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(REVIEW ARTICLE)

The potential of sucralfate as adjunctive therapy in the treatment of periodontal disease: A review

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Abstract

Background: Periodontal disease, a common inflammatory condition caused by bacterial dysbiosis, leads to the destruction of connective tissue and tooth supporting tissue, and has a strong correlation with systemic disease. Sucralfate is a medication commonly used to treat epithelial wounds due to its strong anti-ulcer effects. It is also recognized for its antibacterial and anti-inflammatory properties. However, the regulatory effect of sucralfate on periodontal remains unclear. The article aims to review the potential of sucralfate in the treatment of periodontal disease.

Material and Methods: The literature review within the year 2019-2024 was carried out in ScienceDirect, PubMed and Google Scholar databases with the keywords: sucralfate, periodontal health, periodontal medication, oral health, antibacterial.

Results: Sucralfate demonstrates multiple beneficial properties for periodontal treatment, including forming protective barriers, reducing inflammation, and promoting wound healing. It shows promise in mitigating dental erosion, managing mucositis, and enhancing recovery in postoperative scenarios. However, its localized effects and minimal systemic absorption make it relatively safe, though side effects like constipation and rare cases of aluminum toxicity in renal-compromised individuals were noted.

Conclusions: Sucralfate has significant potential as an adjunctive treatment for periodontal disease, leveraging its cytoprotective, anti-inflammatory, and antibacterial properties. Despite its promise, further research is needed to address the heterogeneity of existing studies and to evaluate its clinical efficacy through standardized trials, enabling its integration into routine periodontal management.

Keywords: Sucralfate; Periodontal Health; Periodontal Medication; Oral Health; Antibacterial

1. Introduction

Periodontal disease is characterized by a persistent inflammatory process that destroys the connective tissues and alveolar bone and tooth supporting tissue. The host's innate and adaptive immune response to a variety of different bacteria connected to periodontal biofilms causes this pathological inflammation [1]. Periodontal disease might be effectively managed by implementing a dual approach that involves both total plaque control and targeted removal or inhibition of pathogenic microflora through systemic or local antibacterial agents. The primary objective of periodontitis treatment is to halt disease progression, prevent recurrence, and restore damaged tissue. Conventional treatment methods typically involve mechanical plaque removal to eliminate or reduce the number of periodontal

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pathogens. However, the microbiological effects of scaling and root planing are often incomplete, potentially allowing bacterial pathogens to recolonize after treatment. The human immune system's reaction to periodontal pathogenic microbes causes periodontitis. The current advanced study suggests that rather than being an infection by a single bacteria, periodontitis is mostly caused by dysbiosis of the bacterial population [2].

Prevention of periodontal disease can be performed by controlling dental plaque mechanically and chemically [3]. Treatment for periodontal disease usually consists of scaling, root planing, and professional cleaning to get rid of tartar and plaque from gum pockets and teeth [4]. Furthermore, some bacteria that are causing the illness can be targeted using antimicrobials and drugs like chlorhexidine and antibiotics [5].

Sucralfate is a complex of aluminum hydroxide with sucrose sulfate and can quickly form a strong and viscous gastrointestinal mucosal barrier with excellent anti-ulcer properties [6]. Sulfate disaccharide is formed by the combination of sucrose octasulfate plus aluminum hydroxide. This substance has cytoprotective properties so it is used for various gastrointestinal conditions and diseases. Several reports also indicate that sucralfate can be used for various skin conditions. Due to its low solubility in water, when dissolved in acidic or alkaline media, sucralfate will dissociate into aluminum salts and sucrose sulfate. In its cytoprotective action, this compound will bind to tissue proteins to form a glycoprotein complex that covers The damaged surface and provides cytoprotection to the area [7].

In the oral cavity, sucralfate can potentially aid in managing conditions such as oral ulcers, mucositis, and other mucosal injuries caused by trauma, infections, or chemotherapy. Additionally, its ability to stimulate prostaglandin production and epithelial regeneration further supports its role in enhancing wound healing. Sucralfate's anti-inflammatory and soothing effects make it a valuable adjunct in oral care, particularly for patients with compromised mucosal integrity.

