Handbook

of

Non-Prescription Drugs

1971 Edition

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George B. Griffenhagen
and
Linda L. Hawkins
Co-editors

Published by the
American Pharmaceutical Association
2215 Constitution Avenue, N.W.
Washington, DC 20037

First Edition
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introduction

As we stated in the introduction of the first two editions of the American Pharmaceutical Association's *Handbook of Non-Prescription Drugs,* self-medication is an integral part of health care today. People like to medicate themselves—self-medication is easy, convenient and generally inexpensive—and it takes some of the load from the already overtaxed physicians. But the self-medicating public must be made to recognize the approximate boundaries of its own therapeutic competence and the dangers inherent in attempting to exceed those boundaries. As APhA Executive Director Apple has written—

"Self-medication is being practiced today with a degree of sophistication that belongs to the Dark Ages. It is national policy for us to practice every possible precaution to protect the patient in the case of drugs which require prescription orders. Nevertheless, some medicaments are available for self-medication that may not be as potent as legend drugs when compared on paper, but there is abundant evidence that their pharmacological action in vivo clearly indicates that they deserve to be labeled 'explosive—handle with care.'"

In reviewing the problems associated with self-medication, M. N. G. Dukes in his excellent treatise *Patent Medicines and Autotherapy in Society* (The Hague, Netherlands, 1963) concludes that "we must continually be on guard against wholesale rejection and condemnation of those practices which may be of help and real benefit to the layman." Dukes continued by noting that depriving the public of home remedies would not necessarily induce people to seek professional medical counsel. They might turn instead to other forms of self-treatment such as folk remedies or the faith healers and charlatans. OTC drugs must therefore be accepted as a normal part of the social scene, but we must also find adequate solutions for the problems caused by their use and particularly by their misuse. Since the traditional source (although not always the only source) of home remedies is the pharmacy, no less authority than former U.S. Public Health Service Surgeon General Leroy E. Burney urged "increased use of, and participation by the pharmacist . . . to improve understanding of the great potential for good of self-medication and, concurrently, when to self-medicate and when to seek professional care. The pharmacist is often the first one contacted by a person with either a minor or serious ailment. The pharmacist, therefore, has a distinct contribution to make in assuring that self-medication achieves its greatest good and least possible harm through his explanation, advice and warning."

To provide the best advice, pharmacists as well as physicians and other members of the health professions, must know the composition of the product before they can render maximum guidance. All health practitioners have always been at a disadvantage in not knowing the full composition of packaged medicines. Even in ancient civilizations few, except those who concocted them, knew the composition of the nostrums sold by the self-appointed healers. But even had the composition been known, ancient civilization would have had very little fundamental knowledge of the pharmacological action of the "active ingredients."

But, as the knowledge of medicine and pharmacy advanced, the "secret remedy" grew in popularity. The introduction of "patent medicines" did not produce disclosure of contents; in fact "patent medicine" makers were even more obscure as to their formulas than were their predecessors. Furthermore, the composition of "patent medicines" varied at the will of the promoter, to the chagrin of the pharmacist who tried to learn the composition of the products which he made available to the self-medicating public.

One of the first actions of the American Pharmaceutical Association when it was founded in 1852 was to ask a committee to "act efficiently in abating this great evil." Many of the profession's leaders in the second half of the 19th century sought to identify the "secret formulas" which were subsequently published in many of the pharmaceutical publications of the period. A classical example of one compilation of the formulas for "secret formulas" was authored by pharmacist A. Emil Hiss and published as a *Thesaurus of Proprietary Preparations* (Chicago, 1898). In the introduction to his 280-page book Hiss wrote—

"Proprietary preparations, like other medicines, are good or bad according to their respective intrinsic merits as medicinal agents. The reproach of proprietary pharmaceuticals as a class consists primarily in the atmosphere of secrecy and mystery with which many manufacturers attempt to surround their preparations. An open proprietary medicine with a clear descriptive name is entitled to full consideration without prejudice, but a secret compound with a meaningless title is presumptively a fraud. Why conceal the composition of a remedy unless it be to impose upon the physician's credulity or to maintain a monopoly not based on the excellence of the product? Why a 'secret' if not to permit extravagant or fraudulent claims as to therapeutic merit."

The sensational disclosures by the muckrakers at the turn of the century subsequently led to the enactment of the 1906 Federal Food and Drug Act, but unfortunately few ingredients were required to be identified on the label of proprietaries. During the ensuing years, the federal law has been tightened insofar as prescription drugs are concerned, so that a quantitative statement of every active ingredient must be identified, but few changes have been made in the full formula disclosure of non-prescription drugs.

The 1938 Federal Food, Drug, and Cosmetic Act did specify certain warnings that were to be carried on various non-prescription drugs, and the Proprietary Association compiled these initially in 1947 in a 100-page booklet entitled *Information on Labeling and Advertising*. But, as an editorial in the *Journal of the American Medical Association* (October 19, 1964) mentions, "warnings on the labels of non-prescription drugs do not sufficiently protect the public from the hazards of excessive use; only education of the public will provide the desired protection."

The public has grown exceedingly interested in knowing more about the drugs they take, but all too many consumers are obtaining such data on home remedies from biased advertising as well as from an ever-increasing number of articles in slick magazines. In 1955, Consumer's Union published the first edition of their book *The Medicine Show*, sub-titled "Some Plain Truths about Popular Remedies for Common Ailments," but it too is an oversimplification of the values and hazards of home remedies—evaluations which are more often than not based on price alone, rather than on an actual evaluation of product composition.

