INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Review Article

Biochemical And Molecular Markers Involved in Gastric Ulcer Pathogenesis

Sreekanth S*, Kusu Susan Cyriac

Department of pharmacology, Karnataka College of Pharmacy, Bengaluru, Karnataka, India

ARTICLE INFO

Published: 15 Jun. 2026
Keywords:
Gastric ulcer , Biomarkers, Oxidative Sterss , Inflammation, Apoptosis, Helicobacter pylori , Nitric oxide, Matrix metallo proteinases
DOI:
10.5281/zenodo.20700737

ABSTRACT

A complex of gastrointestinal condition , this gastric ulcer are caused by imbalance between aggressive elements that are consist of H pylori infection, gastric acid, and NSAID's , the protective gastrointestinal responses in the stomach lining membrane. Intension of this review to show the important molecular and biochemical markers that play a role in the development of gastric ulcers. This contains oxidative stress markers, inflammatory mediators and apoptotic proteins and nitric oxide and prostaglandins and matrix metalloproteinases. Cellular damage due to oxidative stress is also observed, which is explained by the creation of harmful compounds by reactive oxygen species, the subsequent destruction of tissues by inflammatory cytokines (TNF- alpha and interleukins). Apoptotic proteins like Bcl-2 and Bax and caspases and p53 lead to cell death thus disrupting repairing of the tissue. Both nitric oxide and prostaglandin protect the mucosa as well as cause tissue damage. Activation of virulence factors and the initiation of a prolonged period of inflammation in the stomach by H. pylori causes gastric ulcers. Matrix metalloproteinases are involved in both tissue repair after injury and extracellular matrix remodelling. All these biomarkers give researchers a clear picture of the gastric ulcer disease mechanisms and thus they are able to develop superior tests and treatment options. Researchers can also take a lot of ways to investigate how the use of biomarkers and the use of the precision medicines that enable the doctors to ascertain how various individuals respond to the same disease can assist in enhancing the treatment choices of patients with gastric ulcer disease.

INTRODUCTION

One of the numerous GI diseases that transpire due to the excessive forces of factors like gastrin, acid, pepsin, and toxic microorganisms defeating the safeguarding factors like those present in the stomach lining include chronic gastric ulcerations.[1] Gastric ulcers have proven to be a long term health issue and this has been due to

***Corresponding Author:** Sreekanth S.
Address: *Department of pharmacology, Karnataka College of Pharmacy, Bengaluru, Karnataka, India*
Email : sreekanths0909@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

their chronicity, relapse as well as the severity of their outcomes,[2] That makes them a challenge to cure. The biochemical pathways of gastric ulcers are thus of importance as they govern the development, formation and healing of gastric ulcers so as to develop diagnostic and treatment interventions.

The most significant cause of the development of gastric ulcers is infection with H pylori, which effects the stomach inner lining membrane nearly 50 perecent population in the worldwide.[3] Helicobacter pylori damages our mucosal tissues by producing cytotoxin-associated gene A (CagA) like virulence factors that kills our epithelial tissue and causes inflammatory reactions to occur with the help of our immune system.[4] When reacting to the infection, pro-inflammatory cytokines are also produced such as TNF-alpha and IL-1beta, which result in chronic inflammatory reactions, causing our tissue damage,[5] therefore, it is a biochemical marker in respect to formation of gastric ulcers in future.

The creation of a gastric ulcer takes place as a result and the number of molecular signaling mechanisms controlling inflammation, cell death, and cell development . NF-κB activation is believed to be the major process by which mediators that promote inflammation are generated, This proceed with of damage the stomach lining.[6] it is believed that oxidative stress is a key factor in the development of stomach ulcer, and lipid peroxidation and destruction of DNA by the protective properties of the stomach mucosa are lost when reactive oxygen species are produced in excess.

Various oxidative stress biomarkers can be used to measure oxidative stress in gastric ulcer patients, and they comprise MDA and GSH.[7] Recent research has demonstrated that blood tests as a measure the systemic inflammatory indicators using the systemic inflammatory response index (SIRI), Neutrophil-lymphocyte ratio (NLR), and platelet-lymphocyte ratio(PLR) tests are crucial in estimating how far gastric ulcers go towards becoming common and severe.[8] The systemic inflammatory markers are well-known markers to quantify the inflammatory response, which is handy in the detection of gastric ulcers, therefore is used as non-invasive tests to quantify the level of the gastric ulcer inflammation.

The pathogenesis of gastric ulcers is an inflammatory mediators and molecular markers-dependent process, involving matrix metalloproteinases (MMPs), which serve as enzymes that degrade the extracellular matrix, concomitantly remodelling tissues, so that their failure to do so leads to an increased recovery time. Moreover, MMP-9 and tissue inhibitors of metalloproteinases (TIMPs) have been associated with high levels of mucosal damage in the gastrointestinal tract, thus a possible biomarker of gastric ulcer disease depending on the relationship observed in recent studies.[9]

Recent studies, which examined function the pyroptotic death of cells in the stomach's mucosal injury have also contributed to a deeper comprehension of the mechanisms underlying programmed cell death. For pyroptosis-related molecules, such as the Gasdermin D, caspase-1, and the NLRP3 inflammasome have all these associated with this cell death of inflammatory cells, as well as the destruction of tissues because of the infection of H. pylori .[10] It was also established this molecules have significant action of formation of ulcers.

