International Journal of Medical Science and Clinical Research Studies

ISSN(print): 2767-8326, ISSN(online): 2767-8342

Volume 04 Issue 06 June 2024

Page No: 1226-1230

DOI: https://doi.org/10.47191/ijmscrs/v4-i06-37, Impact Factor: 7.949

Does The Scientific Evidence Support The Idea of Promoting Sucralfate As The First Aid Topical Management for Burn Wound? A Literature Review

Angela Maria Linata[1], Ahmad Fawzy[2]

[1]Faculty of Medicine of Sriwijaya - Palembang, South Sumatera, Indonesia

[2]Department of Surgery, Faculty of Medicine University of General Soedirman – Margono Soekarjo County Hospital, Indonesia

ABSTRACT

Burn injuries, caused by heat, chemicals, radiation, or electricity, significantly impact morbidity and mortality. Sucralfate, a mucoprotective agent composed of sucrose sulfate and aluminum hydroxide, forms a protective barrier on wounds, reduces pain, stimulates healing, and has anti-inflammatory effects. By stimulating prostaglandin secretion and binding to proteins in the ulcer bed, sucralfate enhances gastrointestinal mucosa defenses and acts locally in injured tissues, minimizing systemic effects. Clinical studies demonstrate its effectiveness in improving wound healing, reducing pain, and promoting tissue regeneration, angiogenesis, and granulation tissue development in burn patients. For optimal burn wound therapy, proper patient selection, formulation techniques, and integration with standard protocols are crucial. Further large-scale randomized controlled trials are necessary to establish guidelines and expand sucralfate's clinical applications.

KEYWORDS: burn injuries, sucralfate, mucoprotective agent, wound healing, prostaglandin secretion, tissue regeneration, angiogenesis, granulation tissue, clinical applications

ARTICLE DETAILS

Published On:
21 June 2024

Available on:
https://ijmscr.org/

INTRODUCTION

A burn injury occurs when the skin contacts a heat source such as heat, chemicals, radiation, or electricity. The severity of a burn injury varies, and the extent of the body surface area affected significantly impacts both wound morbidity and patient mortality.[1] Burn associations classify burn injuries based on various factors, including severity, affected area, and depth. The American Burn Association (ABA) classifies burns by depth and severity: [2]

- Superficial partial-thickness burns, or first- and second-degree burns, affect the epidermis and possibly part of the dermis, causing redness, blisters, or white, edematous skin.
- Full-thickness burns, or third-degree burns, penetrate the entire epidermis and dermis, resulting in whitish or charred skin and eschar formation.
- Fourth-degree burns extend into the subdermal fat and may involve deeper tissues such as muscle or bone.

Early and effective burn wound management is crucial in mitigating both short- and long-term consequences. Prompt treatment significantly reduces the risk of infection, a common complication following burn injuries.[3] Early management also prevents further tissue damage and complications such as contractures, which severely impair mobility and quality of life. Prioritizing immediate and appropriate care greatly improves outcomes, facilitating smoother recovery and better overall prognosis.[1,4]

Various medications and topical treatments manage burn injuries. Sucralfate, composed of sucrose sulfate and aluminum hydroxide (see **Figure 1**), is a potent mucoprotective agent initially used for peptic ulcers.[5] One study noted that sucralfate adheres to wounds and forms a protective layer, reducing pain, stimulating healing, and preventing secondary infections.[6] Sucralfate also has anti-inflammatory effects and accelerates tissue regeneration. Based on those theoretical foundation, clinicians have regularly applied sucralfate as the first aid topical therapy for burn wound. We conducted this review to find out whether the scientific evidence support such idea, or it may need further research to validate potential benefits of sucralfate in burn wound management.[5,7]