Thus, the problem of product identification was again approached by the American Pharmaceutical Association with the following 1967 official endorsement—

Realizing the need for professional supervision in the area of non-prescription medication and the vital importance of this supervision to the public health, APhA shall continue in its efforts to obtain legislation to require the labeling of non-prescription remedies to include information on the names and quantities of therapeutically active or significant ingredients in the same manner as is now required for prescription legend drugs.

To fill the obvious void of information on formula disclosures, APhA initiated a series of articles on various classes of home remedies in the *Journal of the American Pharmaceutical Association* which was subsequently republished for the first time in September, 1967, as the *Handbook of Non-Prescription Drugs*. The response to the publication was overwhelming. Reviews called the *Handbook* "a first" and "a valuable guide."

Since some 20 percent of the products listed in this *Handbook* still lack the quantitative formula because manufacturers refuse to disclose it on the basis that it is a "trade secret," the APhA in 1968 officially went on record as follows—

"Pharmacists should recommend only those products on which information on the quantitative amounts of all active ingredients is available—such as in the Handbook of Non-Prescription Drugs or on the label."

It should be pointed out that we still are living in a "jargon-jungle" of terminology insofar as designation of self-medicating products is concerned. Even in the 19th century, attempts were

made to distinguish between "proprietary preparations," "patent medicines," "pharmaceutical specialties" and "secret remedies." Since the term "proprietary" indicates proprietorship, it can be considered synonymous with brand-name or trade-name, whether they are prescription or non-prescription drugs. Thus, the often used distinction of "proprietary medicines" to designate those advertised to the public and "ethical OTC (i.e. over-the-counter) drugs to indicate those promoted directly to the health professions, is no longer clearly distinguishable. Another complicating factor is that drugs sold directly to the public may be labeled by brand-name as well as by non-proprietary (generic) name. Most classes of medicinals are probably best identified either as "prescription-legend drugs" (i.e. available only on a prescription order) and "non-prescription drugs."

The terms "drug sundries" has often been used to identify such classes as dentifrices, deodorants, dry skin and chapping aids, etc., but such a term, through common usage, also has included a large array of items which have little or no relationship to health-related products. Under federal law, there are mainly three groupings—drugs, devices and cosmetics, but even here, the distinction between a "drug" and a "cosmetic" is not always clear. Home remedies may be a useful term to include all products contained in this *Handbook*, but even this is by no means universally accepted. Hence, we continue to use the designation "non-prescription drugs" in its broadest sense as the title of this *Handbook*.

This 1971 edition of the *Handbook* has again been enlarged with revised text and updated tables of all products listed. We have endeavored to make this *Handbook* as accurate as possible, but it should be noted that product formulations change from time to time, and the rights of manufacturers are sold, traded or exchanged regularly so that the firm name appearing on the label is constantly changing. The Federal Food and Drug Administration also is implementing the National Academy of Sciences—National Research Council Drug Efficacy Study with an increasing number of announcements in the *Federal Register* that certain products lack substantial evidence of effectiveness as defined by the Federal Food, Drug, and Cosmetic Act. Even as we go to press, some products previously listed have been removed from the market, and hence have been deleted from listing in this *Handbook*. However, other FDA announcements are the subject of actions contesting the findings, and thus such products remain in this *Handbook*. Some manufacturers are submitting new data in an attempt to establish efficacy, or making changes to render the products acceptable - hence formula changes are even more likely to occur in the coming year than in past years.

We are indebted to the authors of the various chapters, each of whom has been given the opportunity of updating his text, and we also are indebted to APhA staff as well as the APhA Committee on Publications for their guidance. We hope that this edition sheds new light on the subject, and will make the reader a little wiser, the self-medicating public a little safer and non-prescription drugs a little more useful.

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antacids

by Richard P. Penna

Among the proprietary products that a pharmacist has to offer his clientele, the antacids offer an opportunity for the practitioner to provide a real service in terms of knowledgeable and informative counsel. The frequent occurrence of mild gastrointestinal disorders, the variety of antacid products available and the increasingly large advertising expenditures for these products place the pharmacist in an ideal position to render meaningful advice to his patrons. Indeed, the number of antacid preparations on the market today is staggering.

In 1968, antacids accounted for total sales of $99.3 million according to *Drug Topics*. This includes $38.6 million in tablets, pills, gums and lozenges (of which there are more than 300 different products on the market), $44.8 million in liquids (of which there are about 175 products on the market) and $5.9 million in powders (of which there are over 100 different products on the market). Milk of magnesia tablets alone occupied a $9.8 million market.

In addition to making a choice from among these preparations, the pharmacist, if he is to render a professional service, must concern himself with his self-medicating patron. He must consider the conditions for which an individual may attempt self-medication, more serious conditions which have symptoms that may mimic the symptoms of hyperacidity and the dangers of self-medication. Satisfied that his patron may safely self-medicate himself, the pharmacist must then choose the product which he believes is best for that patient. This act involves an evaluation of all the antacids he carries in stock and a thorough knowledge of which product is best for the condition his patron is treating.

