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A Review: Effective Ulcer Healing

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Abstract: ***Gastric ulcers, a persistent health issue, have a significant likelihood of recurring and can lead to unexpected complications like bleeding, narrowing, and perforation. In recent decades, advancements in clinical treatments for gastric ulcers have enabled the swift creation of potent anti-ulcer drugs. While traditional treatments for gastric ulcers, including H2-receptor antagonists, are effective, proton pump inhibitors (PPIs) play an essential role in promoting ulcer healing and avoiding complications. Despite the progress made, some patients continue to experience recurrence or persistent issues even with ongoing anti-ulcer treatments. A novel concept known as the quality of ulcer healing (QOUH) was developed, focusing on restoring the mucosal structure and function to help prevent the return of ulcers. While various gastro protective measures have contributed to the successes of QOUH, we discovered that natural product-based gastro protection, particularly a new formulation derived from Artemisia or S-allyl cysteine from garlic, demonstrated significant effectiveness in QOUH, alongside alleviating clinical symptoms with reduced side effects. This review will highlight the significance of QOUH in ulcer healing and the advancements gained from natural products. Reduced side effects, even though various gastro protective measures have contributed to the success of QOUH.***

Keywords: Diabetic Foot Ulcer, Duodenal Ulcer, Wound Healing, Ulcer, endovenous, anti-ulcer

I. INTRODUCTION

The terminology used to refer to wounds associated with chronic illnesses that fail to heal properly has evolved. These injuries are not categorized as complicated wounds. For the definitions provided earlier and within the scope of this document, we refer to these injuries as complicated ulcers. The following characteristics, which have been extensively described, are essential for a straightforward wound to progress into a complicated ulcer: ulcers that have not improved after three months, the presence of infection, reduced surface viability due to tissue death or poor circulation, and a connection to systemic conditions that hinder the healing process. Diabetes is a leading factor in the development of complicated ulcers, with diabetic foot ulcers being a specific type among them. Over 10% of the global population either has diabetes or is at a heightened risk of acquiring it. The worldwide prevalence is at 6.3%, with Oceania showing the lowest rate at 3% and North America the highest at 13%. The prevalence rates for Asia, Europe, and Africa stand at 5.5%, 5.1%, and 7.2%, respectively. Diabetes is a significant cause of non-traumatic amputations of the lower limbs: 15% of individuals with diabetic foot ulcers require amputations, and 25% of diabetic patients (1 in 6) will experience an ulcer during their lifetime.

A. Types Of Ulcer In Human Body

1) Peptic Ulcer Types by Location:
2) Gastric ulcer: In the stomach.
3) Duodenal ulcer: In the duodenum.
4) Esophageal ulcer: In the esophagus, often due to acid reflux.
5) Leg and Foot Ulcers
6) Venous Ulcers: Open wounds on the lower leg, often below the knee and on the inside of the ankle, caused by poor blood flow back to the heart.
7) Arterial Ulcers: Sores on the feet, toes, heels, and ankles resulting from poor blood supply to the tissues.
8) Diabetic Foot Ulcers: A serious complication of diabetes, these are open sores on the foot that can result from poor circulation and nerve damage.
9) Skin Ulcers: Breaks in the skin, which can be caused by various factors, including pressure (pressure ulcers or bedsores) or specific conditions like lichen planes.
10) Mouth Ulcers (Canker Sores): Painful sores inside the mouth, on the lips, tongue, or cheeks, triggered by factors like dental injury, stress, or certain foods.

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11) Genital Ulcers: Sores that appear in the genital area.
12) Corneal Ulcers: Inflammatory or infectious conditions affecting the cornea, the clear front part of the eye.

B. Causes Of Ulcer

Common Causes

1) H. pylori infection: This bacterium harms the mucus lining of the stomach and duodenum, rendering the tissue susceptible to acid damage.
2) NSAID use: Extended use of pain relievers such as ibuprofen, naproxen, or aspirin can reduce the production of prostaglandins, which are crucial for safeguarding the stomach lining, resulting in ulcers.
3) Less Common Causes Other infections: Various viruses, fungi, or bacteria aside from H. pylori may also contribute to the development of ulcers. Medications: Corticosteroids, specific antidepressants, and drugs for bone health can heighten the risk of ulcers, particularly when used in conjunction with NSAIDs.
4) Other health conditions: Severe illnesses like Crohn's disease, stomach cancer, significant burns, or conditions that hinder blood flow can elevate the chances of ulcer formation. Factors That Worsen Symptoms (But Don't Cause Ulcers)
5) Stress: Although not a direct cause, stress can intensify ulcer symptoms. Spicy foods: Likewise, spicy foods do not induce ulcers but can aggravate an existing ulcer, exacerbating the symptoms. Alcohol and caffeine: These substances can boost stomach acid production, potentially worsening ulcer symptoms.

