The case for **sucralfate:** Is it still **relevant?**

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Abstract

Sucralfate is a well-known drug indicated for the treatment of peptic ulcer disease. Since the introduction of other acid-suppressing agents like histamine-2 receptor antagonists and proton pump inhibitors, the use of sucralfate for this indication declined. This article gives an overview of the properties of sucralfate, as well as other indications where it can be the drug of choice.

Keywords: sucralfate, peptic ulcer disease, alternative indications

Introduction

Sucralfate was first introduced in the late 1960s as an ulcer protective agent, then used to treat peptic ulcer disease (PUD). Since the introduction of sucralfate, other agents like the histamine-2 receptor antagonists (H_2-RA) and proton pump inhibitors (PPIs) has been introduced for the same indication. The efficacy of sucralfate for PUD is comparable to both H_2-RA and PPI, but it is also an effective treatment option for various other diseases.

Treatment of various diseases with sucralfate include duodenal ulcers, epithelial wounds, radiation proctitis, burn wounds, Barrett's oesophagus, and chemotherapy-induced mucositis, amongst many other diseases.[1]

Sucralfate is a mucosal protector and exerts its effect by forming a protective layer, increasing bicarbonate production, enhancing the growth of tissue, regeneration and repair thereof.[1] In addition, sucralfate delays gastric emptying, thus increasing its own stay in the stomach.[2] The most common side effect seen with this medication is constipation, amongst other more serious side effects. Sucralfate demonstrates a relatively safe profile since there is insignificant absorption from the gastrointestinal tract (GIT) at less than 2% absorption.[1,2]

Sucralfate has a half-life of 1–2 hours and is excreted in the urine within 48 hours from ingestion.[2] Sucralfate is administered through the oral route on an empty stomach or rectal route, both for local effect, in the dosage form of a tablet or suspension.[2]

Characteristics

Sucralfate is a white amorphous powder.[2] It is a hydrous basic aluminium salt of sucrose octasulfate. Sucralfate is a complex salt of aluminium hydroxide and sucrose sulfate.[2] Sucralfate is insoluble in water with a small quantity (less than 2%) absorbed in the GIT, mostly as the intact sulfated disaccharide. It concentrates in inflamed GIT lesions and is excreted in the urine within 48 hours, with a half-life of 1–2 hours.[2] The pharmacodynamic action of sucralfate is to relieve painful inflammation by generating a protective mechanical barrier on the GIT. Sucralfate increases the number of prostaglandins at the site of injury, which is important for the healing properties of sucralfate.[2] Sucralfate shows drug-drug interactions with theophylline, digoxin, tetracycline, ketoconazole,

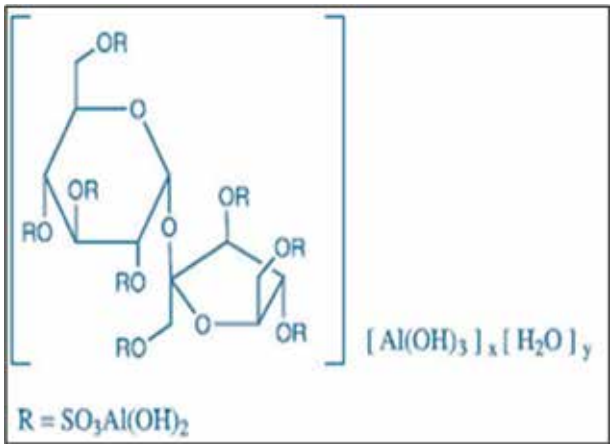

Figure 1: Chemical structure of sucralfate

phenytoin, norfloxacin, ofloxacin and quinidine by primarily inhibiting their absorption.[2]

As represented in Figure 1, the chemical structure exhibits greater stability of glycoside linkage because of the influence of the sulphate groups.

Mechanism of action

The main principle for the mechanism of action of sucralfate is not clear, but some explanations are present.[3]

Sucralfate is a mucosal protective agent that forms a protective barrier or coating over mucus membranes by binding selectively to damaged or inflamed tissue.[4] In an acidic environment or at a low pH, sucralfate forms large complexes with sub-epithelial proteins that could attach to damaged tissue. The sub-epithelial proteins are exposed during mucosal injury.[4,5] The binding of sucralfate to sub-epithelial proteins forms a viscous or gel-like layer to protect the vascular bed and proliferative zone.[5] These proteins include albumin and fibrinogen. It prevents back diffusion or flow of gastric acid and decreases the activity of both pepsin and bile salts.[4,5] The gel-like mucus protector layer prevents the ulcer base from being exposed to acid, pepsin and bile salts.[2] Additionally, sucralfate also inhibits the direct binding of pepsin to ulcer protein and inhibits the absorption of bile acids or bile salts.[4]

Sucralfate polymerises into aluminium hydroxide and sucrose sulfate in the presence of gastric juice or an acidic environment.[6] Sucralfate polymerises at a pH of less than four.[2] The formation of aluminium hydroxide provides buffering properties, while the sucrose sulfate creates polyanions, an acid-resistant, gel-like substance. This gel-like substance forms when polyanions bind to mucins and proteins that are negatively charged and stays there for approximately six hours.[2,5,7] Sucralfate stimulates the synthesis and secretion of mucus and bicarbonate secretion, inducing protective properties and again acting as a buffer in the acidic environment.[5] Figure 2 depicts the mechanism of action of sucralfate.

