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# Stress induced Gastric Ulcers Mechanism and Potential Therapeutic Interventions

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**Abstract**

It is possible that the prevention and treatment of stress-induced stomach ulcers might be revolutionized by the combination of these aforementioned treatments. Utilizing molecular insights, novel and individualized medicines, holistic care, and clinical validation practices, future research may be able to fill in the gaps in the treatments that are currently available. Not only does this method have the potential to enhance patient outcomes and quality of life, but it also has the potential to lessen the financial burden that ulcers like these have on healthcare systems all over the globe.

**Keywords**: Ulcer, Stress, Applications

## Introduction

The spontaneous emergence of ulcers within the mucosal membranes of the stomach is a hallmark of ulcers, a chronic and recurrent condition. Gastric ulcers, which manifest as visible open sores in the stomach lining, have long been acknowledged as a major worldwide health concern. While there are many probable causes of stomach ulcers, such as a Helicobacter pylori infection, the use of nonsteroidal anti-inflammatory medicines (NSAIDs), or unhealthy lifestyle choices like excessive alcohol use, the study of ulcers caused by stress is particularly intriguing [1]. Figures 1.1 and 1.2 show that the persistent challenges of properly managing and treating gastric ulcers have received a lot of attention from the scientific community. These ulcers, which usually result from long-term mental stress, have received a lot of attention from researchers.

The effects of stress on the human body are far-reaching and complex. The digestive system is one of the many physiological systems that it could affect. Increased gastric acid production, reduced blood flow across the mucosa, and impaired mucosal defense mechanisms are some of the physiological changes that stress may bring about in the stomach. These items may cause ulcers in one or more people [2]. Due to the intricate interplay of the problem's components, managing stomach ulcers caused by stress is difficult. Stress-induced stomach ulcers may be treated with phytochemicals, which are naturally occurring compounds in plants, according to recent research. The alkaloids, glycosides, tannins, terpenoids, polysaccharides, and saponins are only some of the phytochemicals that are included in this extensive study. We are primarily concerned in the possible medicinal functions of these phytochemicals. These bioactive compounds have shown great promise in the treatment of ulcers, thanks to their anti-ulcerogenic characteristics, which have been confirmed in both animal studies and human clinical trials.

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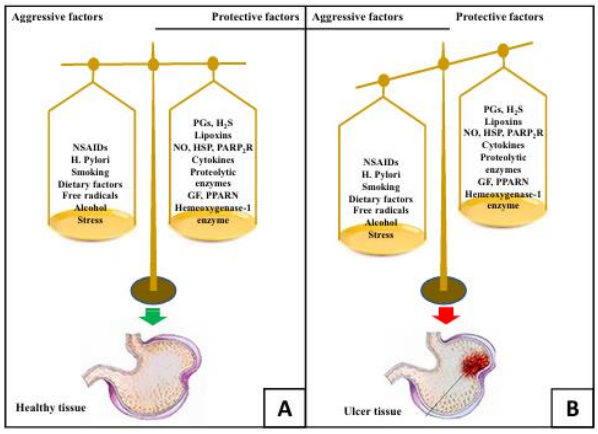


**Fig. 1.1 Gastric ulcer risk factors are shown in Figure A. Regulating the levels of healing-promoting and -inhibiting substances in both healthy mucosa and B. An ulcer may form in the stomach lining if there is an imbalance.**

The effects of stress on the human body are far-reaching and complex. The digestive system is one of the many physiological systems that it could affect. Increased gastric acid production, reduced blood flow across the mucosa, and impaired mucosal defense mechanisms are some of the physiological changes that stress may bring about in the stomach. These items may cause ulcers in one or more people [2]. Due to the intricate interplay of the problem's components, managing stomach ulcers caused by stress is difficult. Stress-induced stomach ulcers may be treated with phytochemicals, which are naturally occurring compounds in plants, according to recent research. The alkaloids, glycosides, tannins, terpenoids, polysaccharides, and saponins are only some of the phytochemicals that are included in this extensive study. We are primarily concerned in the possible medicinal functions of these phytochemicals. These bioactive compounds have shown great promise in the treatment of ulcers, thanks to their anti-ulcerogenic characteristics, which have been confirmed in both animal studies and human clinical trials.