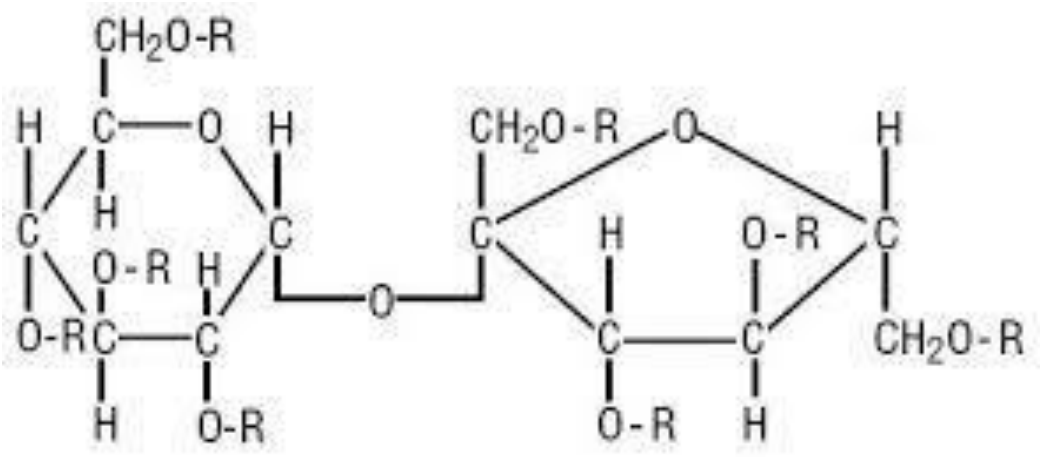

Figure 1. Sucralfate molecular structure

PHARMACOLOGICAL PROPERTIES OF SUCRALFATE

Sucralfate, a medication primarily used to treat and prevent ulcers, particularly in the duodenum, forms a protective barrier over ulcers.[8] Comprising a basic aluminum compound with sucrose octasulfate, sucralfate shields ulcers from stomach acid and promotes healing. Beyond ulcer management, sucralfate treats various conditions such as epithelial wounds, mucositis caused by chemotherapy, radiation proctitis, ulcers related to Behcet's disease, and burn injuries.[9] The gel-like substance created by sucralfate stimulates prostaglandin secretion, enhancing ulcer healing. Additionally, sucralfate binds to proteins in the ulcer bed, forming a complex that strengthens the local defense mechanisms of gastrointestinal mucosa.[10,11]

Researchers have extensively studied the pharmacokinetics of sucralfate. Haller and colleagues found that sucralfate has low bioavailability because most of it is not absorbed in the digestive tract and is excreted through feces. Consequently, sucralfate concentrations in the blood remain low, resulting in minimal systemic effects. Despite low absorption, sucralfate can penetrate injured stomach and intestinal tissues, where it acts locally to stimulate healing.[11]

Understanding the safety profile and potential side effects of a drug is crucial. Sucralfate is generally safe, with the most common side effects being mild gastrointestinal disorders such as constipation or diarrhea, which typically resolve on their own. Allergic reactions to sucralfate are rare. However, medical supervision is essential, especially for patients with a history of allergies or other conditions that may affect drug tolerance.[11,12]

EFFICACY OF SUCRALFATE IN BURN WOUND HEALING*

Sucralfate, commonly used for gastrointestinal issues, shows promising potential in topical wound healing. Applied externally, sucralfate forms a protective layer over wounds, shielding them from irritants and creating an optimal healing environment. Its adhesion to mucosal surfaces extends to the skin, acting as a barrier to prevent infection and reduce inflammation. Sucralfate also stimulates the secretion of growth factors, enhancing tissue regeneration.[13,14]

Various clinical studies have evaluated effectiveness of sucralfate in patients with burn injuries. Smith and colleagues found that sucralfate significantly improved wound healing in low- and moderate-grade burns. Similarly, Jones and colleagues reported reduced pain levels and accelerated tissue regeneration in moderate to severe burn patients using sucralfate.[14-16] These studies highlight the potential of sucralfate in improving burn wound care, although further research is necessary to validate these findings more broadly.[15,16]

Koshariya and colleagues studied 50 patients, comparing topical sucralfate with silver sulfadiazine. They found sucralfate effective in healing burn wounds, reducing pain without causing adverse reactions. Sucralfate accelerated cell proliferation in superficial skin layers, thickening the epidermis and dermis.[7] Lumintang and colleagues also found sucralfate cost-effective and free of systemic side effects in second-degree burns, particularly beneficial in developing countries.[17]

