

Hydrotalcite

The Clay that Cures

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Hydrotalcite (HT) is an anionic clay found in nature. It has a variety of pharmaceutical applications. This article focuses on the versatility of this compound in the prevention and cure of peptic ulcer.

Introduction

The curative properties of inorganic compounds were known even in the early days of civilization. Hippocrates and Paracelsus used mercury and its compounds in many medicinal preparations. In 1909, salvarsan, an arsenic-containing compound was discovered and was effectively used for the treatment of syphilis. Cis-platin is a widely used anti-cancer drug containing platinum. The therapeutic as well as prophylactic use of inorganic compounds is promising, especially when they are well tolerated. The anionic clay, hydrotalcite (*Box 1*) belongs to this category. Hydrotalcite and its structural analogues (commonly called hydrotalcite – type anionic clays) have many medicinal applications.

Peptic Ulcer – Cause and Effects

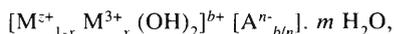
Pepsin is a proteolytic enzyme in the gastric juice. It does its chemical work best at a pH of 1.5 – 2.5. Hydrochloric acid secreted by the parietal cells in the stomach serves the purpose of maintaining this acidic pH. However, when the body's defense fails, lesions are formed in the mucosal lining of the lower oesophagus, stomach or in the first part of duodenum. Thus, the acid-pepsin gastric juice acts upon the stomach wall in an act of chemical cannibalism. This is a debilitating physiological condition called peptic ulcer. Severe burning pain in the stomach (usually in the region between the breastbone and the belly



Box 1. Anionic Clays

Clays are characterised by a layered structure because of which they are slippery when wet. They are broadly classified into cationic and anionic clays. Cationic clays are widely spread in nature. They have negatively charged layers with cations in the inter layer. Structurally, anionic clays are the mirror images of cationic clays and contain positively charged layers and anions in the inter layers.

Anionic clays are represented by the general formula,



where M^{2+} is a divalent or monovalent cation and A^{n-} is the interlayer anion. The value of x is usually between 0.2 and 0.33. The structure of anionic clays is best understood starting from the structure of brucite, $Mg(OH)_2$. The brucite-like sheet is formed by the edge sharing of $M(OH)_6$ octahedra. The isomorphous substitution of M^{2+} ions by trivalent cations leads to the generation of positive charge in the brucite-like sheet. This results in the formation of a layered structure with the charge compensating anions and water in the interlayer region (Figure 1).

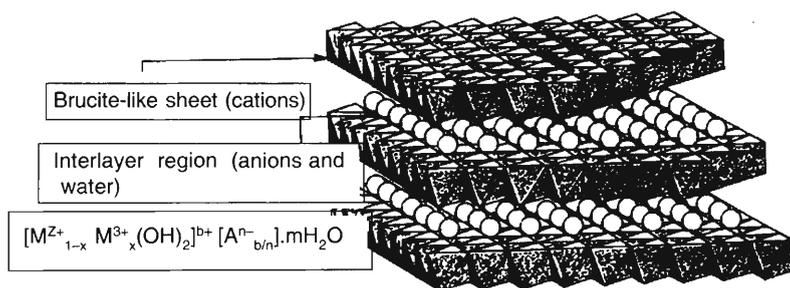


Figure 1. Schematic representation of the hydrotalcite-type anionic clay structure.

button), chronic indigestion, nausea and vomiting are characteristic of gastric or duodenal ulcers. Prolonged use of NSAID's (non-steroidal anti-inflammatory drugs), mental stress, irregular food habits, alcoholism and smoking are known to precipitate acute to chronic ulcers. Peptic ulcer has a bacterial origin as well. *Helicobacter pylori*, a gram-negative bacterium is the prime suspect.

Treatment of Ulcers

In 1971, James Black identified a sub-type of histamine receptor (know as H_2 receptor) as the principal mediator of gastric acid secretion. Antagonists of this receptor showed remarkable

healing effect in peptic ulcers. Later studies have revealed that the inhibitors of the proton pump (the H^+ , K^+ -ATPase operating in the parietal cells) are also rapidly effective and extremely potent anti-ulcer drugs.