In a consideration of gastrointestinal abnormalities commonly treated with self-medication, one is immediately confronted with such medically vague terms as "sour stomach," "upset stomach," "butterflies," "heartburn" and "indigestion." While these terms have been used for years by the public, they remain medically undefined and ambiguous. Some of the conditions which may fall under the category of these phrases are over-eating which causes distention of the stomach due to delayed gastric emptying and swallowed air, [1] gastritis due to foods or substances not "agreeing" with an individual or to ingestion of alcohol and esophageal regurgitation which has now been defined as heartburn [2] but which to the public still includes any pain in the epigastric region. Certainly nausea and vomiting which may be due to a myriad of causes from pregnancy to drug toxicity fall into this area of self-diagnosis.

Peptic ulcer, a condition in which the use of antacids is accepted therapy, is a condition for which self-medicating patients may seek advice from pharmacists. This usually occurs sometime after the physician has diagnosed the condition and treated it only to have the patient abandon treatment after the symptoms have disappeared. The return of symptoms in many cases brings the patient to the pharmacy seeking advice on an antacid to treat his ulcer again. Since the treatment of a peptic ulcer is usually a combination of an antacid and an antispasmodic agent and only the antacid can be provided without prescription, the patient should be urged to see his physician.

Secondly, the mere occurrence of symptoms similar to those of a previous condition does not necessarily indicate that the conditions are the same. In fact, in many cases the self-diagnosis of a gastrointestinal disorder and its subsequent self-treatment with an antacid can be hazardous. It must be recalled that treatment of a pain with an antacid is merely treating the symptom and neglecting the cause. Failure of treatment or the recurrence of symptoms should indicate a physician be consulted.

There are many diseases whose symptoms may mimic hyperacidity, usually as epigastric pain. Acute gastritis, pancreatitis, esophagitis, angina, gallstones, hiatus hernia, pulmonary and coronary infraction can at times manifest themselves as pain in the stomach or "indigestion" and "heartburn." As rare as these cases might be, the pharmacist must be alert to the possibility that a patient requesting a home remedy may be treating himself in vain.

The pharmacist has an obligation to question the patient before deciding to recommend a product. The severity and abruptness of the onset of pain would indicate a more serious condition. In addition the length of time the symptoms have been present or information regarding the recurrence should certainly be facts to consider before a decision on a remedy is made. Recurring symptoms, even though relief is obtained with an antacid, indicate medical investigation is necessary.

Many times an adult will request a remedy for vomiting only to reveal when he is questioned that the remedy is intended for a small child or infant. Vomiting in children and particularly in infants can lead to serious acid-base and dehydration problems and should be promptly referred to a physician. Vomiting in an individual of any age is serious, particularly if it is present for longer than several hours and most certainly if there is blood present.

The mechanism of action of antacid products is generally accepted as a chemical neutralization of the hydrochloric acid present in the gastric fluids. In the treatment of peptic ulcer,

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however, the inactivation of the proteolytic enzyme, pepsin, seems to be an important action as well. This may be a physical absorption of the pepsin onto the antacid particle[3] or, because of the rise in pH above four, an inhibiting reaction of the precursor pepsinogen to pepsin. This reaction takes place in the gastric juice after pepsinogen has been secreted by the chief cells in the gastric lining. Pepsin is considered by many to play an important role in the development of peptic ulcers.

Lastly, the evolution of carbon dioxide by some antacids may play a role in the relief of some conditions of overeating.[1] The sudden production of the gas in the stomach induces belching which aids in the expulsion of swallowed air. In addition the high pH of these antacids hastens gastric emptying which also tends to reduce discomfort.

The evaluation of an antacid is difficult. However, there are certain concepts that can be considered which may bring the problem into sharper focus. Factors which are important to the efficiency and assessment of an antacid are listed in Table I. The first four factors listed in the table are dependent on the physical characteristics of the antacid product in question. The more important of these characteristics are listed in Table II. Certainly in the evaluation of an antacid, we should concern ourselves with how much total acid the product is capable of neutralizing. Likewise the speed of neutralization is important if neutralization of gastric acid can be equated with relief of symptoms. Duration of action is important for duration of relief or for healing purposes.

The ideal pH to which the gastric contents are buffered by the antacid is between pH four and pH five. This optimum range is sufficiently high to inhibit the production of pepsin but low enough to avoid the stimulation of more hydrochloric acid through the "acid-rebound" sequence. The solubility of the antacid is critical because a solution of antacid (e.g., sodium bicarbonate) reacts faster and more completely than a slowly soluble or insoluble product. Unfortunately, an antacid in solution usually has a short duration of activity and, because it usually raises the pH of the gastric fluids above seven, acid rebound is frequent.

The insoluble antacids must depend on surface area for their efficiency. The larger the surface area (smaller particle size), the more contact there exists between the acid and its neutralizer or between pepsin and its adsorbent and the faster the action. Because the chemical is a solid, the reaction is prolonged giving increased length of activity and the pH is usually maintained within desirable limits. The surface area and wettability concept play an important role in the superiority of a liquid over a tableted preparation of the insoluble antacids.[4-5] The insoluble antacids are usually hydrophobic—that is, they do not mix readily with water. A liquid product is milled to a fine particle size and is completely wetted to provide prompt and complete activity. On the other hand, a patient who has to pulverize an antacid tablet with his teeth usually does not obtain the same uniform and small particle size as is present in the liquid. In addition the particles are not sufficiently wetted to provide for prompt action.