II. STUDY OF SOME EFFECTIVE TREATMENTS FOR ACCELERATING DIABETIC FOOT ULCER HEALING

Diabetes is a chronic metabolic disease characterized by elevated blood sugar levels.

A serious side effect of diabetes mellitus, foot ulcers are linked to elevated rates of morbidity, death, and associated costs. Diabetic people frequently have infected foot sores that can develop into cellulitis. Progress. Gangrene and blood infections occur when it is not treated promptly and effectively. Occasionally leads to amputation. Considering the goal of improving the health of individuals with diabetes.

III. MATERIALS AND METHODS

The present study is a systematic review conducted in both English and Persian, exploring articles through search engines, reputable academic websites, and databases such as Magiran, Google Researcher, Embassy, Science Direct, Google Scholar, PubMed, and Springer. To achieve the study's objectives and improve the accuracy of the investigation and comprehension, this in-depth review was executed using the Broome technique. This research used articles published in the last 20 years, which are associated with effective treatments for accelerating the recovery of diabetic foot ulcers. In the initial phase, a total of 38 articles were identified. Among these, 12 relevant articles published in the last two decades were analyzed.

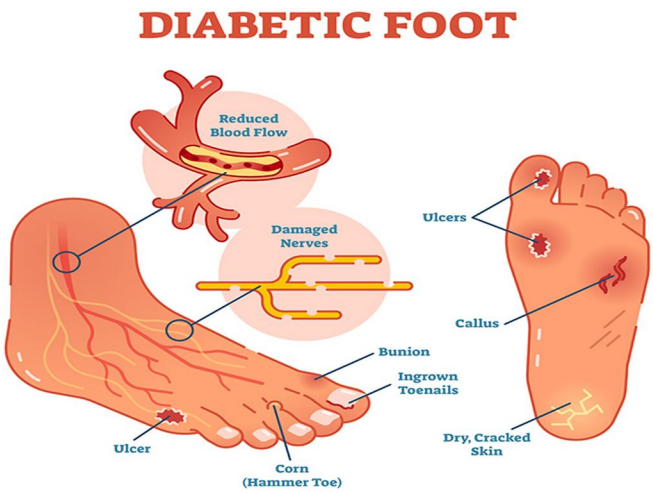

Fig. pathophysiology of foot ulcers in diabetic

IV. PROGRESSIVE HYDROGEL APPLICATIONS IN DIABETIC FOOT ULCER MANAGEMENT

A. *Normal Versus Dysregulated Wound Healing*

Normal wound healing typically follows a series of coordinated steps, each essential for restoring tissue integrity. Unlike acute wounds, diabetic foot ulcers (DFUs) are marked by prolonged inflammation that usually lasts more than four weeks in clinical cases. Although the healing process of DFU wounds resembles that of normal acute wounds, it often reaches a stage where healing stalls. The main stages of wound healing include the hemostasis phase, which involves vasoconstriction, platelet aggregation, and the activation of coagulation factors. When a wound occurs, neutrophils from damaged blood vessels are passively recruited, initiating the inflammatory response. At the same time, local immune cells become activated, leading to increased levels of chemokine's, reactive oxygen species (ROS), and inflammatory cytokines. This activation of local endothelial cells causes vasodilation and increased vascular permeability, a process triggered by nitric oxide (NO) associated with inflammation. Additionally, neutrophils release neutrophil extracellular traps (NETs), and macrophages produce metalloproteinase (MMPs). The subsequent phase of wound repair involves the proliferation and migration of various cells to the injury site. Keratinocytes release epidermal growth factor (EGF), which promotes their proliferation and migration, followed by new blood vessel formation (angiogenesis) and macrophage activation.