***Functioning of Gastric Secretion***

H+ release by parietal cells in response to stomach acid is an ongoing process involving both the periphery and the central nervous system. Factors endocrine (gastrin), paracrine (histamine), and neuronal (acetylcholine, Ach) control acid generation. Receptors H2, M3, and CCK2 are located on the basal and lateral surfaces of parietal cells. Histamine is also generated by enterochromaffin-like cells (ECL), which have certain receptors on them. An AMP-kinase that operates on Gs-adenylyl cyclase The G protein-coupled receptors (GPCRs) set off a response cascade. In parietal cells, the Gq-PLC-IP3-Ca2+ pathway is facilitated by GPCRs and is enhanced by acetylcholine and Gastrin. In parietal cells, the H+, K+ -ATPase is activated by cAMP and the Ca2+-dependent pathway. This enzyme is in charge of the exchange of H+ and K+ ions. It is the job of the proton pump to keep the intracellular pH at around 7.3 and the intracanalicular pH at about 0.8. Hypothalamus, solitary tract nucleus, and vagal nerve of dorsal motor nucleus are the three regions that activate the generation of stomach acid. The dorsal motor nucleus is the origin of the efferent fiber, which, via the vagus nerve, descends to the stomach. When it reaches the enteric nervous system, it connects synaptically with ganglionic cells. The secretion of vagal postganglionic fibers releases acetylcholine (ACh), which increases the production of stomach acid, via its interaction with muscarinic M3 receptors on the basolateral membrane of parietal cells. The central nervous system and the enteric nervous

system is mainly responsible for controlling the release of acetylcholine (ACh) in reaction to olfactory, gustatory, or anticipatory cues about food. Accelerated stomach acid production and release, or "cephalic," is one of the effects of aching [6].

Nonsteroidal anti-inflammatory drugs (NSAIDs) mainly cause damage to the stomach by inhibiting gastric prostaglandin synthesis, as discovered by Sir Vane in 1971(12). Since then, there is a substantial amount of evidence that NSAIDs' ulcerogenic effects are correlated with their ability to suppress prostaglandin creation. Research by Wallace and colleagues suggests that gastrointestinal damage may allow for selective suppression of COX-1 or COX-2, given that the two proteins are not related to each other [16]. However, it was proposed that the dual inhibition of COX-1 and COX-2 is the most important component. It seems that COX-2 is involved in the process of re-establishing the structure of the gastric mucosa, as specific inhibition of COX-2

slows down the healing process of experimental ulcers. Figure 1.9 shows how nonsteroidal anti-inflammatory medications (NSAIDs) harm mucosa by neutrophil adhesion, which in turn releases proteases, free radical oxygen, and capillary blood flow obstruction. Nonsteroidal anti-inflammatory medications (NSAIDs) produce less harm when neutrophil adherence is prevented in mouse models. Conversely, mucoprotection cannot occur without prostaglandins, and more especially PGE2, according to a multitude of research. It seems that NSAIDs significantly impact systemic inflammation by suppressing the COX enzyme, which in turn reduces mucosal prostaglandin synthesis.

Objective-

**Identify Mechanisms:**

- It is the purpose of this research to investigate the physiological and biochemical processes that are involved in the development of stress-induced stomach ulcers. These pathways include oxidative stress, inflammatory responses, and neural control.
- with the purpose of gaining an understanding of the role that mucus production, stomach acid output, and microvascular alterations play in the development of ulcers.

**Evaluate Interventions:**

- Proton pump inhibitors, H2 receptor antagonists, cytoprotectants, and antioxidants are some of the pharmacological treatments that will be evaluated in this study for their efficacy in treating and preventing stomach ulcers.
- The objective of this study is to investigate the potential of herbal and natural chemicals as alternative treatments for ulcers that are caused by stress.

**Aim of the study**

The purpose of this study is to research the processes that are responsible for stress-induced stomach ulcers and to identify novel therapeutic strategies for the control and treatment of these ulcers.

**Limitations of the Study**

**Experimental Models:**

- It is possible that the animal models used in the study of stress-induced ulcers do not adequately replicate the physiological and psychological stress that humans experience.
- It is possible for the findings to be inconsistent if the procedures used to induce stress (such as restraint or immersion in cold water) are not entirely constant.

**Symptoms**

A small ulcer may not cause any symptoms at all, while a large ulcer may result in dangerous bleeding. The most common indications and symptoms of peptic ulcers are a lack of appetite, a sense of fullness, moderate nausea, pain and discomfort in the upper abdomen, sleeplessness owing to pain in the upper abdomen, stools that are bloody or dark, chest pain, exhaustion, and weight loss [21].