Aging and its subsequent effect on crystalline structure has been shown to be responsible for the differences in neutralizing efficiency of various batches of aluminum hydroxide gels. Bassett and Durrant[6] state that there are many variables which affect the types of preparations produced and it is virtually impossible to produce two lots of aluminum hydroxide with identical physical properties. Furthermore, Murphy[7] has shown that for several lots of aluminum hydroxide studied there was a slow but continued change in rate of neutralization upon aging. Aluminum hydroxide gels were found to become less reactive as they aged. This is attributed to a change from the amorphous structure to crystalline structures which are virtually unreactive to hydrochloric acid. Hinkel and coworkers,[8] however, claim a new polymer hexitol complex of aluminum hydroxide is more reactive and less prone to aging effects.

Gastric emptying time has a profound effect on the activity of an antacid.[9] Ulcer patients have a more rapid gastric emptying so that the antacid is quickly squeezed out of the stomach, thereby limiting its effectiveness. Paradoxically, if the pH of the stomach is raised too high it tends to empty more quickly creating the same problem. Recently, it has been shown that if the antacid is administered one hour after meals, gastric emptying is delayed, the product remains in the stomach longer and less frequent dosings are required.[10] The result is a more efficient use of the antacid.

Alterations of the acid-base balance of the body are problems associated with the chronic use of the soluble antacids in particular. The effervescent seltzer type of antacid or sodium bicarbonate contribute large amounts of alkali to the body which, if taken for prolonged periods, may cause complications. Similarly, these products also contain relatively large amounts of sodium which can be troublesome, particularly in the hypertensive or elderly patron with congestive heart failure. The pharmacist must examine his stock of antacids and determine which contain soluble antacids and which contain high amounts of sodium.

Finally, in consideration of the factors which are important to the efficiency and assessment of an antacid product, one must consider the method by which the antacid product was evaluated and consequently the method on which the various claims of superiority are based. From an examination of Tables I and II, it is readily apparent that no one evaluation method can give a complete picture. For example, placing the antacid in a test tube with pH electrodes and measuring pH versus time with the addition of acid can give a limited picture of the product. However, gastric emptying is not accounted for and the stomach's continuing secretion of acid is not considered in this technic. More sophisticated variations of this technic attempt to duplicate gastric emptying and the continuously secreting stomach wall. However, the presence of pepsin which can inhibit some antacids[7] and of food which can also influence the neutralization sequence is neglected.

table I

factors important to efficiency and assessment of an antacid

1. Total neutralizing capacity
2. Speed of neutralization
3. Duration of action
4. pH to which the gastric contents are buffered
5. Gastric emptying time
6. Effect on acid-base balance of body
7. Method of evaluation
8. Side effects

table II

physical factors affecting antacid efficiency

1. Solubility
2. Wettability
3. Surface area (particle size)
4. Disintegration time of non-chewable tablets
5. Reactivity (crystalline structure and age)
6. Administration with respect to meals

Many investigators have attempted to withdraw stomach contents at varying intervals after the administration of antacid and analyze the fluid for acid strength. Still other workers have studied the pH of the stomach by placing pH electrodes into the stomach. [11] Aside from the procedure's being difficult, the pH of the stomach differs depending on the area where the pH is measured. [12] The critical importance of knowing from which portion of the stomach the contents are aspirated or in which part the electrodes are placed is evident when products or various studies are compared. Without such knowledge any comparison is difficult if not impossible. Thus, while each method of evaluation of antacids yields important data, a total concept of the efficacy of one antacid as compared with another is difficult to obtain.

In studying the effect of administering calcium carbonate with respect to meals, Fordtran and Collyns [10] observed that if four grams of the drug are administered one hour after a meal, the acid concentration was depressed for more than three hours. This contrasts sharply with the values recorded by other investigators who found that antacids on an empty stomach kept the pH high for only as long as 75 minutes.[13]

Another interesting fact brought out in the study [10] was that by doubling the dose of antacid (calcium carbonate) one could obtain a proportionately longer period of depressed acid concentration in the stomach. The dose of antacids when administered after a meal is important to the degree and length of neutralization obtained. However, the degree and length of neutralization which are necessary depend to a great extent on the conditions being treated.

Another means of evaluation of drug products, and certainly an important method, is the clinical trial. With all the intra- and extragastric measurements, it is the effect of the drug in the patient that usually tells the story. In this regard, the literature is replete with clinical studies performed to test or prove the qualities of a particular antacid. Plotz and Slanger[14] studied a new antacid preparation, a combination of colloidal tricalcium phosphate and magnesium trisilicate, in 100 patients with excessive gastric acidity as measured by gastric aspiration. The authors noted good to excellent relief in 85 percent of the patients, but no controls were used. Kauvar[15] studied the same preparation in 25 patients comparing it to a well-known product containing magnesium trisilicate and aluminum hydroxide and a placebo in a "three-way double blind technic." He found the new preparation to be statistically superior to the well-known test product or placebo. No information is given, however, regarding the evaluation procedures; secondly, the products were all used in different patients making final judgment of the results somewhat lifficult.