The present day therapeutic treatment of peptic ulcer mainly involves the administration of histamine₂-receptor antagonists like Ranitidine, Famotidine and Roxatidine or a proton pump inhibitor drug like Omeprazole. Antibiotics or antibacterial preparations like bismuth subcitrate and antacids are often supplemented to bring down the malady. In many cases, the safe dosage of antacids is rather insufficient to alleviate the hyperacidity in the stomach. Moreover, the antacids may even worsen the situation by causing an 'acid rebound effect' (flooding the stomach with fresh acid). Hydrotalcite is a rather safe and reliable antacid compared to many of its conventional counterparts.

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The efficacy of hydrotalcite (HT) in ulcer treatment has been demonstrated by the German physiologists Dreyer and Marwiski, in 1991. They have found that the oral administration of HT (2 tablets every 6 hours) to healthy adults decreased the gastric acidity by 31-37% over a 24-hour period, with decreases of $\leq 65\%$ during the 2 hours, immediately following the dose. Further, HT and its clinical formulations show negligible acid rebound effect.

Mechanism of Hydrotalcite Action

The mechanism underlying the mucosal protection shown by HT is still not clearly understood. It is believed that the high anti-peptic activity of HT may be due to its ability to absorb the negatively charged pepsin (the digestive enzyme in the stomach) onto its positively charged surface. Hydrotalcite is also capable of buffering the pH of the stomach at about 4 for a long time. Thus the gastric juice is maintained at a pH that is neither too acidic for high pepsin activity nor too alkaline to trigger the acid rebound. Moreover, the rate of hydrochloric acid



An antacid composition containing hydrotalcite and potassium phosphate remarkably reduces the absorption of aluminium.

neutralisation by HT increases with pepsin concentration. This behaviour is in marked contrast to the behaviour shown by many other antacids. Talcid suspension, a clinical formulation of HT exhibits viscoelastic features similar to those of gastric mucin. Thus it affords mucosal protection, by its ability to mimic the barrier properties of the gastric mucus gel.

Tackling Al absorption

The absorption of Al^{3+} ions from antacids based on aluminium compounds is another matter of concern. This may result in Al accumulation in the body to toxic levels, especially in the cases of renal insufficiency. This can lead to the replacement of calcium ions in the bone matrix by Al^{3+} ions resulting in the softening of bones (a condition known as 'osteomalacia') and neuropathy (the atrophy of brain cells). Hydrotalcite accommodates the hydroxides of Mg and Al in its layers. However, the inherent anion exchange properties of this layered compound can be utilised to reduce the aluminium resorption. An antacid composition containing hydrotalcite and potassium phosphate remarkably reduces the absorption of aluminium. The phosphate ions, which replace the carbonate anions in the interlayer region of the original clay material, can form insoluble aluminium phosphate thereby inhibiting Al resorption.

A Well-shielded Anti-inflammatory Drug

The anion exchange properties of hydrotalcite has also been utilised to produce its salicylate-exchanged derivative. This compound shows pronounced anti-inflammatory properties characteristic of salicylate with negligible ulcerogenic activity. The double hydroxide of magnesium and aluminium in the layers prevents the gastric mucosal damage caused by the salicylate anion. However, the mucosal protective action is not mediated by any prostaglandin production into the gastric lumen. Thus, the anionic clay carrier shields the stomach wall without interfering with the anti-inflammatory action of the charge compensating salicylate anion.



Box 2. Prostaglandins

Prostaglandins are the chemicals present in virtually every tissue and fluid in the body. When cell damage occurs, they are released into the damaged area to cause an inflammatory response. Prostaglandins also play important roles in the sensation of pain, generation of fevers and in the protection of the stomach wall. Salicylates and other non-steroidal anti-inflammatory drugs (Naiad's) inhibit the production of prostaglandins. This can render the stomach walls vulnerable for corrosion from the stomach acid and pepsin, thereby resulting in gastric ulcer (*Figure 2*).

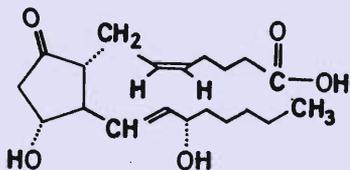


Figure 2. Prostaglandin E2 (the most abundant and the most active of the prostaglandins).

Conclusions

Hydrotalcite proves to be an inimical medicament that attenuates human suffering arising from an agonising physiological disorder. The malady, which is a progeny of the stressful and irregular style of modern life, finds a safe and effective remedy from nature. Man creates ulcer and the clay cures it.

Suggested Reading

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The ideals that have lighted my way and time after time have given me new courage to face life cheerfully, have been Kindness, Beauty and Truth.

Albert Einstein