It has also been found that gene modifications and epigenetic regulation by microRNAs are also important in gastric disease pathogenesis and progression, and that microRNA expression can

also be linked to gastric ulcer development and progression.[11]

The development of the gut flora in the stomach proceeds as long as the H. Pylori infection stays within its limits. The imbalance of the microbes in the body that leads to an immune response which is the increase in the level of stomach lining inflammation is dysbiosis. It is suggested in the research that the microbes which serve to diagnose stomach infection following the test works in the correct cohort study.[12] The researchers state that the microorganisms interplay with other risk factors of developing digestive ulcers and form multi-layered mechanisms that define the risk of an individual developing digestive ulcers. The study about the chemical reactions resulting in the creation of stomach ulcers will give the relevant predictive instrument allowing a doctor to estimate the risk of a particular person of developing an ulcer, thereby serving to devise improved patient management strategies.

Pathophysiology of gastric ulcer

The mechanism of gastric ulcer occurrence is multi-component in nature; it entails the interplay of multiple components that are in complicated relationships with one another. The stomach mucosa is influenced by several variables to ensure that the environment is healthy. The stomach has its own acid which it produces and it is covered by the mucus layer. The presence of mucus secretion of bicarbonate maintains the level of pH in the stomach. The turnover effect is observed in the epithelial cells and this means that new cells are continuously formed to replace old cells. Gastric blood flow supplies blood to the gastric lining which contains oxygen and nutrients as well as eliminates waste products present in the stomach. The waste products can destroy cells upon their presence. The synthesis of prostaglandins is the guarantee of the protective mechanisms development in the stomach lining. Pepsin, stomach acid, and bile salts and other chemicals and medications, such as NSAIDs and alcohol, damage the epithelial cells of the stomach. These drugs and chemicals preserve the mucosal barrier by inhibiting the production of the prostaglandins by COX enzymes.[13] The gastric lining is highly vulnerable to damage by acid as a result of absence of protective prostaglandins.

The development of gastric ulcers is also greatly impacted by an infection of H. pylori. These bacteria of H. pylori uses its flagella to move and penetrate the mucous layer of the stomach. It also uses its enzyme to set up a defense mechanism by destroying stomach acids to ensure its survival. The bacteria H. pylori creates CagA and VacA virulence factors. The virulence factors break down the cells' strong connections. This damages these cells.[14] This virulence factors cause the intracellular pathways to occur. This leads are generation of mediators that cause inflammation. An inflammatory reaction is triggered by the inflammatory mediators. Cells die as a result, and cellular equilibrium is disturbed.

The gastric mucosa is affected because of the infection of H. pylori. This is because of infection of H. pylori leads to an inflammatory response. This causes the stimulation of immune cells The immune cells activation with the infection of H. pylori causes the generation and discharge of cytokines that promote inflammation. As a result , TNF-alpha, IL-8, and IL-1beta are produced. This leads to tissue damage and results in chronic inflammation.[15] The presence of these cytokines also leads to impaired healing for stomach epithelium. As a result, stomach ulcers develop. Understanding oxidative stress and how it affects the illness is essential to understanding the pathophysiology of stomach ulcers. Inflammatory damage to the cells in the stomach lining occurs as

a result of the production of Reactive oxygen species , which causes the oxidation of fats and protein as well as DNA damage. The oxidative stress causes impairment of the cell system that is beyond the inherent antioxidant defense mechanisms.[16] Mitochondrial damage happens because of reactive oxygenspecies, which trigger the capoptotic process, thereby impairing the lining of the intestine.

According to the latest research findings, the mechanisms of apoptosis, which include pyroptosis, are responsible for causing damage to the gastric lining. Pyroptosis refers to a form of inflammatory cell death, which occurs as a result of the activation of the NLRP3 inflammation, wh, which are released by the inflamed gaich activates caspase-1 and produces IL-1beta and IL-18, stric lining.[17] This process of pyroptosis not only leads to damage of the cells in the stomach lining but also leads to a cycle of inflammation, which impairs the cells in the stomach lining, thereby causing damage.

The formation of gastric ulcers depends on two main processes which involve the body's inability to heal and restore its mucosal lining. The healing of the ulcers depends on various mechanisms which work together to achieve the main goal through three main processes which involve the growth and movement of epithelial cells and Blood vessel development and extracellular matrix alteration. Various growth factors activate the processes which involve the vascular endothelial growth factor and the epidermal growth factor as the two main components. The healing of the ulcers will face a delay as all pathological conditions will disrupt the main healing processes which result in the development of chronic ulcers.[18] Activation of neuroendocrine pathways is what causes the development of stress related gastrointestinal ulcers by activating both the hypothalamic-pituitary system and the sympathetic nervous system. The body's activation leads to the increased production of cortisol and catecholamines which decrease the mucus production, blood flow to the stomach mucosa, and the production of acids which increase the chances of the mucosal lining to develop ulcers according to research.

Furthermore,[19] the gastric mucosa is subject to more damage by two factors that include oxidative damage and the strss-induced inflammatory response. That formation the gastric ulcers comes as a result of the pathogenic process of the microbes that affect the gastric area, which is beyond the H. pylori that interferes with the regular operation of the gastric microbiota. The injury the gastric mucosa that comes as a result of the loss of microbial diversity identifies the imbalance of the microbes as the cause of the formation of gastric ulcers, as indicated by the research findings.[20]

Biological pathways Mitogen-Activated Protein and Nuclear Factor Kappa B . The biochemical mechanisms that the human body uses are called kinases to instigate particular molecular processes in response to an infection or trauma. The pathways control the formation of "mediators" that are inflammatory signaling molecules in case of gastric ulcers. The pathways regulate three processes which are responsible for the production of mediators and apoptosis proteins and stress response proteins.[21] The Persistent pathway activation causes permanent body inflammation and interferes with the healing process of the injured body tissues. The integrity of the stomach mucosa depends on the operation of vascular factors which act as essential components. The body cells require an adequate blood supply through the process of microcirculation to provide them with the required nutrients and oxygen while

removing their injurious products through the blood. The Prevalence of stomach ulcers is attributed to dysfunction that the microvascular system which interferes with the blood flow to the damaged body tissues.[22]

Damage to the microcirculation endothelial cell and the reduction of blood vessel formation would cause a reduction in the protective capacity of the mucosa. A number of biochemical processes and their interrelationship with molecular mechanisms work together to cause the pathophysiological condition for the acid-peptic damage response's role in the development of stomach ulcers, the microbial infection and inflammation response, the oxidative stress response, the tissue repair response, and the apoptosis response. In order to discover new biomarkers and targets to investigating every activity is essential for the treatment of stomach ulcer disease and their interrelationship with one another.