B. *Healing of Duodenal Ulcer with an Antacid Regimen*

A double-blind clinical trial was carried out over 28 days with 74 patients who had endoscopically confirmed duodenal ulcers to evaluate the effectiveness of a high-dose antacid treatment in promoting the healing of duodenal ulcers. Among the patients undergoing antacid therapy, 28 of 36 achieved full ulcer healing, compared to 17 of 38 in the placebo group ($P<0.005$). The antacid therapy showed no superior effectiveness compared to the placebo in reducing ulcer symptoms. The existence or lack of symptoms in the fourth week of treatment did not consistently indicate if an ulcer crater was present or not. In patients receiving a placebo, smokers were less likely to heal compared to non-smokers ($P=0.03$). Other than mild diarrhea, no major side effects from the antacid therapy were observed

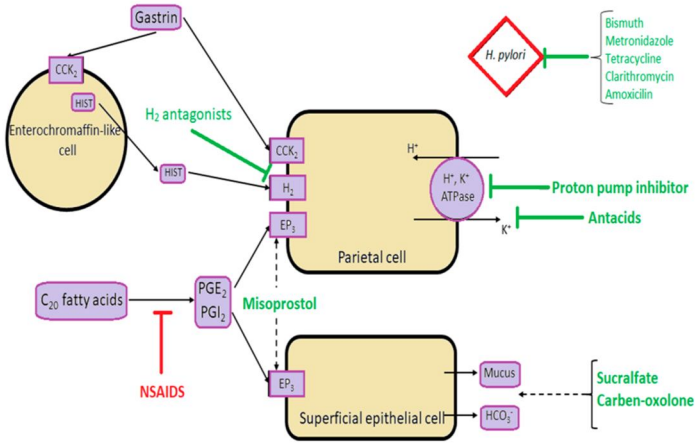

Fig. Treatment Of Antacid In Duodenal Ulcer

C. *Endovenous Ablation Of Incompetent Perforating Veins Is Effective Treatment For Recalcitrant Venous Ulcers*

Endovenous closure of ineffective saphenous veins has been noted to aid in the healing of venous ulcers; however, there is limited data on the efficacy of perforator ablation (PA) for healing stubborn venous ulcers. We share our experience with PA in cases of venous ulcers that did not respond to extended compression treatment

D. *Ulcer Management prior to Endovenous Ablation*

Before undergoing endovenous ablation for incompetent perforator veins, patients received treatment at our specialized wound care center for a minimum of three months, with an average duration of thirty-four months. During this time, they were treated with debridement, as well as systemic and topical antibiotic therapies, topical growth factors, and skin replacements, alongside biweekly three and four-layer compression therapy. To reassess for any lingering reflux in the superficial venous system and specifically to evaluate the limb for incompetent perforating veins, patients with ongoing ulcers who showed no signs of healing, as measured by our software system, had repeat duplex ultrasound performed after three months of compression therapy.

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E. Plant Used for Treating Peptic Ulcer

Numerous plant-based products, nutrients, and herbs have been shown to help prevent or treat peptic and stomach ulcers. There aren't many human trials available, but many in vitro or animal studies have shown promise. Although a wide range of botanical products have been shown to exhibit antiulcer activity, the majority of the literature that has been documented has focused on their pharmacological effects in experimental animals. With the exception of a few phytogenic substances (i.e. There is little clinical evidence to support the use of herbs as gastro-protective agents (such as aloe, liquoricen , and chilli), and consequently, little information on their safety and effectiveness. Despite this, a number of botanical products have low toxicity and high efficacy, making them potentially useful for therapeutic purposes. Finally, since the majority of anti-inflammatory medications used in modern medicine have antiulcer properties, compounds with such properties as flavonoids, aescin, aloe gel, and many others are of special therapeutic importance.