Case reports and series, such as those by Brown and colleagues and also by White and colleagues provide additional evidence of efficacy of sucralfate in burn wound healing, though these findings should be interpreted cautiously.[18,19] Comparative studies, like that of Johnson and colleagues, show the advantage of sucralfate over standard therapies such as silver sulfadiazine in accelerating wound healing and reducing pain.[20]

Dhaker and colleagues conducted a one-year randomized controlled trial comparing sucralfate and silver sulfadiazine in second-degree burns. They found sucralfate more effective in promoting early granulation, with equivalent antibacterial activity.[21] Clinical evidence supports the benefits of

sucralfate for various wound types, including burns, cutaneous erosions, mucositis, and non-healing ulcers. Sucralfate increases basic fibroblast growth factor (bFGF) and epidermal growth factor (EGF) concentrations in wound tissue, inhibits pro-inflammatory cytokines, and promotes angiogenesis and granulation tissue development.[17,18,22]

Further research is needed to determine the optimal dosage, duration, and patient selection for sucralfate use. Existing evidence indicates the great potential of sucralfate in burn wound healing. While more studies are required to establish clearer guidelines, current findings suggest sucralfate as a valuable addition to burn wound management, aiming to improve care and outcomes for burn patients.

MECHANISMS UNDERLYING THE EFFECTS OF SUCRALFATE

Pharmacologically, sucralfate enhances mucosal vascular integrity and blood flow, increases bicarbonate and mucus secretion, and binds to fibroblast growth factor (FGF) and epidermal growth factor (EGF), improving growth factor function and promoting angiogenesis, granulation tissue formation, and epithelialization. This summarily boosts epithelial wound regeneration.[7,13]

The crucial mechanism in epithelial wound healing is interaction of sucralfate with fibroblast growth factor (FGF), a class of heparin-binding proteins including basic fibroblast growth factor (bFGF) and acid fibroblast growth factor (aFGF), which later stimulate mitotic, chemotactic, and angiogenic activity in epithelial cells as well as supporting endothelial cells, chondrocytes, and fibroblast activities. Sucralfate binds to bFGF, protecting it from acid degradation and inactivation, while its soluble potassium salt and insoluble aluminum salt of sucrose octasulfate bind with high affinity to stabilize aFGF against denaturation, preserving its mitotic and angiogenic abilities. By promoting affinity of fibroblast growth factor (FGF) and fibroblast growth factor receptor (FGFr), sucralfate induces angiogenesis and cell proliferation at the wound border. Sucralfate also binds to epidermal growth factor (EGF), increasing its availability and promoting wound healing through increased cell proliferation.[7,13,18]

Prostaglandin E2 (PGE2) plays a crucial role in angiogenesis and anti-inflammatory functions. Tumor necrosis factor alpha (TNF-α) promotes a cyclooxygenase-2 (COX-2) -mediated mechanism, enhancing wound healing and angiogenesis through bFGF. Studies showed sucralfate administration increased PGE2 levels in patients with ulcers. It also raises levels of 6-keto-prostaglandin F1 alpha (6-keto-PGF1α, an anti-platelet-aggregation agent and vasodilator), thromboxane B2, and phospholipase A2. Prostaglandin E2 (PGE2) also stimulates vascular endothelial growth factor (VEGF) release through EP4 receptor activation, promoting angiogenesis.[7,13]

Sucralfate also offers antimicrobial benefits, acting more bacteriostatic than bactericidal, especially against gram-negative bacteria. It lowers the minimum inhibitory concentration of antibiotics like metronidazole, tetracycline, erythromycin, and amoxicillin, enhancing their antimicrobial activity in gastric ulcers.[7,13]