**Reported Antiulcer activity**

**A.F.S.C Viana et al. (2013)**How well an ethanolic preparation of Cenostigma macrophyllum Tul's leaves protects the digestive system. Researchers examined the effects of Cm-FHA, a variety of A. acuminata, on rats. Rats were subjected to the induction of ulcers using a variety of different models. The following models were included: ethanol-induced ulcers, ischemia-reperfusion ulcers, cold restriction stress ulcers, indomethacin ulcers, and HCl/ethanol ulcers. The extract was made using four kilos of dried CmFHA leaves, which were extracted using 95% ethanol. Subsequently, the ethanol extract was subjected to a treatment using a 1:2 mixture of methanol and water. It was successively extracted using ethyl acetate. The concentrated extract was then suspended in a solution of 1:2 methanol and water and extracted using hexane. In an ethanol-induced ulcer model, Cm-FHA showed a gastroprotective effect at 100 and 200 mg/kg, resulting in a 40% decrease in lesion development.

***Endogenous gastro-protective mediators***

It is possible to preserve the endogenous mediators by reducing the prevalence of major risk factors for stomach ulcers. Prostaglandins play an important role in mucosal defense because they may enhance blood flow to the mucosa, protect epithelial cells from cytotoxin damage,

and reduce the generation of inflammatory mediators [66]. Lipoxin-A4 regulates trans-epithelial electrical resistance and aids in the resolution of inflammation, two important functions of mucosal defense. Furthermore, by reducing leukocyte adherence within the stomach's microcirculation, it protects the stomach from aspirin's harmful effects. Inflammation regulation is one area where nitric oxide is involved. Changes in mucosal immunocyte activity, epithelial permeability, and bicarbonate secretion may be effected by its interactions with prostaglandins. Increased mucosal resilience to ulceration is a direct result of this [67].

**Hypothalamic Pituitary axis and Stress**

Both short-term stress in childhood and long-term stress in adulthood may affect the gastrointestinal tract. When the gastrointestinal system experiences stress, it may alter permeability and motility, which in turn affects the pain circuitry. Potential risk factors for later life include immunological stressors including allergies, infections, metabolic and nutritional deficits, and maternal deprivation, as well as early-life stressors like physical and emotional abuse, the loss of a caregiver, and maternal illness [72]. An inflammatory response inside the central nervous system, along with physical and mental stresses, sets off a chain reaction that might provide positive or negative feedback. These responses are controlled by stress hormones secreted by the pituitary gland and the brain, which are called corticotropin-releasing hormone (CRH) and adrenocorticotropic hormone (ACTH), respectively.

**Conclusion**

In conclusion, this study demonstrates that phytochemicals can be used in conjunction with conventional treatments to treat stomach ulcers caused by stress. Emerging research demonstrates that they possess protective capabilities via a variety of methods, which makes them attractive candidates for ulcer care. Numerous health advantages may be attributed to phytochemicals, which are secondary metabolites that are present in plants. In addition to their antioxidant and anti-secretory properties, flavonoids have gastroprotective properties. Since they can alter pH levels and ulcer indices, there is evidence that alkaloids and terpenoids have gastroprotective properties. Tannins and saponins, which can be found in a wide range of plants, have the potential to control acid secretion, making them effective against ulcers. There are anti-inflammatory and antioxidant properties associated with polysaccharides. In terms of treating and preventing ulcers, it appears that herbal medications and conventional treatments can work together. The preventive activities that phytochemicals have against stress-induced stomach ulcers put an emphasis on the therapeutic potential of these compounds. To fully comprehend their processes and translate the findings into real-world applications, additional research is required. In order to effectively manage stress-induced stomach ulcers, further study should include the use of phytochemicals as supplementary choices.

Ulcers or sores in the mucosa of the stomach, caused by stress, are a dangerous medical disease. These ulcers form when the delicate equilibrium between inflammatory mediators, stomach acid, pepsin, oxidative stress, and protective chemicals including mucus and bicarbonate production is upset. Depression, anxiety, and other mental health issues, as well as physical pressures like serious sickness or surgery, are the main culprits in causing this imbalance. An upregulation of cortisol and catecholamine synthesis occurs when these stresses stimulate the hypothalamic-pituitary-adrenal (HPA) axis. Hormonal shifts brought on by stress make oxidative stress worse, cut off blood flow to the mucosa, and slow down the healing process—all of which create an environment where ulcers thrive. The following are some of the main mechanisms that cause stomach ulcers brought on by stress:

**Oxidative Stress:** Excessive production of reactive oxygen species (ROS) damages the stomach's epithelial cells and breaches the mucosal barrier.

**Inflammation:** The generation of cytokines such as interleukin-1 (IL-1) and tumor necrosis factor-alpha (TNF-) is a major factor in mucosal injury, which is caused by the activation of inflammatory pathways.

