Handbook of Non-Prescription Drugs

1973 Edition

Published by the

AMERICAN PHARMACEUTICAL ASSOCIATION

Handbook

of

Non-Prescription Drugs

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

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

First Edition
Published September, 1967
1969 Edition
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introduction

As we stated in the introduction of the first three 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.

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."

Despite the fact that considerable publicity has been given to the lack of, and need for, quantitative disclosure of active ingredients in OTC drugs, many people still are surprised that a number of manufacturers continue to hide their products' contents behind the cloak of secrecy. Regulations restricting the use of hexachlorophene promulgated by the Food and Drug Administration on September 27, 1972, provide a classical example of the need for quantitative disclosure of all ingredients

in all pharmaceutical products. Since the law then in existence did not require manufacturers to provide quantitative disclosure of all ingredients in the absence of NDA (New Drug Application) clearance, the FDA drew up the best list it could from available sources, including the last edition of this *Handbook*. The list provided the names of 409 products containing hexachlorophene, but the quantitative amounts were unknown in 222 of the products.

Many point to the Drug Listing Act of 1972 as the means of obtaining the quantitative listing of each drug's active ingredients by June 1, 1973. But the legislative history of this act indicates that the quantitative data will still remain "confidential information" in FDA files.

As reported in the Introduction to the 1971 Edition, FDA was 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. Prior to 1938, no preclearance was required for drugs. From 1938 to 1962 anyone wishing to market a drug not generally recognized as safe had to submit to FDA a New Drug Application (NDA) containing evidence of its safety. Then, in 1962, the law was changed to require evidence of effectiveness as well as safety for any new drug that had been marketed since 1938. FDA contracted with the National Academy of Sciences-National Research Council to review some 4,000 drugs that had been marketed since 1938, but only about 400 of these were non-prescription drugs. Thus, a proposed notice, followed on May 11, 1972, by a final notice in the *Federal Register* entitled "Procedures for Classification of Over-the-Counter Drugs," established FDA review of all OTC drugs to provide basic information of safety (i.e., low incidence of adverse reactions or significant side effects), effectiveness (i.e., a reasonable expectation that the drugs will provide clinically significant results), and accurate labeling (i.e., directions shall be clear, complete and truthful).

In testifying before the Senate Subcommittee on Government Regulation on December 7, 1972, FDA Commissioner Charles C. Edwards described the end results of the study as the preparation of "comprehensive monographs" on a number of classes of OTC drugs. Each "monograph will detail the acceptable product formulations, doses of the active ingredients, and acceptable claims and manufacturing standards. . . . We believe the monograph approach is the only manageable approach to the evaluation and regulation of a large group of drugs (estimated to be well over 100,000) which are available without prescription for self-medication," stated Dr. Edwards. But the time estimate for completing the work of the review panels and publishing proposed monographs for all classes is three years, and "final implementation will take additional time," noted Dr. Edwards.

The 1973 Edition of this *Handbook* thus fills the void until FDA completes its study, and even the tables of products may continue to serve as a useful supplement to the FDA monographs. This 1973 Edition of the *Handbook* has again been enlarged, with revised text as required, and extensive updating of all products listed in the tables. We have endeavored—as in past editions—to make this *Handbook* as accurate as possible, but it should be noted that product formulations frequently change; the proprietary rights of manufacturers are sold, traded or exchanged; and new products appear as old products are removed from the market. As the FDA survey moves forward, it is anticipated that this trend will increase rather than diminish.

We are indebted to the authors of the various chapters, each of whom was given the opportunity to update his text, and we appreciate the cooperation of manufacturers in providing us with product information. We thank the APhA Committee on Publications for its guidance, and take special note of APhA staff who provided assistance in the monumental task of compiling the information as well as the editing and publishing, including Donald E. Prescott and Anthony T. DiSalvo.

We hope that this edition—as past editions—will continue to better equip the pharmacist and other members of the health professions with facts to make the self-medicating public a little safer and non-prescription drugs a little more useful.

George B. Griffenhagen
Linda L. Hawkins
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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 (over $42.5 million in 1971) 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 1971, antacids accounted for total sales of $108.8 million according to *Product Management*. This includes $41.1 million in tablets, pills, gums and lozenges (of which there are more than 300 different products on the market), $51.9 million in liquids (of which there are about 175 products on the market) and $5.3 million in powders (of which there are over 100 different products on the market). Milk of magnesia tablets alone occupied a $10.3 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.