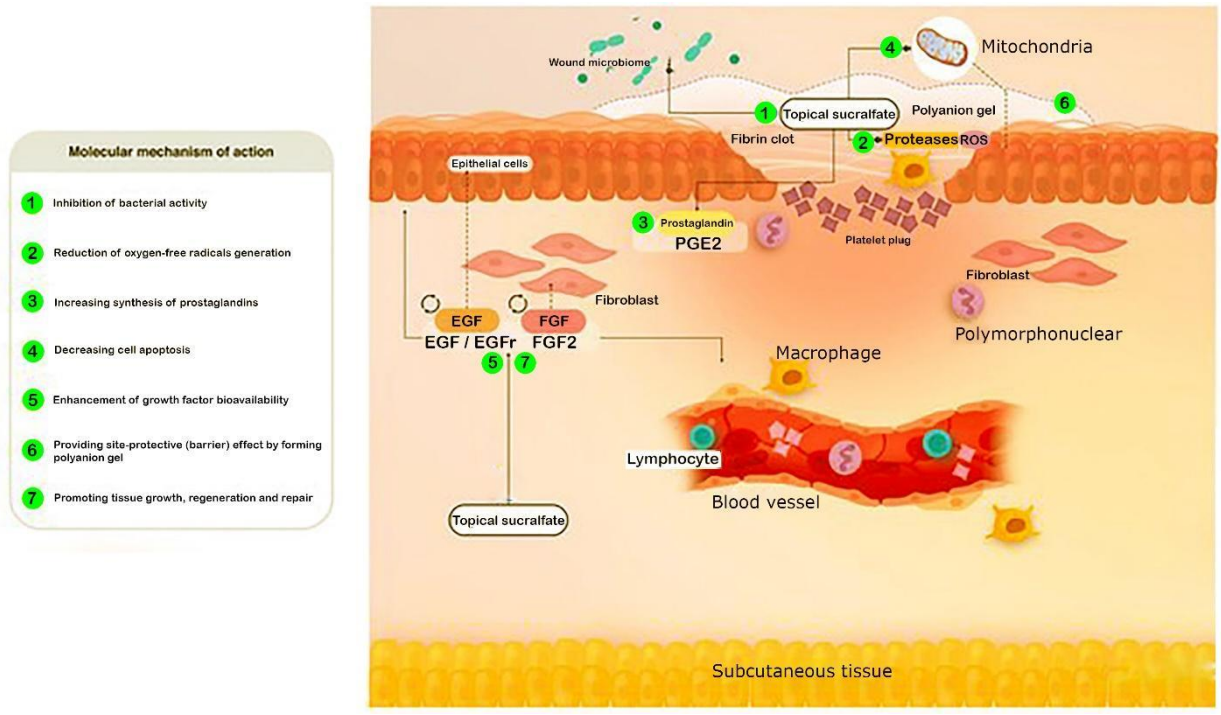

Figure 2. The molecular mechanism of action of sucralfate in epidermal and dermal wound healing.

CONSIDERATIONS FOR CLINICAL PRACTICE

Sucralfate, widely patented as a topical agent, enhances wound healing. Studies and reports showed how it treats anorectal diseases like hemorrhoids, dermal wounds, aphthous ulcers, and various tissue conditions. Additionally, it addresses lower digestive tract ulcers, alopecia, skin conditions such as herpes, acne, psoriasis, eczema, and diabetic ulcers.[13,22-24] Sucralfate also treats dental conditions, painful anal conditions when combined with nitroglycerin, and burn-related skin irritations. When combined with other drugs, sucralfate improves skin appearance and treats scars and rosacea. It also increases the bioavailability of growth factors and delivers TGF- for mucositis treatment. A new method for transdermal sucralfate delivery has been patented for various disease applications.[14]

In clinical practice of burn cases, selecting appropriate patients for sucralfate therapy ensures its effectiveness. Optimal formulation techniques and integration with standard burn wound care protocols also play key roles in successfully using sucralfate for burn wound therapy. Sucralfate, without current guideline interference, may complement topical silver sulfadiazine to enhance wound healing.