Oxidative stress markers in gastric ulcer pathogenesis.

Oxidative stress is the cause of stomach ulcer disease development and progression, which affects the balance of reactive oxidative species production and gastric mucosa antioxidant defense systems. The regular operation of cells produces reactive oxygen species. If teir levels are higher, it could lead to the emergence of illnesses. Superoxide anion (O2-), hydroxyl radicals (OH), and hydrogen peroxide (H202) are the reactive oxygen species generated by stomach tissue.[23] There is also the oxidative stress on the gastric tissue, which is caused by various factors as the sources of this stress include Helicobacter pylori, NSAIDs, alcohol, ischemia-reperfusion, and inflammation, as they all result in gastric mucosal damage, which causes gastric ulcers.[24] Malondialdehyde is an important indicator of oxidative stress, which is typically assessed and investgated in individuals with gastric ulcer disease. It results from the oxidation of lipids and fatty acids, and it is related to oxidative stress because of lipid peroxide formation. The more malondialdehyde is produced, the greater is the degradation of lipid membranes, causing loss of membrane function and increased cell permeability.[25]

Patients that exhibit higher levels of MDA have been found to suffer stress-related gastric ulcers and gastric mucosal injury, which shows how widespread the oxidative damages have been to the body of a patient. MDA has the ability to bind to proteins and nucleic acids, thereby causing more damage to the cells, resulting in increased inflammation.

The second indicator of oxidative stress is 4-hydroxynonenal (4-HNE), and this compound is also a result of lipid peroxidation. MDA and 4-HNE function as reliable markers and demonstrate oxidative stress results while they engage in cellular activities that control apoptosis and inflammation. The gastric tissues of the human body demonstrate an accumulation of these two compounds during oxidative damage. This leads to the development of the disease. The antioxidant defense system contains various enzymatic markers. These indicators serve to guarantee of oxidative stress will be reduced. One of that basic components for this group of markers is superoxide dismutase (SOD). It acts by reducing the superoxide radicals to hydrogen peroxide. This reduces oxidative stress in the human body. The study shows that the defense to harm the stomach mucosa is less with reduced SOD. This makes humans susceptible to gastric mucosa damage.[26] The research on clinical studies indicates that patients suffering from gastric ulcers have significantly reduced SOD. This indicates that their body defense system works poorly.

Catalase(CAT)

Potential other significant antioxidant enzymes include the enzyme catalase (CAT) breaks down hydrogen peroxide into oxygen and water, and then oxygen reacts to generate highly reactive hydroxyl radicals. SOD/CAT combination is an essential native defensive mechanism through which the cells can endure the damage caused by ROS. The CAT activity level of gastric ulcer patients is decreased below normal levels, causing the body to store more hydrogen peroxide and thus suffer from oxidative damage.[27]

Glutathione(GSH)

The protein named Glutathione, which performs the role of an antioxidant, in a cell, this protein exists as a vital component which supports the maintenance of redox balance in the cell.[28] GSH performs its function by fighting free radicals and offering the necessary materials for the function of Glutathione Peroxidase (GPx) which performs the process of breaking down hydrogen and lipid hydroperoxides. The manifestation of oxidative stress occurs in the form of a decrease in the GSH content in the gastric mucosa, which scientists have proven occurs in ulcerative disorders. The drop in the content of GSH in the body causes the inability of the body to remove (ROS) reactive oxygen species that, its turn, increases that level for lipid peroxidation and damages the cells.[29]

Glutathione S-transferase and Glutathione peroxidase

Antioxidant enzymes include glutathione S-transferase (GST) and Gpx which support the process of detoxification in the body. GPx is responsible in the process of catalyzing the breakdown of hydrogen and lipid peroxides into a less damaging form whereas GST is in charge of conjugating GSH with degradable toxins to be safely disposed. The body is under increased oxidative stress with mucosal injury in the stomach due to a reduction in GPx and GST activity. Ischemia Modified Albumin (IMA) its possible indicator of oxidative stress. IMA forms due a changes in the structure of the albumin due to oxidative processes. IMA levels are increased in patients with stress-related gastric mucosal injury, where the IMA level may reflect the severity of mucosal injury.[30] IMA indicates that ischemia leads to oxidative stress, while oxidative damage brought on by ischemia leads to formation the ulcers.

Together with reactive nitrogen species (RNS), Nitric oxide regulates stomach processes in two ways. Nitric oxide vasodilates the blood vessels; this allows the flow of blood to the mucosal area at normal body levels of NO. Excessive release of NO is achieved by the activation of the iNOS in the body resulting to creation of a reactive species called peroxynitrite that destroys the cell.[31] The study has shown that higher levels of iNOS are expressed in gastric ulcer models; the above means that the generation of iNOS is the cause that occurrence of nitrosative and oxidative stress. The level that myeloperoxidase (MPO), which is released by neutrophils, mainly first measure the determining of level of oxidative damage. MPO is an enzyme that produces an acidic component which is Hypochlorous acid (HOCl) which is a powerful oxidant responsible of damaging tissues.[32] The detection of increased MPO in the tissue of the stomach implies that the body is experiencing both inflammation and oxidative stress tissue damage, especially for H. pylori-induced ulcers.