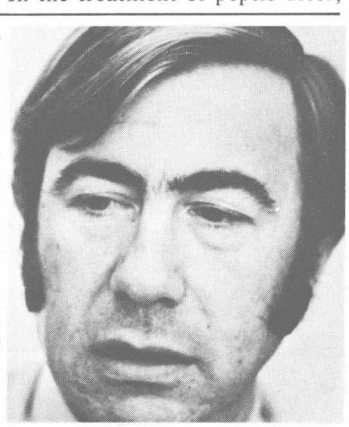
Secondly, the mere occurrence of symptoms similar to those of a previous condition does not necessarily indicate that the conditions are the same. In fact, in many cases the self-diagnosis of a gastrointestinal disorder and its subsequent self-treatment with an antacid can be hazardous. It must be recalled 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 infarction 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,



Community pharmacist, clinical instructor of pharmacy, APhA staff member—such has been the career of ***Richard P. Penna.*** *From 1966 to 1973 he was executive secretary of the APhA Academy of General Practice of Pharmacy. Prior to that Penna was assistant clinical professor of pharmacy at the University of California school of pharmacy, San Francisco Medical Center, from which he received his BS in 1958 and his PharmD in 1959. While on the faculty of the University of California, he was also a practicing community pharmacist in Redwood City, California. Penna served as the first president of and helped organize both the Peninsula (California) Pharmaceutical Society and San Mateo County (California) Pharmaceutical Association. He now serves as APhA Assistant Executive Director for Professional Affairs.*

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 co-workers,[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 an 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 procedures 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 difficult.

In 1961, Schwartz[16] compared a new formulation 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 co-workers[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 co-workers 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 rapid 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.

(continued on page 13)

examples of antacids

product	manufacturer	dosage form	sodium bicarbonate	calcium carbonate	aluminum hydroxide	magnesium oxide or hydroxide	magnesium trisilicate	dihydroxyaluminum aminoacetate	other	sodium *(a)*
Al-Caroid	Breon	tablet	—	450 mg	30 mg	30 mg	—	—	papain 32.5 mg	—
Al-Caroid	Breon	powder	—	76.14%	4.8%	4.8%	—	—	papain 4%	—
Alkalade	De Pree	suspension	—	1.2 Gm/ 15 ml	300 mg	—	—	—	—	—
Alglyn	Brayten	tablet, magma	—	—	—	—	—	500 mg/ tab 250 mg/ 5 ml	—	—
Alka-Seltzer	Miles	tablet	1.904 Gm	—	—	—	—	—	aspirin 324 mg monocalcium phosphate 200 mg citric acid 1.055 Gm	—
Alkets	Upjohn	tablet	—	800 mg	—	65 mg	—	—	mag. carb. 130 mg	—
Aludrox	Wyeth	tablet, suspension	—	—	500 mg/tab 500 mg/5 ml	***	—	—	—	15 mg/ 15 ml
Alzinox	Smith, Miller & Patch	tablet, magma	—	—	—	—	—	500 mg/tab or 5 ml	—	—
Amitone	Mitchum-Thayer	tablet	—	420 mg	—	—	—	—	glycine 180 mg mint flavor	—
Amphojel	Wyeth	tablet, suspension	—	—	320 or 600 mg/tab susp *	—	—	—	—	18 mg/ 15 ml
A.M.T.	Wyeth	tablet, suspension	—	—	150 mg/ tab	—	250 mg/tab 650 mg/ 5 ml	—	—	18 mg/ 15 ml
Bell-Ans	Bell & Co.	tablet	264 mg	—	—	—	—	—	wintergreen willow charcoal 38.8 mg ginger 0.0003 ml	—
BiSoDol	Whitehall	tablet	—	*	—	*	*	—	peppermint	0.036 mg/tab
BiSoDol	Whitehall	powder	*	—	—	—	—	—	peppermint mag. carb.* bismuth subnitrate*	471 mg/3 Gm
Buffertabs	Durst	tablet	—	190 mg	gel 32 mg	—	—	—	bismuth subcarbonate 65 mg mag. carb. 125 mg aminoacetic acid 48 mg	—
Calcium Carbonate & Soda	Lilly	tablet	1.95 Gm	650 mg	—	—	—	—	—	—
Camalox	Rorer	suspension	—	*	*	*	—	—	—	—
Chooz	Plough	chewing gum	—	*	—	—	*	—	peppermint oil	—
Creamalin	Winthrop	tablet, liquid	—	—	320 mg/ tab or /5 ml	75 mg/ tab	—	—	mint flavored liquid	9 mg/ 15 ml
Dicarbosil	Arch	tablet	—	489 mg	—	—	6 mg	—	mag. carb. 11 mg oil of peppermint	2.7 mg/ tab
Di-Gel	Plough	tablet, liquid	—	—	*	*	—	—	mag. carb.* tab simethicone 25 mg/tab or /tsp	—
Ducon	Smith Kline & French	suspension	—	375 mg /5ml	720 mg	350 mg	—	—	mint flavor	15 mg/5 ml