In 1961, Schwartz[16] compared a new formation of specially processed aluminum hydroxide and an older formulation of the same product. Intragastric pH measurements were made on 11 ulcer patients and six normal patients. Eighty-five ulcer patients were then treated with the new formulation. It was shown that the newer formulation gave higher intragastric pH values for a longer period of time than the old formulation. However, in the clinical trial portion only the new formulation was used; therefore any claim as to clinical superiority was invalid.

The clinical trial, although a valuable tool, is in many cases conducted in such a manner that a true evaluation of the product tested cannot be made. As stated by Berk [17]

Many reports claiming to establish the value of certain drugs consist of clinical observations having largely to do with subjective response on the part of the patients. The subjective improvement reported to occur is percentagewise often significantly different from that obtained with conventional management not employing these drugs. Despite this, control groups of patients treated with placebos and with an orthodox regimen are all too frequently omitted.

calcium carbonate

Among the antacids used, either alone or in combination, calcium carbonate remains a popular drug. Indeed calcium carbonate has recently received notoriety as being the antacid of choice. [18–19] Kirsner *et al*[20] found calcium carbonate the most effective antacid when compared with aluminum hydroxide (various brands). In another study, McKenna[21] found calcium carbonate to be the most effective antacid but frequent dosages were necessary to maintain adequate relief. In studying heartburn due to pregnancy, Cook and coworkers[22] checked 50 pregnant patients with complaints of gas, bloating, nausea and postprandial pain or discomfort. A combination product of calcium carbonate, magnesium carbonate and milk and cream solids, brought improvement in 88 percent of the patients. Again no controls were used in this study.

When an *in vivo* test was made utilizing the intragastric pH electrode,[13] Harrison and coworkers found that a dose of one gram of calcium carbonate raised the pH of the stomach to seven within 15 minutes. The pH remained above six for 45 minutes, returning slowly to three. The effect of a four-gram dose of calcium carbonate given one hour after meals has already been discussed. Kirsner and Palmer[23] found that the intragastric pH ranged between 3.7 and 5.8 during hourly administrations of four grams of calcium carbonate and 90 cc of milk. Of the antacids studied, they concluded calcium carbonate was the most effective.

In a very comprehensive review, considering economic factors as well, Brody and Bachrach[24] arrived at a similar conclusion—that calcium carbonate is an inexpensive, rapid and potent neutralizer and can be considered the antacid of choice. Side effects can, however, become a problem with this agent, particularly if taken in high and frequent doses for prolonged periods. Constipation is the most common effect seen. Usually this can be controlled by adding a magnesium carbonate or oxide to the formulation. In certain instances, however, constipation remains such a significant problem that therapy must be discontinued. Nevertheless, for the occasional user, this usually presents little difficulty.

Increased blood levels of calcium have been demonstrated by Stiel and co-workers[25] in six of 28 peptic ulcer patients treated with 30 to 40 grams of calcium carbonate daily. Berreras[26] observed similar effects in ulcer patients after four hourly doses of two grams of calcium carbonate. In addition, Berreras observed a significant rise in gastric acidity and acid output following the administration of the antacid.

Another potential side effect from calcium carbonate is the formation of urinary calculi. This can be caused by both high calcium and alkali intake. This effect, as serious as it is, still is quite rare and its association with calcium carbonate ingestion has been debated. [24] The indications are that rather than self-medicating with calcium carbonate for a prolonged period, an individual would do well to consult his physician.

sodium bicarbonate

Sodium bicarbonate is still one of the most frequently used antacids we have today. In therapeutic doses of four grams, it is rapidly acting and effective. In cases of simple discomfort due to overeating, sodium bicarbonate is effective in inducing gastric emptying belching. While effective for the occasional user, the drug can be harmful if used chronically.

examples of antacids

product	dosage form	manufacturer	sodium bicarbonate	calcium carbonate	aluminum hydroxide	magnesium oxide or hydroxide	magnesium trisilicate	dihydroxyaluminum aminoacetate	other	sodium *(a)*
Al-Caroid	powder and tablet	Breon	–	76.14% 450 mg	4.8% 30 mg	4.8% 30 mg	–	–	4% papain T.32.5 mg	–
Alkalade	suspension	De Pree	–	1.2 Gm/ 15 ml	300 mg	–	–	–	–	–
Alglyn	tablet or magma	Brayten	–	–	–	–	–	500 mg/ tab 250 mg/ 5 ml	–	–
Alka Seltzer	tablet	Miles	1.904 Gm	–	–	–	–	–	aspirin 324 mg cal. phosphate 196 mg citric acid 1.055 Gm	–
Alkets	tablet	Upjohn	–	800 mg	–	65 mg	–	–	mag. carb. 130 mg	–
Aludrox	tablet and suspension	Wyeth	–	–	500 mg/tab 500 mg/5 ml	***	–	–	–	13.5 mg/ 15 ml
Alzinox	tablet and magma	Smith, Miller and Patch	–	–	–	–	–	500 mg/tab or 5 ml	–	–
Amitone	tablet	Thayer	–	420 mg	–	–	–	–	glycine 180 mg mint flavor	–
Amphojel	tablet and suspension	Wyeth	–	–	320 or 600 mg/tab susp.*	–	–	–	–	24.6 mg/ 15 ml
A.M.T.	tablet and suspension	Wyeth	–	–	150 mg/ tab	–	250 mg/tab 650 mg/ 5 ml	–	–	25.5 mg/ 15 ml
Bell-Ans	tablet	Bell & Co.	264 mg	–	–	–	–	–	willow charcoal 38.8 mg gingerine 0.0003 ml	–
Belglyn	tablet	Brayten	–	–	–	–	–	500 mg/ tab	belladonna alkaloids*	–
BiSoDol	tablet	Whitehall	–	*	–	*	*	–	peppermint	0.036 mg/tab
BiSoDol	powder	Whitehall	*	–	–	–	–	–	peppermint mag. carb.* bismuth subnitrate*	471 mg/3 Gm
Calcium Carbonate & Soda	tablet	Lilly	1.95 Gm	–	–	–	–	–	–	–
Camalox	suspension	Rorer	–	*	*	*	–	–	–	–
Chooz	chewing gum	Pharmaco	–	*	–	–	*	–	peppermint oil	–
Creamalin	tablet and liquid	Winthrop	–	–	320 mg/ tab or /5 ml	760 mg/ tab	–	–	mint flavored liquid	9 mg/ 15 ml
Cremo Carbonates	magma	Merck Sharp and Dohme	–	100 mg/ 5 ml	–	–	–	–	chloroform 10 mg bis. subcarb. 200 mg. mag. carb. 200 mg	–
Dicarbosil	tablet	Arch	–	489 mg	–	–	6 mg	–	mag. carb. 11 mg oil of peppermint	2.7 mg/ tab