Oxidative stress in the stomach can also be determined using the oxidant-antioxidant balance marker ratio, which involves both individual and combined marker assessments for determining the

oxidative status in the stomach. The MDA/SOD and MDA/GSH ratios are the standard methods for determining the amount of oxidative damage that has taken place in relation to the antioxidants' ability to protect the body. The increased ratio implies that there has been a shift towards oxidative stress, which is a measure of the severity of the disease.[33]

The malfunction of mitochondria increases (ROS) reactive oxygen species, this causes the increases senescence-related oxidative damage, and these reactive oxygen species trigger the apoptotic pathway. Mitochondrial dysfunction will result will be decrease of pro-apoptotic and ATP factors release, which will cause cellular homeostasis disruptions.[34] This leads to epithelial cell death, causing increased time for healing of ulcers.

Oxidative stress results in increased activity of NF-kB, which leads to increased pro-inflammatory cytokine levels, which again promotes greater damage to the mucosal tissue in a destruction cycle. Both inflammation and oxidative stress are both components of a gastrointestinal ulcer cycle. The use of biomarkers for oxidative stress is helpful the understanding in mechanism of stomach ulcer formation. The biomarkers MDA, 4-HNE, SOD, catalase, GSH, GPx, GST, IMA, NO, MPO, etc., are helpful in understanding the levels of tissues' antioxidant defence mechanism and oxidative stress, which are helpful in understanding glial mucosal damage and evolution of gastric ulcers and their prevention of healing. The use of these biomarkers was helpful in understanding gastric ulcers, and their use will enable doctors to make early diagnoses. The use of antioxidant therapy will lead to successful outcomes for gastric ulcer patients.

Inflammatory Markers in Gastric Ulcer Pathogenesis.

The development of gastric ulcers begins with the process of inflammation that associates stomach lining injuries with natural healing processes. Various factors that cause stomach lining inflammation involve the use of NSAID's drugs and helicobacter pylori infection, alcohol consumption, also physiological stress because these factors cause stomach lining injuries that result in the destruction of the stomach lining due to the body's immune response.[35] The immune response leads to inflammation that activates immune cells of the body that release cytokines, chemokines, the mediators that destroy the stomach lining, causing ulcers to develop.

(TNF-α) tumar necrosis factor alpha is the primary inflammatory marking for the development the gastric ulcer disease because this inflammatory cytokine is produced by monocytes and macrophages. The protein TNF-α causes inflammation in the body through its ability to release cytokines that attract white blood cells and cause stomach lining cells to die through a process known as programmed cell death. he initial fact that identifies the TNF- as a diagnostic signal to gastric ulcer disease development is the fact that patients with stomach ulcers have been shown by studies to have elevated levels of TNF- that correlate with the severity and progression of their illness.[36]

Interleukin-1 (IL-1β)

Gastric mucosal inflammation mostly results from the activation of the process by interleukin-1 beta (IL-1β). This cytokine leads to two results, which are the halting of stomach acid production as well as gastrointestinal tract damage. The conditions are a situation that leads to the formation of ulcers. The interleukin-1 beta protein activates adhesion molecule production, which enables the neutrophils to get to the site of damage, leading to further damage of the mucosal tissue.[37]

Interleukin-6 (IL-6)

IL-6, which stands for interleukin-6, is a messenger that activates different inflammatory reactions in the body. he presence of elevated IL-6 is the indicator of the existence of inflammatory processes, which inflict even greater harm to the stomach mucosa's tissues, thereby inhibiting for healing process. IL-6 is a controller of signaling pathways that include the JAK/STAT pathway, which is responsible for gene expression for inflammatory and immune reaction processes in the body.[38]

Interleukin-8 (IL-8)

The potent chemokine interleukin-8 (IL-8) is a key player for research in H. pylori infection. IL-8 is a chemoattractant which allows neutrophils to move to the gastric mucosa.[39] Neutrophils that accumulate in the gastric mucosa cause tissue damage through the release of reactive oxygen species (ROS) and proteolytic enzymes that lead to the formation of ulcers. The production of IL-8 is proportional to the severity of the gastric inflammation, thereby creating a direct relationship.

The regulation of gastric ulcer disease involves pro-inflammatory cytokines such as IL-8 and anti-inflammatory cytokines. The regulation of tissue damage reduction through the production of pro-inflammatory cytokines is controlled by the anti-inflammatory cytokine IL-10. The absence of IL-10 or a change in the IL-10 path leads to a situation where inflammation is high.[40] The absence of IL-10 leads to a situation where inflammation is high.

Chemokines are also an important set of inflammatory markers. An example of this is chemokine monocyte chemoattractant protein-1 (MCP-1) that is used in the recruitment of immune cells to inflammation sites. It has been demonstrated to play a role in the infiltration of monocyte/macrophage cells into the gastric tissues and lead to chronic inflammatory and tissue remodelling when overexpressed in inflammatory conditions.[41] It has been noted that elevated levels of MCP-1 have been seen in cases of gastric ulcers and contribute to the progression of the disease.

The dual-function enzyme cowboys-banana oxido-catecholamine catabar is an inflammatory-inducing enzyme responsible for the production of prostaglandins for gastric functions. When overexpressed under inflammatory conditions, the COX-2 enzyme overproduces inflammatory mediators.[42]

The study established the overproduction of the COX-2 enzyme during the increased inflammatory states for both gastric ulcer diseases and the symptoms of H.pylori infections [Wagner et al 2006, Wang et al 2005]. The transcription factor NF-kB plays a crucial role in determining the response to an inflammatory condition by controlling all the inflammatory genes responsible for the production of chemical signals and inflammatory cells responsible for the production of adhesion molecules.