product	manu-facturer	dosage form	sodium bicar-bonate	calcium car-bonate	aluminum hydroxide	magne-sium oxide or hydroxide	magne-sium tri-silicate	dihydroxy-aluminum amino-acetate	other	sodium *(a)*
Eno	Beecham Inc.	powder	2.68 Gm /5 Gm	—	—	—	—	—	tartaric acid 2.32 Gm	—
Fizrin	Glen-brook	powder	1.82 Gm	—	—	—	—	—	aspirin 324 mg sod. carb. 400 mg citric acid 1.5 Gm	—
Gelumina	Amer. Pharm.	tablet	—	—	250 mg	—	500 mg	—	sorbitol 18.8 mg lactose sod. saccharin	0.3 mg/tab
Gelusil	Warner-Chilcott	liquid, tablet	—	—	250 mg/ tab or/4 ml	—	500 mg/ tab or/4 ml	—	mint flavor alginates	5.7 mg/4 ml 5.1 mg/tab
Gelusil-Lac	Warner-Chilcott	powder	—	—	1 Gm/pack	—	2 Gm/pack	—	high protein, low fat milk solids	7.5 mg/ pack
Gelusil M	Warner-Chilcott	liquid, tablet	—	—	*	*	*	—	(liq.) alginates (tab.) mannitol	5.7 mg/5 ml 6.1 mg/tab
Gustalac	Geriatric Pharma-ceutical Corp.	tablet	—	300 mg/ tab	—	—	—	—	defatted skim milk powder 200 mg	—
Krem	Mallin-ckrodt	tablet	—	400 mg	—	—	—	—	mag. carb. 200 mg cream & milk powder 500 mg mint or cherry flavor	—
Kudrox	Kremers-Urban	suspen-sion, tablet	—	—	susp gel*	susp*	—	—	hydro magma paste 600 mg/tab susp sorbitol	—
Maalox	Rorer	suspen-sion	—	—	*	*	—	—	—	16.8 mg/ 15 ml
Maalox #1	Rorer	tablet	—	—	†	†	—	—	—	1 mg
Maalox #2	Rorer	tablet	—	—	**	**	—	—	—	2 mg
Magnatril	Lannett	tablet, suspen-sion	—	—	260 mg/tab susp*	130 mg /tab susp*	454 mg/tab 260 mg/tsp	—	—	—
Magne-sium-Aluminum Hydroxide Gel USP	Philips Roxane	suspen-sion	—	—	760 mg /30 ml	1.15 Gm /30 ml	—	—	sorbitol* sod. saccharin* peppermint	50.4 mg /30 ml
Malcogel	Upjohn	suspen-sion	—	—	330 mg/ 5 ml	—	660 mg/ 5 ml	—	—	—
Maxamag Suspension	Vitarine Co.	suspen-sion	—	—	gel*	*	—	—	—	—
Mucotin	Warner-Chilcott	tablet	—	—	250 mg	650 mg	450 mg	—	gastric mucin 65 mg	—
Mylanta	Stuart	tablet, liquid	—	—	200 mg	200 mg	—	—	simethicone 20 mg	0.79 mg/tab 11.7 mg/15 ml
Mylanta II	Stuart	liquid, tablet	—	—	400 mg	400 mg	—	—	simethicone 30 mg	8 mg/5ml 1.5 mg/tab
Pepto-Bismol	Norwich	liquid	—	—	—	—	—	—	bismuth subsalicylate* salol* zinc phenol-sulfonate*	—
Pepto-Bismol	Norwich	tablet	—	350 mg	—	—	—	—	bismuth subsalicylate* glycocoll	—