product	dosage form	manu-facturer	sodium bicar-bonate	calcium car-bonate	aluminum hydroxide	magne-sium oxide or hydroxide	magne-sium tri-silicate	dihydroxy-aluminum amino-acetate	other	sodium *(a)*
Di-Gel	tablet and liquid	Plough	–	–	*	*	–	–	mag. carb.* tab simethicone 25 mg/tab or /tsp	–
Fizrin	powder	Glenbrook	1.82 Gm	–	–	–	–	–	aspirin 324 mg sod. carb. 400 mg citric acid 1.45 Gm	–
Gelusil	liquid and tablet	Warner-Chilcott	–	–	250 mg/ tab or /5 ml	–	500 mg/ tab or /5 ml	–	mint flavor	19.5 mg or /15 ml
Gelusil-Lac	powder	Warner-Chilcott	–	–	1 Gm/pack	–	2 Gm/pack	–	high protein, low fat milk solids	6.5 mg/ pack
Gelusil M	liquid and tablet	Warner-Chilcott	–	–	*	*	*	–	(liq.) alginates (tab.) mannitol	5.7 mg/5 ml 6.1 mg/tab
Gustalac	tablet	Geriatric Pharma-ceutical Corp.	–	300 mg/ tab	–	–	–	–	defatted skim milk powder 200 mg tab	–
Krem	tablet	Neisler	–	400 mg	–	–	–	–	mag. carb. 200 mg cream & milk powder 500 mg mint or cherry flavor	–
Kudrox	suspension and tablet	Kremers-Urban	–	–	susp. gel*	susp*	–	–	hydro magma paste 600 mg/tab susp. sorbitol	–
Maalox	suspen-sion	Rorer	–	–	*	*	–	–	–	16.8 mg/ 15 ml
Maalox #1	tablet	Rorer	–	–	†	†	–	–	–	1 mg
Maalox #2	tablet	Rorer	–	–	**	**	–	–	–	2 mg
Magnatril	tablet and sus-pension	Lannett	–	–	260 mg/tab susp*	130 mg/tab susp*	454 mg/tab 260 mg/tsp	–	–	–
Magnesium-Aluminum Hydroxide Gel USP	suspen-sion	Philips Roxane	–	–	760 mg /30 ml	1.15 Gm /30 ml	–	–	sorbitol* sod. saccharin* peppermint	50.4 mg /30 ml
Malcogel	suspen-sion	Upjohn	–	–	330 mg/ 5 ml	–	660 mg/ 5 ml	–	–	–
Maxamag Suspension	suspen-sion	Bryant-Vitarine	–	–	gel*	*	–	–	–	–
Mucotin	tablet	Warner-Chilcott	–	–	250 mg	650 mg	450 mg	–	gastric mucin 65 mg	–
Mylanta	tablet and liquid	Stuart	–	–	200 mg	200 mg	–	–	simethicone 20 mg	0.79 mg/tab 11.7 mg/15 ml
Phosphaljel	suspen-sion	Wyeth	–	–	–	–	–	–	al. phosphate gel (4% est.)	39 mg/ 15 ml
Ratio	tablet	Warren-Teed	–	400 mg	–	–	–	–	mag. carbonate 50 mg	0.6-0.8 mg/tab
Riopan	tablet or suspen-sion	Ayerst	–	–	–	–	–	–	magaldrate 400 mg/tab or /5 ml	2.1 mg/ 15 ml
Robalate	tablet and sus-pension	Robins	–	–	–	–	–	500 mg/ tab or /5 ml	–	28 mg/15 ml 0.11 mg/tab
Rolaids	tablet	Amer. Chicle	–	–	–	–	–	–	dihydroxy al. sod. carbonate 330 mg	53 mg/ tab
Sippyplex	powder	Purdue Frederick	–	–	1 Gm/8 tsp	–	2 Gm/8 tsp	–	vitamins defatted dry milk solids 32.77 Gm/ 8 tsp	–