2. Material and Methods

For the purpose of this study, we investigated the English-language literature on sucralfate potential in dentistry by using the databases ScienceDirect, PUBMED, and Google Scholar. Research and literary studies conducted between the years 2019 and 2024 were included. It was determined that sucralfate, periodontal health, periodontal medication, oral health, antibacterial. were the parameters for the search.

3. Results and Discussion

3.1. Sucralfate and Protective Potential

Periodontitis is the inflammatory disease in the tooth-supporting tissue, resulting from the interaction between periodontal pathogenic bacteria and host immune response. It is characterized by symptoms such as swollen or bleeding gums (gingivitis), discomfort, and sometimes bad breath. In severe cases, it can cause gum recession, loss of supporting bone, and tooth mobility, potentially leading to tooth loss [8]. Increasing the protection of the mucosal barrier on the periodontal tissue might decrease the prevalence of periodontal disease.

Sucralfate is a compound formed from the combination of aluminum hydroxide and sulfated sucrose. Sucralfate can rapidly form a strong and viscous mucosal barrier in the gastrointestinal tract, providing excellent anti-ulcer and anti-bacterial properties[6] . Sucralfate can also reduce pain by preventing the production of inflammatory cytokines from damaged epithelial cells and can accelerate wound healing. It encourages angiogenesis and fibroblast growth, both of which are essential for the formation of granulation tissue and the healing process [9]. Sucralfate acts as a physical barrier, facilitating the rapid binding of epidermal growth factors at wound sites and promoting their accumulation. This process stimulates the proliferation of epithelial cells and supports angiogenesis, enhancing wound healing by encouraging granulation tissue formation [10].

3.2. The Mechanism of Action of Sucralfate as Protective Barrier

Recent studies indicate that sucralfate can provide protective effects against hydrochloric acid-induced dental erosion. In a controlled experiment, sucralfate suspensions were tested on hydroxyapatite crystals and dental enamel. The results demonstrated that sucralfate significantly reduced surface loss in both enamel and root dentine compared to controls, suggesting its ability to form an acid-resistant barrier that protects dental tissues from erosive agents like gastric acid. This finding highlights sucralfate's potential as a preventive measure against dental erosion, particularly for patients with conditions that lead to increased acid exposure in the oral cavity [11]. In pursuit of new preventive strategies, sucralfate, an aluminum salt of sucrose octasulfate, stands out as a promising agent, because it binds to

proteins and glycoproteins, including mucins, forming an acid-resistant gel-like coat and releasing aluminum hydroxide [12], [13].

3.3. Sucralfate and Oral Mucositis

A study demonstrated that high-potency sucralfate enhances the activation of growth factors, aiding in the treatment of chemotherapy-induced mucositis affecting the oropharynx and digestive tract. The treatment involved administering 1.5 g of sucralfate three times daily at the onset of mucositis for two days, followed by a twice-daily dosage of 1.5 g throughout cancer therapy and continuing for two weeks after the treatment concluded [12].

The using Sucralfate as an oral rinse significantly reduced pain within the first week post-surgery. Pain scores in the Sucralfate group decreased by 44.1% by day 3, compared to a 50.26% reduction in the control group only by day 7. This pain relief aligns with previous studies on post-tonsillectomy wounds, where Sucralfate formed a protective barrier over wounds, shielding them from environmental irritants. Sucralfate's coating effect lasts 5–6 hours, necessitating frequent reapplication. Its systemic absorption is minimal (2–5%), and adverse effects, such as bloating and constipation, are rare. Sucralfate suspension used as an oral rinse can serve as an effective topical pain reliever for postoperative intraoral wounds healing by secondary intention. It has minimal impact on the healing process and poses a low risk of systemic side effects [14].

