Drug Interactions with Antacids
Mechanisms and Clinical Significance

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Summary
Concomitant use of antacid preparations with other medications is common. The potential for antacid-drug interactions is dependent upon the chemistry and physical properties of the antacid preparation. The intragastric release of free aluminum and magnesium ions has potent effects on gastrointestinal function and on drug pharmacokinetics. Antacid-drug interactions may occur secondary to changes in gastrointestinal motility or alterations in gastric and urinary pH. Direct adsorption also results in decreased drug bioavailability. Human drug interaction studies are usually performed with healthy volunteers; extrapolation of these results to clinical situations may not always be valid. However, the current literature would suggest that significant interactions with antacids do occur with certain members of the quinolone, nonsteroidal anti-inflammatory drug (NSAID)
Dyspepsia is a common human experience, and relief can often be found through the use of oral antacids. The ready availability of over-the-counter preparations and the commonality of dyspeptic symptoms in the general public makes antacid use one of the most common forms of self medication.[1] Medications such as nonsteroidal anti-inflammatory drugs (NSAIDs) and antibiotics are common sources of dyspepsia which is often self treated with antacids. Thus, the potential for a drug-antacid interaction exists in many therapeutic situations.

Many patients do not consider antacids to be drugs and hence do not volunteer details about their use unless specifically asked. Concomitant antacid ingestion should be suspected in any case of unexplained therapeutic failure. Patients need education regarding possible interactions and, thus, sound physician knowledge about potential drug-antacid interactions is essential.

The purpose of this review is to summarise briefly the relevant chemical properties of the commonly used antacid preparations and discuss potential mechanisms by which antacids may interfere with normal drug pharmacokinetics. A review of newer literature regarding drug-antacid interactions of interest follows.

1. Mechanisms of Antacid Interactions With Drugs

1.1 Antacid Composition and Chemistry

By definition, antacids are basic compounds which when taken orally neutralise hydrochloric acid in the stomach by various chemical reactions. Hydroxide is the basic anion used most commonly in antacid formulations, but phosphate, trisilicate, carbonate and citrate are also used. Aluminium, magnesium and calcium are the cations used in virtually all antacids (table I).[2]

1.1.1 Aluminium Based Antacids

Aluminium is used in its hydroxide, phosphate, carbonate and aminoacetate forms. The hydroxide form \([Al(OH)_{3}]\) has a high acid neutralisation capacity, but this reaction occurs at a very slow rate relative to other antacids. This makes its use as a sole compound in antacid formulation somewhat limited.[3] Work on the physical structure of aluminium hydroxide gel has demonstrated that the compound exists as a large macromolecular aggregate with a relatively low surface area. Disaggregation is required for acid neutralisation, and this fact probably explains the slow rate of acid neutralisation.[4] The intragastric chemical reaction is as follows:

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Al(OH)_{3} + 3HCl \rightarrow Al^{3+} + 3Cl^{-} + 3H_{2}O
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The significance of this reaction for drug interactions is that free aluminium ion is released and becomes available for intraluminal binding and absorption to drugs. This binding property of aluminium ions is utilised in the treatment of hyperphosphataemia in chronic renal failure. Aluminium ions can also cause changes in gastrointestinal motility, which may have a profound impact on drug absorption.[5]

1.1.2 Carbonate Antacids

Sodium bicarbonate and calcium carbonate have been used since antiquity for the treatment of dyspeptic symptoms.[6] The intragastric reaction with acid occurs rapidly, resulting in the formation of sodium and calcium salts, respectively. Sodium is readily absorbed by the gut, leading to a net base excess. This is of no consequence in most circumstances as excess alkali is promptly excreted in the urine. The capacity of the kidney to excrete bicarbonate is immense, and more than 1000 mmol/day