product	dosage form	manufacturer	sodium bicarbonate	calcium carbonate	aluminum hydroxide	magnesium oxide or hydroxide	magnesium trisilicate	dihydroxyaluminum aminoacetate	other	sodium *(a)*
Soda Mint	tablet	Lilly	330 mg	–	–	–	–	–	oil of peppermint	44 mg/ tab
Syntrogel	tablet	Sauter	–	71 mg	144 mg	–	–	–	mag. peroxide 86 mg	–
Titralac	tablet and suspension	Riker	–	420 mg/ tab 1 Gm/5 ml	–	–	–	–	glycine 180 mg/tab 300 mg/5 ml	37 mg/ 15 ml
Tricreamalate	liquid	Winthrop	–	–	300 mg/5 ml	–	600 mg/ 5 ml	–	–	123 mg/ 15 ml
Trisogel	capsule and suspension	Lilly	–	–	100 mg	–	300 mg	–	–	48 mg/ 15 ml (in suspension)
Trisomin	tablet	Lilly	–	–	–	–	500 mg	–	–	–
Tums	tablet	Lewis-Howe	–	489 mg	–	–	6 mg	–	mag. carb. 11 mg oil of peppermint	2.7 mg/ tab
WinGel	tablet and liquid	Winthrop	–	–	††	††	–	–	–	16 mg/ 65 ml
Zylase	tablet	Bryant-Vitarine	–	300 mg	–	–	–	–	mag. glycinate 50 mg amylase 7.5 mg protease 4 mg cellulase 0.75 mg	–

* Quantitative statement not provided
† Amounts listed as 400 mg combined hydroxides of magnesium and aluminum. Individual concentrations are not listed.
** Amounts listed as 800 mg combined hydroxides of magnesium and aluminum. Individual concentrations are not listed.
*** Amounts in one teaspoonful or one tablet equivalent to 1/4 teaspoonful milk of magnesia.
†† Amounts listed as 410 mg combined hydroxides of magnesium and aluminum, per tablet or /5 ml liquid. Manufacturer states 20% of each ingredient.
(a) Amounts determined from the literature; if amounts are not given, it does not necessarily mean that sodium content is absent.

First of all, the high pH to which the gastric fluids are raised will usually stimulate the production of more hydrochloric acid. Secondly, the alkalinity of the drug when administered for prolonged periods can cause alkalosis and even urinary calculi. Thirdly, the high intake of sodium can cause difficulty for the hypertensive individual or the patient on a restricted salt diet.

aluminum hydroxide

Aluminum hydroxide either alone or in combination with magnesium compounds is perhaps the most popular antacid in use today. In addition to its antacid activity, it is postulated that some of the value of aluminum hydroxide in the treatment of peptic ulcer lies in its ability to adsorb pepsin.[3,27] Like calcium carbonate, aluminum antacids are constipating and, thus, are usually mixed with magnesium compounds to offset this effect. Many times, however, the desired effect is not achieved and constipation continues to be a problem in some individuals. In addition to its adsoprtion of pepsin, aluminum can combine with phosphate, causing an increase in fecal phosphate and a decrease in urinary phosphate. This will not be a problem in the occasional user or even in the ulcer patient who uses large quantities because usual diets are high in phosphate. In some patients with conditions predisposing to low phosphate intake or poor absorption, however, difficulties may arise from low phosphate levels. Aluminum hydroxide is notable in that there is virtually no effect on the body's acid-base balance.[28]

Kirsner and Palmer[23] gave 16 cc of aluminum hydroxide gel hourly with 90 cc of milk and found an average intragastic pH of 2.2. There are many clinical reports[29-31] dealing with the use of aluminum hydroxide in peptic ulcers, most of which are uncontrolled. As was mentioned previously, aluminum hydroxide products vary in their capacity to neutralize acid. Brody and Bachrach[24] found neutralizing capacities varying from 367 cc to 684 cc of 0.1 N hydrochloric acid per ounce. Variations may occur between batches of the same product, the aging factor having a great deal to do with the problem.[7]

Hinkel and coworkers[8] have reported that new, highly reactive polymeric aluminum hydroxide hexitol complex exhibits a better neutralizing profile than the conventional aluminum hydroxide preparations. This product was tested clinically by Schwartz[16] and although he found a more acceptable pH-time profile in intragastric pH, his clinical investigation was uncontrolled and therefore no conclusion can be made regarding the clinical superiority of this compound. Furthermore, these tests fail to provide evidence that aging does not affect the new formulation as it does the old.

magnesium trisilicate

Magnesium trisilicate has a higher adsorption potential than aluminum hydroxide[33] and thus may be of greater value than aluminum hydroxide in the treatment of peptic ulcer because of the increased adsorption of pepsin. Comparative *in vitro* studies have been done to evaluate magnesium trisilicate with other antacids. Johnson and Duncan[32] found that for short observation periods, magnesium trisili-

cate falls below calcium carbonate, sodium bicarbonate and aluminum hydroxide in neutralizing activity. During longer periods of observation, however, magnesium trisilicate was found to be less effective than calcium carbonate, but more effective than aluminum hydroxide. [33]

Magnesium trisilicate has not been demonstrated to produce alkalosis and administering an excess will seldom raise the pH of the stomach above seven. The amount of magnesium absorbed is insignificant. Although many clinical trials testify to its effectiveness in the treatment of peptic ulcer, controls are absent, thus a statement regarding its clinical usefulness would be unfounded.