3.4. Sucralfate and Antibacterial Properties

When exposed to gastric juice, sucralfate breaks down into aluminum hydroxide, providing mild buffering properties, and sucrose sulfate. The sucrose sulfate then binds to positively charged proteins and mucins on the surface, forming an acid-resistant, gel-like polyanion substance [11]. Sucralfate suspensions demonstrated greater effectiveness in protecting root dentine, likely due to the inability of the fluoridated solution to penetrate the collagen matrix left by erosive acids. In both enamel and root dentine, the specially prepared sucralfate suspension with a pH of 5.9 was less effective in preventing dental erosion compared to the commercial version, despite having the same pH. The commercial formulation includes sodium hydroxide, which acts as a buffering agent and may provide additional protection against dental erosion. This protection likely stems from the combined effects of the sucralfate film forming on the surface, the buffering action of sodium hydroxide, and the aluminum hydroxide released during sucralfate dissociation [11].

Sucralfate enhances mucosal protection by increasing mucus hydrophobicity, viscosity, and sulfation, as well as its aluminum and carbohydrate content, thereby improving its resistance to acid. It also stimulates mucus production by promoting prostaglandin synthesis. In addition to its effects on mucus, sucralfate supports tissue growth, regeneration, and repair by binding epidermal growth factors and tissue growth factors to the affected tissues, aiding in the healing process [12] .

3.5. Sucralfate as Antioxidant

Sucralfate, a cell-protective agent, has been utilized for over three decades to treat duodenal peptic ulcers and reflux esophagitis. This compound, a combination of sucrose and sulfate-aluminum, adheres strongly to proteins like albumin and fibrinogen on inflamed mucosal surfaces in the gastrointestinal tract. This adherence forms a stable, insoluble complex that creates a protective barrier over ulcerated areas, shielding the damaged epithelium. Recent studies have demonstrated that high concentrations of SCF can reduce the production of reactive oxygen species, enhancing mucosal healing in experimental models of duodenal conditions, highlighting its antioxidant properties [15].

One critical defense mechanism supported by sucralfate involves the maintenance of intercellular junctions, particularly tight junctions. Oxidative stress plays a significant role in the disruption of these junctions, leading to tissue inflammation. Research indicates that a decrease in TJ proteins correlates with elevated oxidative stress levels, exacerbating tissue damage and inflammation [15].

3.6. Sucralfate as Anti-Inflammatory agent

Sucralfate is known for its anti-inflammatory effects, which may be useful in managing skin disorders associated with inflammation and itching [16]. At the molecular level, sucralfate has been found to stimulate the activation of genes related to Epidermal Growth Factor (EGF) and basic fibroblast growth factor (bFGF), along with their receptors. This leads to a marked increase in the expression of EGF and its receptors in tissues affected by ulcerative conditions [17], [18]. Sucralfate plays a multifaceted role in skin health, demonstrating its capacity to enhance wound healing, alleviate inflammation, and strengthen the skin's barrier function. Its topical application has been shown to reduce pain levels, speed up the wound healing process, and lower the need for analgesics. As a result, topical sucralfate is considered a safe, effective, and practical option for post-hemorrhoidectomy care [18].

3.7. Sucralfate and Wound Healing

The topical application of sucralfate has emerged as a prominent area of research for its potential therapeutic uses. Building on the findings of Masuelli et al., highlighted that sucralfate supports tissue repair by stimulating epithelial growth factor production, reducing inflammation, and exhibiting antioxidant effects. These attributes strongly support its topical application. In earlier literature, Masuelli et al. had already advocated for the use of sucralfate as a topical agent [12], [19].

Its potential extends to standalone use or in combination with other treatments for various conditions. Some of the suggested applications, supported by varying levels of scientific evidence, include managing anorectal disorders like hemorrhoids, aphthous ulcers, dermal wounds, and subcutaneous injuries. Other potential uses involve treating dermal ulcers (e.g., bedsores), stomatitis, and skin conditions such as alopecia, acne, psoriasis, eczema, and herpes symptoms. Additionally, it has been proposed for conditions like shingles, athlete's foot, ringworm, itchy skin, and rosacea, particularly when combined with other drugs. Sucralfate has also shown promise in alleviating irritation and discomfort from burns, as well as in addressing skin damage caused by inflammation, infection, or burns [19].