product	manu-facturer	dosage form	sodium bicar-bonate	calcium car-bonate	aluminum hydroxide	magne-sium oxide or hydroxide	magne-sium tri-silicate	dihydroxy-aluminum amino-acetate	other	sodium *(a)*
Phillips' Milk of Magnesia	Glen-brook	liquid, tablet	—	—	—	2.27-2.62 Gm/30 ml 311 mg/tab	—	—	—	—
Phosphal-jel	Wyeth	suspen-sion	—	—	—	—	—	—	al. phosphate gel (4% est.)	39 mg/ 15 ml
Ratio	Warren-Teed	tablet	—	400 mg	—	—	—	—	mag. carbonate 50 mg	0.6-0.8 mg/tab
Riopan	Ayerst	tablet, suspen-sion	—	—	—	—	—	—	magaldrate 400 mg/tab or /5 ml	0.7 mg/tab or/5ml
Robalate	Robins	tablet, suspen-sion	—	—	—	—	—	500 mg/ tab or /5 ml	—	0.14 mg/tab 3.05 mg/5ml
Rolaids	Amer. Chicle	tablet	—	—	—	—	—	—	dihydroxy al. sod. carbonate 330 mg	53 mg/ tab
Silain-Gel	Robins	liquid	—	—	gel 282 mg	85 mg	—	—	simethicone 25 mg	4.78 mg/5ml
Silain-Gel	Robins	tablet	—	—	co-dried with mag. carb. 282 mg	85 mg	—	—	simethicone 25 mg	7.68 mg
Sippyplex	Purdue Frederick	powder	—	—	1 Gm/8 tsp	—	2 Gm/8 tsp	—	vitamins defatted dry milk solids 32.77 Gm/8 tsp	—
Soda Mint	Lilly	tablet	330 mg	—	—	—	—	—	oil of peppermint	89 mg/ tab
Syntrogel	Sauter	tablet	—	71 mg	144 mg	—	—	—	mag. peroxide 86 mg	—
Titralac	Riker	tablet, suspen-sion	—	420 mg/ tab 1Gm/5 ml	—	—	—	—	glycine 180 mg/tab 300 mg/5 ml	37 mg/ 15 ml
Tricreama-late	Winthrop	liquid	—	—	300 mg/5 ml	—	600 mg/ 5 ml	—	—	123 mg/ 15 ml
Trisogel	Lilly	capsule, suspen-sion	—	—	100 mg/cap 150 mg/5 ml	—	300 mg /cap 583 mg /5 ml	—	—	48 mg/ 15 ml
Trisomin	Lilly	tablet	—	—	—	—	500 mg	—	—	—
Tums	Lewis-Howe	tablet	—	489 mg	—	—	6 mg	—	mag. carb. 11 mg oil of peppermint	2.7 mg/ tab
WinGel	Winthrop	tablet, liquid	—	—	††	††	—	—	—	16 mg/ 65 ml
Zylase	Vitarine Co.	tablet	—	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 ¼ 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 intragastric 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 co-workers[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

Comparative *in vitro* studies have been done to evaluate magnesium trisilicate with other antacids. Johnson and Duncan[31] found that for short observation periods, magnesium trisilicate 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.[32]

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[33] compared a new antacid compound, dihydroxyaluminum aminoacetate (DHAA), with aluminum hydroxide and magnesium trisilicate, both separately and together. They used 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,[34] 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,[34] hydrated magnesium aluminate (Monalium hydrate) compared favorably with other antacid compounds. In similar comparative *in vitro* study, von Seemann[35] 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[36] found hydrated magnesium aluminate to be clinically effective and to maintain a desirably low acid level in the stomach on hourly dosages. Sohmer[37] 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 co-workers[38] 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 controlled clinical trials.

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 nonprescription 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 are 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 with symptoms which mimic hyperacidity. Some of these conditions may be relieved tem-