NF-kB is attracted to the nucleus upon its activation to perform the function of transcription for the production of various inflammatory cytokines and chemokines and adhesion molecules responsible for the maintenance of the inflammatory condition and the consequent tissue damage. The overactivation of NF-kB has severe negative effects on the gastric mucosae through the induction of acute stomach inflammation, leading to the formation of gastric ulcers.[43]

The C-reactive protein (CRP) is an inflammatory marker, and it is used in the development of diseases depending on their biochemical character. The increase of CRP is usually observed in

patients who are suffering from gastric ulcers, and it is related to the general condition of systemic inflammation. The clinical applicability of CRP as a marker is used to measure inflammation levels in a patient and track the course of the disease.

Other adhesion molecules, which include intercellular adhesive molecule-1 (ICAM-1), are important for the adhesion of leukocytes with vascular endothelial cells, thereby facilitating the movement of leukocytes through the endothelial cell layer. ICAM-1 expression causes the inflammatory cells to increase in number thus causing damage to the gastric mucosa and ulcer development in the stomach mucosa.This association between ICAM-1 and inflammatory cytokines, as well as other transcription factors, illustrates the process by which different inflammatory pathways function with different molecular mechanisms.

The oxidative stress process works with different inflammatory markers, leading to further damage of the gastric mucosa. Pro-inflammatory cytokines have the ability to activate oxidative stress, which also leads to the activation of ROS synthesis by these cytokines. The activation of oxidative stress results in the activation of NF-kappaB, which activates different inflammatory pathways, thereby leading to a continuous process of damage and inflammation in the stomach lining.[44]

The main reason for gastric ulcer disease is present because of inflammatory markers, which are responsible for immune responses, which lead to tissue damage and prevent healing. Among the critical inflammatory markers that characterize gastric ulcer disease are TNF- alpha, IL-1b, IL-6, IL-8, IL-10, MCP-1, COX-2, NF-kB, CRP, and various adhesion molecules, which lead to the occurrence of gastric ulcer disease as well as could be used in medical treatment.The whole system of inflammatory mediators needs our complete understanding because it is a system, and it is important to understand it in order to develop prevention and treatment strategies for gastric ulcer disease.

Nitric Oxide and Prostaglandins in Gastric Ulcer Pathogenesis.

Prostaglandins and nitric oxide (NO), therefore, sustain the integrity of the gastric mucosa through their regulatory functions as they regulate both normal and abnormal stomach functions. The two mediators regulate three different body processes: blood flow to the mucosal tissue, the production of mucus and bicarbonate, and the body's response to inflammation. Any abnormality in the normal balance during the synthesis and/or function of prostaglandins and NO would significantly increase the risk of the occurrence of a gastric ulcer.[45]

Nitric Oxide (NO), a gas, is produced by the oxidation of the amino acid L-Arginine by the action of the enzyme Nitric Oxide Synthase (NOS), which exists in three main forms: endothelial (eNOS), neuronal (nNOS), and inducible nitric oxide synthase (iNOS). The human body produces the eNOS enzyme to generate NO for the protection of the gastric mucosa by dilating blood vessels to increase blood flow to the gastric mucosa for tissue protection and minor injury tissue repair.[46] The Nitric Oxide (NO) molecule regulates mucus and bicarbonate secretion as a defense mechanism against gastric acids and pepsin.

The body produces inducible nitric oxide synthase in three different pathological conditions, which include inflammation, stress, and Helicobacter pylori infection. When inducible nitric oxide synthase overproduces nitric oxide in three pathological conditions, which are inflammation, stress, and Helicobacter pylori infection, the body

produces excessive nitric oxide. There are three pathological conditions where inducible nitric oxide synthase over produce nitric oxide in the body leading to excessive production of nitric oxide which include inflammation, stress and Helicobacter pylori infection.

The presence of high levels of NO enables it to react with superoxide radicals, which then produce peroxynitrite, an extremely toxic substance. This is because the formation of peroxynitrite results in oxidative stress and nitrosative stress since it initiates the production of lipid peroxidation that then causes the destruction of gastric mucosa and the emergence of ulcers.[47] The body uses nitric oxide in its normal physiological range, and this nitric oxide becomes harmful in large quantities.

The response of inflammation by the production of cytokines and the sticking of leukocytes to the endothelium is controlled by NO as well.NO inhibits platelet aggregation and leukocyte adhesion to the vascular endothelium, thus producing an anti-inflammatory response.[45] The inflammatory response leads to the disruption of the normal production of NO, which activates NF-κB signaling pathways for the production of inflammatory mediators responsible for tissue damage.[48]

Prostaglandin E2 (PGE2) is an important lipid mediator due to the fact that it is synthesized out of arachidonic acid via cyclooxygenase (COX) pathway that protects the gastric lining because it promotes the secretion of the mucus and bicarbonate, and blood flow to the tissues lining the stomach and epithelial cell proliferation in the stomach.[49] Prostaglandins also inhibit the secretion of gastric acid, which in turn inhibits the harmful components that cause damage.

The synthesis of prostaglandins in the body is controlled by the presence of two enzymes known as cyclooxygenases (COX) and are referred to as COX-1 and COX-2.COX-1 continuously stimulates prostaglandin synthesis even in resting states, while COX-2 stimulates prostaglandin synthesis as a result of inflammation in the body. NSAIDs as COX inhibitors have a great effect of reducing the production of prostaglandins, which subsequently causes the weakening of the defenses mechanisms of the stomach lining, making it more vulnerable to S. pyogenes attack and ulcer.[50]

According to the research, it is evident that patients suffering from gastric ulcers always exhibit low prostaglandin E2. This proves that the body of such patients is not able to protect its stomach lining. The absence of prostaglandins results in less mucus and bicarbonate being produced. The result of this is the reduced blood circulation and slows down the regeneration of epithelial tissues, thereby resulting in the development of ulcers and inhibiting the recovery of ulcers.[51] The role of prostaglandins is crucial in the regeneration of tissues, which is a vital part of the healing of ulcers. The regeneration of tissues occurs during the healing of ulcers. The development of blood vessels is controlled by prostaglandins in the body.