3.8. Sucralfate Comparison with Fluoride

Sucralfate is primarily known for its mucosal-protective properties. It forms a gel-like coating on the mucosa, which can protect against erosive agents such as hydrochloric acid. In dental applications, sucralfate has been shown to provide a protective effect against acid-induced erosion, particularly in enamel and dentine. It binds to proteins and creates an acid-resistant barrier that helps prevent further erosion. Research indicates that sucralfate provides significant anti-erosive protection against hydrochloric acid-induced dental erosion. In studies, sucralfate suspensions demonstrated lower surface loss in enamel compared to control groups and were effective in protecting root dentine from erosion. While primarily used for gastrointestinal issues, sucralfate's protective qualities are being explored for managing dental erosion due to gastric acids. Its application in dentistry is still emerging, focusing on its role in protecting teeth from acid-related damage [11].

Sodium fluoride works by enhancing the remineralization of enamel and inhibiting demineralization. It strengthens tooth enamel by incorporating into the hydroxyapatite structure of teeth, making them more resistant to acid attacks from bacteria. Fluoride also has antibacterial properties that reduce the metabolic activity of caries-causing bacteria [20]. Fluoride has a long-established reputation for preventing dental caries and promoting enamel remineralization. It is effective in reversing early decay and preventing future cavities, making it a critical component of preventive dental care. Fluoride treatments have been shown to significantly reduce the prevalence of caries when used correctly. While fluoride is effective, excessive exposure can lead to dental fluorosis, particularly in children whose teeth are still developing. The American Dental Association emphasizes the importance of using fluoride appropriately to avoid potential adverse effects [21].

Turssi et al (2019) found that Sucralfate suspension has shown superior protection for root dentine compared to a stannous-containing fluoride solution, despite the fluoride solution's proven effectiveness. The lower pH of the $NaF/SnCl_2$ solution (4.5) compared to sucralfate (5.9) may influence binding capabilities, but sucralfate's performance is likely due to its ability to form a stronger protective layer. This is likely because the fluoride solution cannot penetrate the collagen matrix left by erosive acids. Root dentine provides more binding sites than enamel due to its higher protein content and larger surface area, facilitating better adhesion and protection. Additionally, the presence of sodium hydroxide in the sucralfate formulation, along with aluminum hydroxide's buffering capacity, enhances its protective effects against dental erosion [11].

3.9. Side Effects in Dental Medicine

Sucralfate is considered relatively safe due to its localized action and minimal systemic absorption. However, constipation is its most common side effect, affecting 1% to 10% of users. In diabetic patients, cases of hyperglycemia have also been observed. Other reported adverse effects include skin rashes, formation of stomach bezoars, metal toxicity, headaches, dry mouth, nausea, vomiting, flatulence, and low phosphate levels (hypophosphatemia). Rare but severe complications, such as cerebral edema and pulmonary embolism, have been associated with accidental intravenous administration of sucralfate [22].

Long-term use of sucralfate generally results in negligible aluminum retention, except in individuals with renal impairment. In patients with uremia, aluminum absorption from the gastrointestinal tract increases to levels comparable to those seen with aluminum hydroxide. To minimize the risk of aluminum toxicity, sucralfate should be used with caution or avoided in patients with end-stage renal disease [12].

Limitations of the study

The present systematic review is characterized by some limitations. Firstly, the electronic search of the articles was done in only three databases, ScienceDirect, PubMed and Google Scholar, and included studies published only in English. Furthermore, studies published before the specified period (2019-2024) were excluded from this review. However, some material or discussion also comes from journals before 2019. At the same time, the studies included in this review exhibit heterogeneity in their design, data collection methods, and the populations studied. Additionally, a limitation of this review is the absence of an evaluation of the quality of the studies included.

4. Conclusion

Sucralfate exhibits significant potential as an adjunctive treatment for periodontal disease and related oral health conditions. Its ability to form protective barriers, reduce inflammation, and enhance tissue healing underscores its versatility in dental applications. Despite its promising attributes, the current evidence is limited by the heterogeneity of studies and the lack of robust clinical trials specifically targeting periodontal disease. Future research should focus on standardized methodologies to evaluate sucralfate's efficacy comprehensively, enabling its integration into clinical practice for improved periodontal management.

Compliance with ethical standards

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All authors acknowledged their equal contribution, read the manuscript, and gave their approval.

Disclosure of conflict of interest

We declare that there was no major conflict with this article.

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