F. Clinical study on Vitamin U, Belladonna and Aluminum Capsules II combined with Omeprazole in Treatment of Gastric Ulcer

Patients in the control group received oral capsules covered with enteric Omeprazole prior to breakfast at 0.5 hours, one grain per time, once a day. Patients in the treatment group receive vitamin U, Belladonna and Aluminum Capsule II, similar to those in the control group, at the dose of one grain each time, three times a day. The two groups received six weeks of treatment. After treatment, the effectiveness was assessed and compared between the two groups by comparing the symptom scores, the size of the ulcer, the pH of the digestive juice, the serum factor levels, the frequency rate and the Helicobacter pylori eradication rate. After treatment, the levels of two groups of IL-6 and IL-8 were significantly lower, but the levels of two groups of EGF and VEGF we real so significantly lower .In the same group, the difference was statistically significant(P0.05). Furthermore, serum factor levels in treatment and control groups differ significantly (P0.05). After treatment, control and treatment groups had a rate of eradication of Helicobacter pylori of 70%–7 percent and 90%–2 percent, respectively, and were different (P0.05). After a six-month follow-up period , the recurrence rate in control and treatment groups was19 per cent and 4 per cent, respectively. The difference between the two groups is (P0.05).In conclusion, the combination of vitamin U, belladonna and aluminum capsule II with omeprazole capsules coated with intestinal coatings has clinically beneficial effects on the treatment of gastric ulcers. It can also improve the pH level of the stomach and alleviate symptoms of the intestine.

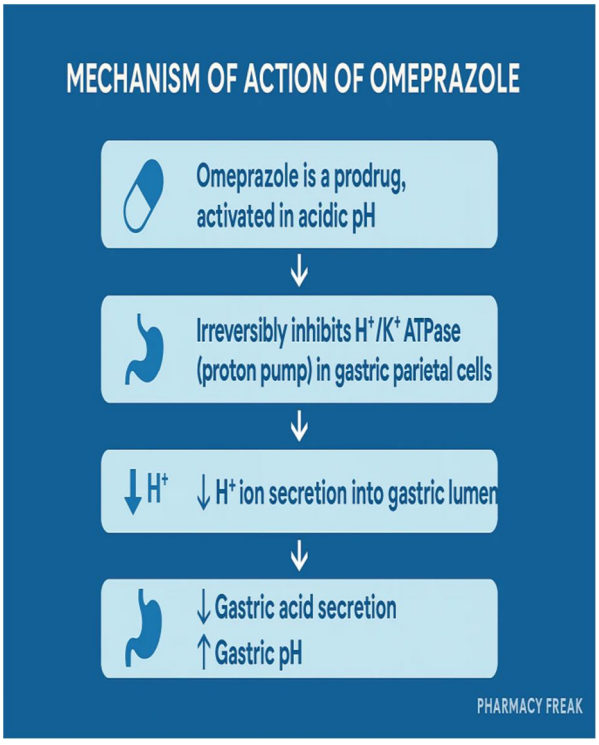

Fig. Mechanism of Action of Omeprazole

G. Clinical efficacy of vitamin B in the treatment of mouth Ulcer

Vitamin B complex is a combination agent commonly used to treat oral ulcers, including vitamin B1, vitamin B2, nicotinamide, pantothenic acid, vitamin B6, folic acid, and vitamin B12. Vitamin B1 (thiamine) plays an essential role in the body's energy transformation and proper function of muscles and nerves. Vitamin B3, often referred to as niacin, mainly promotes enzyme activity and participates in the transfer of hydrogen during biological oxidation. Vitamin B2 or riboflavin is related to oral and genital mucosa inflammation and plays an important role in normal growth, muscle development and hair health. Pantothenic acid, also known as vitamin B5, promotes the metabolism of carbohydrates, fats, and proteins, leading to energy production in the body. Vitamin B6 plays a role in the physiological function of several enzymes and in the metabolism of fats and amino acids. Folic acid and B12 are two interconnected B vitamins; various studies have shown that they contribute to the production of red blood cells in bone marrow, but a lack of any of these vitamins can cause anemia. This meta-analysis aimed to investigate in depth and quantitatively whether vitamin B complex treatment has a positive impact on the healing of mouth ulcers.

V. RESULT

Relevant literature, including comparative retrospective studies, outcomes from case reports, randomized controlled trials (RCTs), and systematic reviews, were identified after applying the inclusion and exclusion criteria. Through the use of substances that either neutralize acidity or inhibit acid production, medical treatment may aim to reduce the impact of pepsin and acid. Both the reduction of pepsin activity and an elevated pH level contribute to diminished peptic activity. Another category of compounds enhances mucosal defense by stimulating the secretion of mucus, bicarbonate, and mucosal growth, or by forming a protective barrier over the ulcer crater.