**Altered Gastric Acid Secretion:** Stress may cause changes in neural regulation, particularly via the vagus nerve, which can cause an increase

in stomach acid production. This, in turn, can worsen mucosal damage.

**Reduced Mucosal Blood Flow:** Stress may narrow blood vessels, which can lead to ischemia and cut off oxygen and nutrients needed for mucosal tissue repair.

Pharmacological treatments, including proton pump inhibitors (PPIs) and H2 receptor antagonists, have been the mainstay in the treatment of stress-induced ulcers. These chemicals have a profound effect on lowering stomach acid production, which in turn helps with symptom relief and expedites recovery. A variety of adverse effects, including as nutritional malabsorption, drug interactions, and an increased risk of infections, have been associated to their long-term use. Furthermore, many therapies focus on symptom relief rather than addressing the root reasons, which creates a vacuum in the comprehensive treatment of the problem. New study suggests that non-pharmacological approaches and natural ingredients might be useful as complementary or alternative medicine. The antioxidant, anti-inflammatory, and mucoprotective properties of curcumin, flavonoids, and polyphenols have been shown to show promise in preclinical research. Furthermore, the physiological impacts of stress may be mitigated via the use of stress management strategies such as physical exercise, meditation, and mindfulness. Ulcers may be less likely to form as a consequence of this. Adopting a balanced, antioxidant-rich diet and making lifestyle changes are additional strategies that encourage holistic ulcer care, in addition to avoiding triggers like smoking and excessive alcohol intake. In order to find novel therapy targets, the researchers are doing this study to better understand the biology of stress-induced stomach ulcers. The overarching goal of this research is to find a better way to treat these ulcers. This will be achieved by exploring innovative alternatives to current pharmaceutical and non-pharmacological treatments. Patients with stress-induced stomach ulcers may have better results, higher quality of life, and lower healthcare costs if conventional medication and alternative therapies could work together.

**Innovative Therapies**

**Novel Pharmacological Agents:** Despite the continued benefits of proton pump inhibitors (PPIs) and H2 receptor antagonists, the limitations of these medications necessitate the creation of alternative treatments. Selective inflammatory inhibitors that target specific cytokines like IL-1 and TNF-, as well as mucosal protectants that strengthen the gastric barrier without affecting acid production, have the potential to significantly advance treatment.

**Synergistic therapies,** in which natural chemicals and conventional pharmaceuticals are combined, have the potential to increase effectiveness while simultaneously reducing side effects. Curcumin, a natural substance that helps reduce inflammation and oxidative stress, can be added to proton pump inhibitors (PPIs) as a supplement to help improve overall results. The most effective medication dosages and combinations will be the primary focus of future research.

**Personalized Medicine**

**Biomarker Discovery:** Genomic and proteomic techniques may be used to find biomarkers that are related with stress-induced stomach ulcers. These biomarkers may include genetic predisposition, inflammatory mediators, or levels of stress hormones. These biomarkers have the potential to facilitate early identification and the development of individualized treatment programs depending on the risk profile of a person.

**Tailored Therapies:** Personalized medicine has the capacity to deliver focused therapies by gaining a knowledge of individual variability in response to stress and therapy. Examples of people who could benefit from specialized anti-inflammatory medications or antioxidant supplements include those who have a hereditary tendency to heightened inflammatory reactions.

**Clinical Translation**

It is necessary to confirm the results of preclinical research via rigorous clinical trials, which are conducted on a large scale. The purpose of these trials is to evaluate the safety, effectiveness, and long-term effects of conventional and alternative medicines in a variety of patient groups, with the goal of assuring that the results can be generalized.

**Alternative treatments:** The evaluation of the efficacy of alternative and non-pharmacological

treatments, such as acupuncture, herbal medications, and probiotics, will result in an expansion of treatment alternatives. This entails defining optimal doses for clinical usage and standardizing processes for use in clinical settings.

**Safety and Accessibility:** Innovative medicines should have a priority on safety, particularly for vulnerable groups such as the elderly or those who suffer from chronic diseases. In addition, accessibility and cost-effectiveness are two factors that need to be taken into consideration in order to guarantee equal healthcare delivery.

**Impact of a Multi-Faceted Approach**

It is possible that the prevention and treatment of stress-induced stomach ulcers might be revolutionized by the combination of these aforementioned treatments. Utilizing molecular insights, novel and individualized medicines, holistic care, and clinical validation practices, future research may be able to fill in the gaps in the treatments that are currently available. Not only does this method have the potential to enhance patient outcomes and quality of life, but it also has the potential to lessen the financial burden that ulcers like these have on healthcare systems all over the globe.

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