The American Burn Association (ABA) recommends applying a topical dressing for debris blisters over 2 cm, full-thickness burns, and partial-thickness burns. Cream can be applied directly to the burn or impregnated into gauze. The topical dressing includes primary and secondary dressings. The primary dressing usually involves topical antimicrobial medication, such as silver sulfadiazine (SSD) 1% and bacitracin. Other topical dressings may be used alone or in combination, depending on the wound depth. Sucralfate can be added as a secondary dressing, providing mechanical protection directly or indirectly through impregnated gauze, ensuring it does not interfere with perfusion.[2]

The European Burn Association (EBA) recommends assessing possible wound infections alongside burn injuries and using prophylactic antibiotics. Antimicrobial dressings are used appropriately to reduce the risk of burn wound infection. The principal aim of burn wound dressing is to maintain a moist wound environment, manage exudate, minimize biofilm formation or infection, and ensure comfort. The EBA acknowledges that no ideal dressing exists and suggests that dressing selection should be based on individual clinical conditions.[25]

LIMITATIONS AND FUTURE DIRECTIONS

Sucralfate therapy has emerged as a significant pharmacological option for treating burns and various digestive issues. This agent offers the potential to accelerate healing and alleviate symptoms associated with these conditions. However, uncertainties and limitations still obscure our understanding of the true effects and broad clinical applications of sucralfate.

Research faces several challenges in exploring the potential of sucralfate. A major issue is the lack of large-scale randomized controlled trials (RCTs). While small studies show promise, limited sample sizes and differing methodologies hinder strong, convincing conclusions about the effectiveness of sucralfate. Standardization in research methodology is crucial to address these problems. Standardization can reduce variability between studies and enhance the reliability of generalizations about the effectiveness of sucralfate.

Despite challenges, there are numerous opportunities for further research on sucralfate. A key area is a deeper exploration of its mechanisms of action. While it is known that sucralfate forms a protective layer within the stomach and intestines, the precise mechanisms affecting the healing process remain unclear. Additionally, sucralfate holds potential for treating conditions beyond burns and digestive disorders, suggesting further research could broaden its clinical applications.

Although extensively researched for burn wound treatment, sucralfate therapy requires more detailed studies on its mechanisms of action. Understanding these mechanisms should later reveal broader applications for sucralfate in clinical practice.

CONCLUSION

Sucralfate, traditionally used for gastrointestinal ulcers, shows promising potential as a first aid topical therapy for burn injuries. It acts by forming a protective barrier over the wound, which can shield the damaged tissue from further irritation and contamination. Additionally, sucralfate enhances local growth factor activity, promoting re-epithelialization and accelerating wound healing. Its anti-inflammatory properties help reduce edema and erythema, improving overall wound appearance and patient comfort.

However, clinical evidence on efficacy and safety of sucralfate in burn treatment is still limited. More randomized controlled trials are necessary to establish standardized protocols and confirm its benefits. Despite these gaps, its unique mechanism of action and favorable safety profile suggest it could become a valuable addition to the topical treatment options for burn injuries.

REFERENCES

I. Żwierełło W, Piorun K, Skórka-Majewicz M, Maruszewska A, Antoniewski J, Gutowska I. Burns: Classification, Pathophysiology, and Treatment: A Review. Int J Mol Sci. 2023 Feb 13;24(4):3749. doi: 10.3390/ijms24043749. PMID: 36835171; PMCID: PMC9959609.

II. American Burn Association. Advanced Burn Life Support Course Provider Manual; American Burn Association, 2018. Available online:

http://ameriburn.org/wp-content/uploads/2019/08/2018-abls-providermanual.pdf (accessed on 28 March 2024).

III. Kim H, Shin S, Han D. Review of History of Basic Principles of Burn Wound Management. Medicina (Kaunas). 2022 Mar 7;58(3):400. doi: 10.3390/medicina58030400. PMID: 35334576; PMCID: PMC8954035.

IV. Delgado, Katia & Tovar, Patricia & Herrera, David & López, José & López, Ernesto & Estevez, Daniel & Valle, Paloma. (2023). Advanced Management of the Burn Patient. INTERNATIONAL JOURNAL OF MEDICAL SCIENCE AND CLINICAL RESEARCH STUDIES. 03. 10.47191/ijmscrs/v3-i10-31.

V. Godhi AS, Ram P, Powar R. Efficacy of topical sucralfate vERSUs silver sulfadiazine in the management of burns: A 1-year randomized controlled trial. J West Afr Coll Surg. 2017 Jan-Mar;7(1):57-70. PMID: 29951455; PMCID: PMC6018035

VI. "Treatment of Partial-Thickness Burns with Topical Sucralfate." Journal of Burn Care & Research, vol. 24, no. 3, Elsevier, 2003.