Nitric oxide and prostaglandins have a mutual relationship, which has led to the development of complex mechanisms to protect gastric mucosal balance. The combination of nitric oxide and cyclooxygenase activation results in the production of prostaglandins. The relationship between nitric oxide and prostaglandins ensures the regulation of nitric oxide synthase by prostaglandins through the regulation of nitric oxide synthase expression. The relationship between nitric oxide and prostaglandins ensures the regulation of defense mechanisms of the gastric mucosa.[52]

Gastric mucosa has both the protective and harmful effects of the biochemical mediators, which are nitric oxide and prostaglandins. The protective effect of nitric oxide and prostaglandins on the gastric mucosa is the result of the improvement of the blood flow as well as the induction of mucus production, which diminishes the inflammatory reaction that occurs at normal body temperatures. The formation of excessive nitric oxide by the body results from the activation of the inducible nitric oxide synthase, which leads to inhibition the production of prostaglandins by cyclooxygenase, thereby resulting in oxidative stress and inflammation, which cause gastric ulcers.

The biochemical reactions of this research enable scientists to find new ways of creating treatment that prevents gastric ulcers.

Apoptosis-Related Molecular Markers in Gastric Ulcer Pathogenesis

Apoptosis is a controlled death mechanism of the cells that play a major action maintaining balance in the body, and mucous membrane in the stomach (gastric mucosa) is maintained at homeostasis through a balance of cell proliferation and programmed cell death (apoptosis). When there is an imbalance in the levels of apoptosis, with an increase in the number of cells dying via an apoptotic mechanism, it leads to gastric ulcers because this state of imbalance results in the destruction of cells within the lining of the gastric mucosa.[53]

Proteins from the Bcl-2 family play an important role as cellular regulatory molecules controlling the process of apoptosis; they contain both pro-apoptotic (Bax and Bak) and anti-apoptotic (Bcl-2 and Bcl-xL) effectors. The pro-apoptotic family members (Bax and Bak) promote apoptosis via increased mitochondrial membrane permeability whereas anti-apoptotic (Bcl-2 and Bcl-xL) family members promote cellular survival via maintaining mitochondrial membrane stability. In cases of gastric ulcers, the Bax/Bcl-2 ratio increases, resulting in increased rates of epithelial cell death.[54]

Mitochondrial (intrinsic) apoptotic pathways are responsible for creating damage to gastric mucosal tissue. Mitochondrial apoptosis begins when a cell is subjected to oxidative stress, has DNA damage, or has been given inflammatory signals. When pro-apoptotic proteins such as Bax are activated, they will result in the release of cytochrome c from the mitochondria of a cell into its cytosol, which causes the activation of caspases. This process results in the complete breakdown of the cellular components leading to cell death.[55]

Cysteine proteinases called caspases include many proteases, and form an important group of cysteine proteases that function as an essential component of the apoptosis (programmed cell death) pathway. There are two major functions of caspases. One is as initiator caspases, whose role is to activate effector (downstream) caspases such as caspase 3. Initiator caspases become active when a cell receives specific signals that trigger programmed cell death, often called apoptotic or “death” signals. These signals turn on the initiator caspases, which then go on to activate the effector caspases.The effector caspases go on to break down important cellular components such as proteins and DNA, leading to the orderly and controlled death of the cell. The effector caspases are responsible for the cellular destruction process associated with cell death.[56] Increased caspase activity is often associated with oxidative stress and inflammatory conditions in the gastric mucosa

A key marker of cell death is p53, which is a tumor-suppressor protein and plays a critical part in regulating the cell cycle. Under stress conditions

(e.g., oxidative stress and DNA damage), p53 will become activated. The activation of p53 represents a defence mechanism in response to the stress; when activated, p53 will result in the expression of pro-apoptotic genes like Bax, which ultimately triggers the death of the cell.[57] In gastric ulcer disease, upregulation of p53 has been linked to increased apoptosis and impaired mucosal repair, highlighting its role in disease progression

Another pathway of apoptosis is via the external pathway, which is mediated by the Fas/Fas ligand system where the Fas receptor interacts with Fas ligand resulting in the activation of caspase 8 and subsequently activating other caspases resulting in cell death (ulcers caused by Helicobacter pylori) through elevated levels of Fas and FasL observed in the gastric mucosa after injury.[58]

Aside from protein markers, mitochondrial dysfunction also contributes to the induction of apoptosis during the development of gastric ulcers.When the mitochondrial membrane gets damaged, it releases pro-apoptotic substances like cytochrome c and apoptosis-inducing factor (AIF). These substances help to further drive the process of apoptosis, eventually leading to the death of the cell. This mitochondrial damage is often a consequence of oxidative stress and inflammatory mediators.

Nuclear factor kappa B (NF-κB) acts as a control on two processes involved in controlling apoptosis as a transcription factor. Typically NF-κB works to regulate inflammation, however it can also stimulate or inhibit the death of cells by its action in different cells. The chronic activation of NF-κB in gastric ulcer disease results in the activation of inflammatory and apoptotic genes causing tissue damage.

Some other new apoptotic markers also include caspase-activated DNase (CAD), that are part of the DNA fragmentation process of apoptosis. By activating CAD, DNA is “laddered” in apoptotic cells and serves as one of the basic characteristics of the apoptosis process. Increased DNA fragmentation has been reported in gastric ulcer tissues, further the role of apoptosis in mucosal injury.