When referring to sucralfate's ability to induce tissue growth, regeneration and repair, the mechanism is not clear, but histological examinations have delivered a proposed mechanism.[1,3] Sucralfate stimulates the formation of collagen, vascular and granulation tissue as shown by histological examinations done in a study by Saei et al.[3]

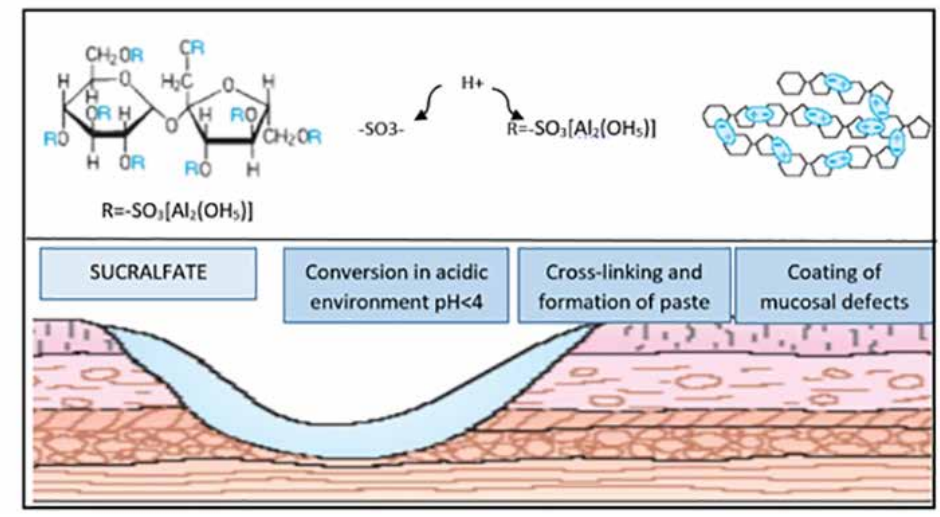

Figure 2: Mechanism of action of sucralfate

Sucralfate also promotes the binding of epidermal growth factor while exhibiting antioxidant effects, which promotes wound healing.[3] It is suggested that the antioxidant effect of sucralfate might contribute to both the healing and protection of damaged mucus surfaces.[3]

Indications

Duodenal ulcers

Sucralfate is approved for short-term treatment (8 weeks) of duodenal ulcers. It acts by forming an impenetrable local viscous substance, which shields the gastric mucosa from pepsin (digestive enzyme), polygalacturonic acid and bile salts. The effectiveness of sucralfate therapy in duodenal ulcers is comparable to cimetidine and intensive antacid treatment. The recommended dose is initial therapy of 1 g four times per day for eight weeks, followed by 1 g twice daily maintenance therapy.[1]

Dyspepsia

Sucralfate therapy has shown improvement in the incidence and severity of dyspepsia or indigestion, especially in reducing dyspeptic symptoms while on nonsteroidal anti-inflammatory drugs (NSAIDs). The efficacy is comparable to that of cimetidine therapy.[1]

Epithelial wounds

Evidence suggests that sucralfate has antibacterial activity and promotes tissue repair. For this reason, it can be used to promote healing in epithelial wounds. This includes second- and third-degree burns, ulcers in the perineal area, perineal dermatitis, mucositis, epidermolysis bullosa and desquamation during radiotherapy. Sucralfate also promotes healing and reduce pain after a haemorrhoidectomy. A study found that when combined with an antibacterial cream such as mupirocin, sucralfate can significantly contribute to reducing the size of ulcers in a shorter period.[8]

Chemotherapy-induced mucositis

High potency polymerised cross-linked sucralfate (HPPCLS) is used in preventing and treating oral mucositis in patients receiving chemotherapy. Using HPPCLS therapy resulted in quick reversal or complete prevention of ulceration within the digestive tract, thereby preventing chemotherapy treatment breaks. The recommended dosage for adults is 1 g four times daily (can be used up to 57 days) and for children under 12, 14 mg/kg/dose two to three times daily, dependent on the severity or predicted risk.[9]

Radiation proctitis

Sucralfate therapy displayed a reduction in the incidence of acute proctitis and a decrease in symptom severity and complications due to proctitis. The administration of sucralfate is associated with reduced rectal pain and discomfort in patients undergoing pelvic