dihydroxyaluminum aminoacetate

In 1949 Hammarlund and Rising[34] compared a new antacid compound, dihydroxyaluminum aminoacetate (DHAA), with aluminum hydroxide and magnesium trisilicate, both separately and together. They use a potentiometric titration of products purchased on the commercial market. They found DHAA to have the fastest and most prolonged action. Similarly, Breidenbach and Martin,[35] using an *in vitro* acid neutralizing technic found that DHAA and hydrated magnesium aluminate conformed more to the ideal pH-time curve than did the combined hydroxides of magnesium and aluminum and the magnesium trisilicate-aluminum hydroxide gel mixtures. Again the absence of controlled, clinical trials makes a final comparison difficult.

hydrated magnesium aluminate

As mentioned in the above study, [35] hydrated magnesium aluminate (Monalium hydrate) compared favorably with other antacid compounds. In similar comparative *in vitro* study, von Seemann[36] found the new compound to possess high acid combining power, prolonged activity and ability to maintain pH levels between 3.0 and 5.5 longer than any other compound tested. In a combination of clinical and intragastric pH study, Figueroa and Klotz [37] found hydrated magnesium aluminate to be clinically effective and to maintain a desirably low acid level in the stomach on hourly dosages. Sohmer [38] in another study observed similar results. Although these studies show the compound is effective, comparative clinical data are lacking as are controlled studies.

dihydroxyaluminum sodium carbonate

Dihydroxyaluminum sodium carbonate combines the antacid properties of aluminum hydroxide and sodium bicarbonate. [10] Rapid neutralization of acid accompanied by release of carbon dioxide is followed by prolonged neutralization with the pH rarely straying into the alkaline region. Confirming their *in vitro* studies with intragastric pH measurements, Packman and coworkers [39] concluded that this compound was superior to aluminum hydroxide, calcium carbonate and sodium bicarbonate. Although this compound has been shown to be effective, its relative effectiveness must await the conclusion of the controlled clinical trial.

There are many proprietary antacids which are combinations of antacids with other drug products. In the absence of adequate literature in this area, it is safe to conclude that there is little justification for the addition of antihistamines, caffeine, bromides, salicylates or low dose antispasmodics to the antacid already in the product. In many cases the drug additive is present in an ineffective dosage. For example, some antispasmodics in non-prescription stomach remedies are present in one-tenth their usual therapeutic doses. While this low dose may be effective, such a conclusion cannot be made in the face of a lack of adequate published clinical work. The combination products of analgetics and antacids is effective in treating minor pain and may find usefulness when a headache is associated with hyperacidity.

Side effects from antacid therapy are varied. The side effect which should arouse the most concern is the possibility of an individual self-medicating himself for a condition which requires medical supervision. As was mentioned earlier, there are many serious conditions, the symptoms of which may mimic simple hyperacidity but, although in some cases relieved by antacids, should be medically cared for. The pharmacist finds himself in an ideal position to detect these cases and refer them to a physician for proper treatment. Therefore, the pharmacist routinely questions his patrons who chronically use antacids.

The chronic use of antacids has been associated with other problems although these have been rare. Talbot [40] reports a patient who consumed one roll of a popular calcium carbonate antacid per day for a period of four years. The patient had calcium deposits in the cornea and other tissues plus renal insufficiency and alkalosis. Withdrawal of the product and high intake of fluids reversed the condition. Herman and Goldberg[41] report a case of silicone-containing kidney stones formed in a patient who consumed per day for two to three years 30 to 35 tablets of a magnesium trisilicate-aluminum hydroxide combination product. Brettschneider and coworkers[42] report on two cases of intestinal obstruction due to antacid therapy; however, these patients were in debilitated states, so the conclusions must be viewed in this respect. Potyk[43] reports on a patient who experienced an intestinal obstruction from undissolved antacid tablets containing aluminum and magnesium hydroxides. The patient had not chewed the tablets prior to swallowing. Surgery was required to relieve the obstruction and 150 intact tablets were found in the obstructed intestinal segment.

Another problem which can be associated with the chronic administration of antacids is the high sodium intake. This can arise even from the "non-sodium" antacids. Listed are available sodium contents of various products. While for many of the metallic hydroxide products, sodium content will be of little concern, high doses (for prolonged periods in susceptible individuals) would certainly bring the problem of the contribution of sodium from antacids into the picture.[44] This is another reason for exercising caution in chronic users, particularly the elderly who are more prone to sodium problems. Certainly the sodium-containing antacids should be restricted for short term usage. Thus, the pharmacist should be particularly aware of chronic users of this particular class of antacids.

In conclusion, one can safely state that the antacid field is saturated with contenders for honors as the antacid of choice. Obviously, since the choice of an antacid depends on the condition being treated, none has qualified for this position. The ultimate test of a compound's comparative effectiveness, the clinical trial, has suffered from a notable defect —lack of proper controls. Also many of the clinical trials are performed on ulcer patients and so results should not be applied to use of the product in "upset stomach," "sour stomach," or nausea and vomiting.

The final decision on whether to recommend a product and which product to recommend remains with the pharmacist—as indeed it should. It is up to the pharmacist to use his knowledge, background and experience to provide for his client the utmost in professional guidance in recommending a product or in refusing to dispense a product and referring his client to a physician.

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