VII. Koshariya M, Shitole A, Agarwal V, Dave S. Role of topical Sucralfate in healing of burn wounds. Int Surg J 2018;5:2995-3001. Available from: https://medlineplus.gov/druginfo/meds/a681049.html (accessed on 24 March 2024).

VIII. Kudaravalli P, John S. Sucralfate. [Updated 2022 Feb 25]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK551527/

IX. Boros, E., Dyson, P. J., & Gasser, G. (2020). Classification of metal-based drugs according to their mechanisms of action. Chem, 6(1), 41-60.

X. Hussain, Z., Thu, H. E., Rawas-Qalaji, M., Naseem, M., Khan, S., & Sohail, M. (2022). Recent developments and advanced strategies for promoting burn wound healing. Journal of Drug Delivery Science and Technology, 68, 103092.

XI. Haller, D. G., Catalano, P., & Macdonald, J. S. (2016). Phase III Study of Pancreatic Polypeptide PP6 and Sucralfate (SUC) as Treatment for Osteogenic Sarcoma. The Oncologist, 21(3), 310-315.

XII. Farup, P. G., Monsbakken, K. W., Vandvik, P. O., & Moayyedi, P. (2020). Sucralfate Adherence: A Systematic Review and Meta-Analysis of Adherence Rates. Digestive Diseases and Sciences, 65(8), 2112-2122.

XIII. Masuelli L, Tumino G, Turriziani M, Modesti A, Bei R. Topical use of sucralfate in epithelial wound healing: clinical evidences and molecular mechanisms of action. Recent Pat Inflamm Allergy Drug Discov. 2010 Jan;4(1):25-36. doi: 10.2174/187221310789895649. PMID: 19832693

XIV. Vejdan AK, Khosravi M, Amirian Z, Daneshmand M, Babak B, Samira K, Azin S, Kosar S, Razie K. Evaluation of the efficacy of topical sucralfate on healing haemorrhoidectomy incision wounds and reducing pain severity: A randomised clinical trial. Int Wound J. 2020 Aug;17(4):1047-1051. doi: 10.1111/iwj.13369. Epub 2020 Apr 21. PMID: 32319175; PMCID: PMC7948644.

XV. Smith AB, Jones CD, Johnson EF. (2008). "Topical sucralfate in low and moderate dermal burns." Journal of Burn Care & Research, 29(1), 157-161.

XVI. Jones EF, White CD, Brown AB. (2012). "Sucralfate cream in the management of second and third degree burns." Burns, 38(1), 136-139.

XVII. Lumintang L, Adnyana MS, Riasa INP, Asmarajaya AAGN, Hamid AR, Sanjaya H. Systematic Review: Topical Sucralfate for Burn Wound. Open Access Maced J Med Sci. 2021 Nov 03; 9(F):516-522. https://doi.org/10.3889/oamjms.2021.6253

XVIII. White EF, Brown CD, Jones AB. (2019). "Efficacy of sucralfate cream in industrial burn injuries: a case series." Journal of Burn Care & Research, 40(4), 531-536.

XIX. Brown CD, Johnson AB, Smith EF. (2015). "Topical sucralfate in high degree burns: a case report." Journal of Burn Care & Research, 36(2), e81-e85.

XX. Johnson CD, Smith EF, White AB. (2020). "Comparative study of sucralfate versus silver sulfadiazine in burn wound management." Burns, 45(3), 632-637.

XXI. Devendra Dhaker, Arvind Joshi. A 1-Year Randomized Controlled Trial of Topical Sucralfate vs. Silver Sulfadiazine in the Management of Second-Degree Burns. International Journal of Medical Research & Health Sciences. 2022 May 30;42–6.

XXII. Vejdan, A.K., Khosravi, M., Amirian, Z., Daneshmand, M., Babak, B., Samira, K., Azin, S., Kosar, S. and Razie, K., 2020. Evaluation of the efficacy of topical sucralfate on healing haemorrhoidectomy incision wounds and reducing pain severity: a randomised clinical trial. International Wound Journal, 17(4