and 1.94 A. No other bands were observed, indicating that hydrotalcite was the only crystalline phase present. However, it is unlikely that the sample is composed only of hydrotalcite, as the Al:Mg ratio calculated from the aluminum and magnesium content is 1:1.5. This is outside the 1:2 to 1:5 range for hydrotalcite (5) and suggests an excess of aluminum. Thus, sample N probably contains some form of amorphous aluminum hydroxide in addition to hydrotalcite.

Sample O had X-ray diffraction bands at 4.810, 2.739, 2.377, 1.800, 1.578, and 1.498 A. Sample P had a similar X-ray diffraction pattern, with diffraction bands at 4.811, 2.737, 2.378, 1.800, 1.578, and 1.498 A. These d-spacings are characteristic for magnesium hydroxide (brucite) and the relative intensities of the diffraction peaks suggest that it is the dominant crystalline phase in both sample O and sample P. Thus the magnesium hydroxide has retained its structural integrity in the process used for production of these two codried gels.

While the infrared spectra of these samples show the usual broad hydroxyl stretching frequency at about 3450 cm^{-1}, samples O and P show, in addition, a very sharp band at 3697 cm^{-1}. The 3697-cm^{-1} frequency is unique for magnesium hydroxide (brucite) and shows that all or part of the original magnesium hydroxide is present. The absence of the

Table III. Elemental Composition by Energy Dispersive Spectrometry (EDS) and Physical Properties

Sample	Morphology[a]	Particle composition by EDS				Surface area (m^2/g)
		Total examined	Contained			
			Al + Mg	Al	Mg	
Aluminum hydroxide–magnesium carbonate codried gel						
K	a,b	6	2	4	0	85
L	a,b,c	5	1	3	1	37
M	a,b	7	3	4	0	42
Aluminum hydroxide–magnesium hydroxide codried gel						
N	b	6	3	2	1	157
O	a,b,c	4	1	1	2	34
P	a,b,c	6	1	3	2	32

[a] a, platy; b, aggregates of plates; c, cubic.

Table IV. Antacid Properties

Sample	PAT	ANC (mEq/400 mg)	Rossett–Rice test[a] Lag (min)	R-R time (min)	Buffering pH	pH-stat T-50 (min), pH 3, 37°C	% Neutralized in 70 min, pH 5, 37°C
			Aluminum hydroxide–magnesium carbonate codried gel				
K	3.7	12.0	1.0	10.0	3.6	2.4	16.0
L	3.7	11.5	a	a	a	10.6	8.4
M	3.8	11.6	7.0	6.8	3.3	5.6	6.8
			Aluminum hydroxide–magnesium hydroxide codried gel				
N	3.8	12.0	a	a	a	10.7	20.4
O	5.6	13.6	2.2	6.9	3.8	5.5	0.7
P	5.6	13.3	a	a	a	5.8	0.7

[a] a, pH did not reach 3.0.

3697-cm^{-1} band in sample N shows that the magnesium hydroxide in the initial mixture has been transformed. The X-ray diffraction pattern shows the resulting material to be hydrotalcite. The presence of hydrotalcite is also confirmed by the infrared band at 1363 cm^{-1} which is not seen in the infrared spectra of samples O and P. This band is assigned to unperturbed carbonate stretching and probably arises from exchangeable carbonate in the anionic layer of hydrotalcite.

Samples O and P exhibit bands at 1507 and 1435 cm^{-1} which are carbonate bands arising from perturbation of the stretching vibrations of carbonate bound to aluminum by unidentate bonds. These bands suggest the presence of amorphous aluminum hydroxycarbonate.

The morphology and elemental composition of particles of samples N, O, and P also revealed the diversity of this type of antacid (Table III). Platy particles, aggregates of platy particles, and cubic particles were observed. In this group, of the 16 particles which were examined, 5 contained both aluminum and magnesium, 6 contained only aluminum, and 5 contained only magnesium. The surface area of sample N was 5 times greater than the surface area of samples O or P. The primary crystallite dimension of these antacids could not be determined due to the presence of amorphous and crystalline phases.

The antacid properties of the aluminum hydroxide–magnesium hydroxide codried gels are presented in Table IV. All three samples passed the preliminary antacid test, although the pH of samples O and P was higher than that observed for any of the 16 samples studied in both parts of this series. The higher pH may be caused by the magnesium hydroxide in the sample. Samples O and P also showed a significantly higher acid neutralizing capacity than the other samples in the study. In the Rossett–Rice test, only sample O raised the pH to 3.0 and exhibited a buffering pH at a dose of 400 mg. Samples O and P exhibited a faster rate of acid neutralization at pH 3, 37°C, than sample N. The slower rate of acid neutralization of sample N is surprising in view of its high surface area. The presence of magnesium hydroxide in samples O and P may have affected the antacid properties. Thus, the composition of the amorphous and crystalline phases in the three samples of this type of antacid influences the rate of acid neutralization. As has been observed for all samples in this study, the rate of acid neutralization at pH 5.0, 37°C, was very slow for the three samples in this group.

ACKNOWLEDGMENT

This work was supported in part by Bayer AG.

REFERENCES

1. S. M. Beekman. Preparation and properties of new gastric antacids. I. Aluminum hydroxide-magnesium carbonate dried gels. *J. A.Ph.A. Sci. Ed.* 49:191–200 (1960).
2. H. W. Schmank, J. M. Holbert, and S. M. Beekman. Synthesis and evaluation of new high-capacity gastric antacids. *J. Pharm. Sci.* 54:1285–1289 (1965).
3. S. M. Beekman. Preparation and properties of new gastric antacids. V. Aluminum hydroxide-magnesium hydroxide dried gels. *J. A.Ph.A. Sci. Ed.* 51:675–679 (1962).
4. C. L. Peterson, D. L. Perry, H. Masood, H. Lin, J. L. White, S. L. Hem, C. Fritsch, and F. Haeusler. Characterization of antacid compounds containing both aluminum and magnesium. I. Crystalline powders. *Pharm. Res.* 10:998–1004 (1993).
5. C. J. Serna, J. L. White, and S. L. Hem. A structural survey of carbonate-containing antacids. *J. Pharm. Sci.* 67:324–327 (1978).