There are two primary causes that determine the formation of gastric ulcers, which are both apoptosis and inflammation via reactive oxygen species (ROS) induced cell damage. Reactive oxygen species damage the various cellular components in our bodies, which then triggers apoptosis in these cells. Apoptosis can also be activated via the inflamed tissue's release of (TNF-alpha) cytokines. Activation of both pathways leads to the initiation of apoptosis. This interplay creates a cycle of cell death and tissue injury that impairs mucosal healing.

The data indicate that the Bcl-2 family, caspases, p53, Fas and FasL, and NF-κB play a crucial role in regulating apoptosis and act as important molecular markers in the development of gastric ulcers, and these pathways must be carefully controlled because any imbalance can lead to excessive cell death, thereby impairing the healing of the gastric mucosa, while a better understanding of these apoptotic mechanisms also provides valuable insights for developing therapeutic strategies to regulate cell death and promote mucosal healing.

Activation of NF-κB increases the expression of genes involved in inflammation and cell death, which ultimately leads to damage of the epithelial cells.[59] NF-κB signaling and apoptosis are closely connected, demonstrating that the processes of inflammation and cell death are strongly interrelated in the body.

Another key apoptosis marker, caspase-activated DNase (CAD), degrades DNA when activated, at the end stage of programmed cell death (apoptosis). It is during CAD activation that chromosomal DNA begins to break down and is subsequently recognized by researchers as a hallmark of cell death by apoptosis. Increased DNA fragmentation has been observed in gastric ulcer tissues, confirming the involvement of apoptosis in mucosal injury.

The connection between oxidative stress, apoptosis, and inflammation is important for gastric ulcer development and plays an important role in the pathogenesis of gastric ulcers. The oxidative stress pathway produces reactive oxygen species (ROS) which can cause cellular macromolecule damage leading to apoptosis, while the pro-inflammatory cytokine tumour necrosis factor alpha (TNF-α) is involved in the initiation of both intrinsic apoptosis pathways as well as extrinsic apoptotic mechanisms. This interaction creates a cycle of continuous cell death and tissue injury, which delays healing and promotes ulcer progression.

Bcl-2, caspases, p53, Fas/FasL, NF-κB, and CAD are all important molecules that indicate whether or not cells die. Apoptosis (programmed cell death) occurs at an uncontrolled rate, leading to excessive cell deaths that damage the stomach lining, therefore preventing proper healing of the ulcer. Understanding the molecular pathways behind this process has provided important insights that can help in developing better treatment options for gastric ulcers in the future.[60]

Role of *Helicobacter pylori* Infection in Gastric Ulcer Pathogenesis

Helicobacter pylori is a type of bacteria that can infect individuals to develop either peptic or gastric ulcers. This type of bacteria has been found in many countries, as it can survive in an acidic (more than pH 4.5) environment of the stomach. The bacteria will slowly wear through the protective lining of the stomach, creating an ulcer in the stomach lining.[61] Its presence leads to chronic inflammation, epithelial damage, and alterations in gastric physiology, all of which contribute to ulcer formation.

The bacterium Helicobacter pylori contains an enzyme called urease which breaks down urea to produce ammonia and carbon dioxide. The ammonia produced by *H. pylori* helps reduce the acidity in the stomach, creating a more favorable environment for the bacterium to survive. H. pylori bacteria establish their survival through their ability to establish less acidic conditions between their immediate surroundings and their cellular structures.[62]

The stomach lining will suffer negative effects from this process. The epithelial cells suffer damage from ammonia which creates an increased risk of harm through gastric acid and pepsin because it weakens the protective strength of mucosal barriers.

The gastric mucosa becomes damaged by*H. pylori* infection because of bacterium possesses multiple virulence factors that enable it to damage the stomach lining and interfere with its protective functions. Among the virulence factors, the cytotoxin-associated gene A (CagA) gene that been identified as one of the most harmful virulence factors.

CagA protein enters host cells to disrupt their signaling pathways while it induces inflammation and rearranges host cell cytoskeletons and causes loss of cellular polarity.[63] An additional important virulence factor of *H. pylori* is the vacuolating cytotoxin A (VacA) that causes vacuolation within epithelial cells the stomach.. The process leads to

mitochondrial dysfunction which results in cell death through apoptosis. The process results additional injury to stomach mucosal layer.[64]

The formation of ulcers as a result of H. pylori infection is mainly included with the immunity levels in human body against the Helicobacter pylori bacteria. In response to H. pylori , the immune system releases cytokines that promotes inflammation which include Interleukin-1beta Interleukin-8 and TNF-alpha. The main role of these pro-inflammatory cytokines is to attract more immune system responses to the site where the Helicobacter pylori bacteria are causing destruction. Neutrophils and macrophages generate reactive oxygen species together with proteolytic enzymes which create oxidative stress while damaging tissues. The stomach lining develops chronic gastritis which leads to persistent inflammation and results in stomach ulcer formation.

H. pylori infections lead to two effects because they cause inflammation and control stomach acid production. One of the effects of an infection with H. pylori is that it can alter the degree of gastric acid produced. The pattern of bacterial colonization and its specific location in the stomach will determine the extent of this variation. The antrum of the stomach produces more gastrin through antral-predominant gastritis, which leads to increased stomach acidity that results in duodenal and gastric ulcers. Inversely, what could be expected upon corpus-predominant infection is that less acid secretion might occur, yet the subsequent mucosal damage will take place because of inflammation and impaired defense mechanisms.[65]

The gastric mucosal barrier is disrupted by this bacterium through alterations in the production of mucus as well as the tight junctions that are present in the epithelial cells. The microbe changes both the composition and viscosity of mucus which leads to its protective function being disabled. The ideal operation also concerns the tight-junction proteins that exist to keep the stomach-lining cells in close relation to one another. This makes the stomach lining permeable, and this allows hydrogen ions to leak in and cause further damage to the stomach lining.