VI. CONCLUSIONS

The significance of eradicating H pylori in cases of ulcer disease is clear, yet formulating a treatment strategy can be perplexing. Our review of the literature on eradication shows that 7–14-day treatment courses combining a proton pump inhibitor with clarithromycin and metronidazole are highly effective and generally well accepted. Vitamin B accelerates the healing of ulcers, lowers the chances of recurrence, and enhances the treatment's efficacy. Overall, vitamin B offers considerable clinical advantages for addressing mouth ulcers.

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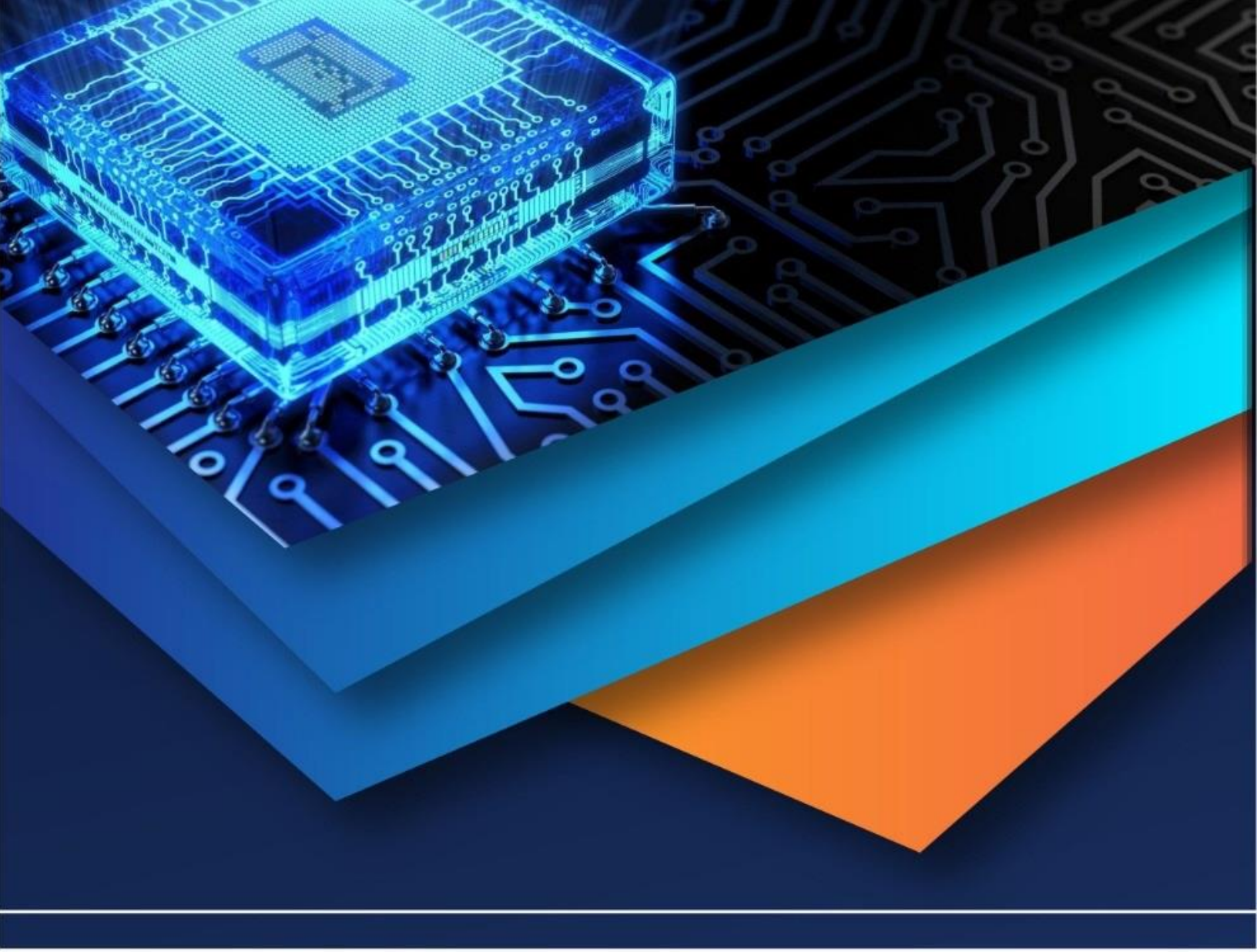

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