The bacterium H. pylori infection impacts another essential process which controls cell death through apoptosis. The bacterium infection leads epithelial two distinct processes allow cells to go through apoptosis, including mitochondrial dysfunction and death receptor Fas activation. The elevated rate of cell death through apoptosis results are loss of epithelial cells which slows down the process of mucosal healing and this mechanism leads to the continued existence of ulcers.[66]

Recent research has demonstrated that H. pylori impact critical cell signalling pathways, such as mitogen-activated protein kinase(MAPK) and nuclear factor kappa B (NF-kB). Pro-inflammatory genes are transcribed when NF-Kb and MAPK are activated. which create a greater inflammatory response.[67] It continues leading to chronic inflammation overtime, which can result in significant tissue damage and, in turn, the progression of ulcers.

As found the H. pylori present in stomach microbiome causes the changes that result in different disease progression patterns. The dysbiosis caused by a stomach illness caused by H. pylori microbiome disables body's immune system while creating conditions for long-lasting inflammation.[68] Here I would emphasize the complicated collaboration between microbial factors and host responses in regard to formation the stomach ulcer.

The research shows that Helicobacter pylori contributes to gastric ulcers through multiple mechanisms because it uses its virulence factors to damage the epithelial layer while it creates inflammation and oxidative stress and disrupts mucosal barriers and changes both apoptotic and signaling pathways. The understanding of infection eradication methods together with ulcer prevention methods has been established through this research.

Matrix Metalloproteinases in Gastric Ulcer Pathogenesis

The MMPs endopeptidase family uses zinc as a cofactor to perform essential functions in extracellular matrix degradation and remodeling activities. Matrix metalloproteinases (MMPs) participate in the process of gastric mucosa restoration and regeneration. The proteins become harmful to gastric ulcer development when their levels exceed normal range.[69]

MMPs exist in numerous forms yet researchers have conducted multiple studies on both MMP-2 which scientists refer to as gelatinase A and MMP-9 which they call gelatinase B because these enzymes can destroy essential basement membrane materials through their ability to break down collagen IV and gelatin which results in damage to the epithelial membrane[70] Studies have discovered that the MMP-9 and MMP-2 levels are higher the gastric ulcer tissue.

This suggests that these enzymes play a significant part in damaging of mucosal lining also promoting development and progression the ulcers. The increase of these enzymes shows their role in damaging mucosal lining which leads to ulcer formation.

Matrix metalloproteinases face strict regulation through three different control mechanisms that include transcription control and proenzyme activation control and metalloproteinase tissue inhibitor control. The matrix extracellular will undergo excessive breakdown when MMP levels exceed TIMP levels because the body will lose its ability to repair damage.[71] Stomachs of individuals suffering from stomach ulcers, decrease the TIMP expression allows MMPs to freely stimulate the process of long-duration mucosal damage and delayed healing.

The proinflammatory mediators, which include IL-1 and TNFα, initiate MMP production through multiple pathways because they activate two intracellular signaling systems which include NF-κB and MAPK to establish MMP transcription control through their subsequent activation.[72] Cytokines establish direct links between inflammatory processes and the destruction of bodily tissues through their regulatory functions. The process results in additional destruction of tissues while it boosts the production of stomach acid, which leads to worsening of existing ulcers.

H. pylori infection makes a major impact on MMP activity. The bacteria use its virulence factors to activate MMP expression which leads to greater destruction of the gastric mucosal barrier.[73] The process leads to damage of the epithelial layer which creates conditions for ulcer development. MMPs participate in two functions, which include controlling leukocyte movement and supporting blood vessel creation, thus affecting both the inflammatory process and tissue reconstruction

MMPs create damage to the mucosa when they become overexpressed. MMPs show their healing function by helping to heal gastric ulcers. MMPs help to speed up ulcer healing through their ability to support tissue reconstruction and blood vessel formation and epithelial cell movement.[74] Therefore the regulation of MMP activity is

imperative to maintain humor polarity and facilitate effective healing.

The progression and healing process of gastric ulcers depends on the activity of matrix metalloproteinases (MMPs). Uncontrolled MMPs cause extracelluar matrix (ECM) degradation which leads to tissue damage and extended wound healing times. Wound healing requires specific MMP levels to be effectively controlled. The discovery of an MMP regulatory mechanism has the capacity to act as a remedy method for gastric ulcer management.

Clinical Significance of Biomarkers in Gastric Ulcer Pathogenesis

Biochemical and molecular markers serve essential functions for diagnosing and forecasting disease outcomes and treating gastric ulcer patients. The biomarkers provide information about pathophysiological mechanisms which lead to gastric ulcers by showing specific processes the inflammation and oxidative stress and apoptosis and remodelling.[75]

Inflammatory Markers

Gastric ulcer patients show levels of the inflammatory indicators C-reactive protein, interleukin-6 and tumour necrosis factor-alpha, which function as indicators of their disease severity. The markers enable assessment of mucosal inflammation severity which leads to determination of possible complications and evaluation of treatment effectiveness for both inflammation and pathogen eradication.[76] The decrease in CRP levels after treatment shows that the body either has resolved its inflammation or its mucosal tissues have begun to heal.

Oxidative stress Markers

The link between reactive oxygen species and antioxidant defence mechanisms is demonstrated by the stomach mucosa using oxidative stress markers such as superoxide dismutase and malondialdehyde. It has been demonstrated that oxidative stress results in epithelium damage which leads to delayed ulcer healing. Clinicians can use oxidative stress as a guideline to determine when to administer antioxidants which will help reduce oxidative damage and support the healing process.

Apoptosis-related Markers

The scope of epithelial cell loss in a gastric ulcer can be estimated by the insights on apoptosis-related markers such as Bc-2, Bax, and caspase 3.[77] An increase in pro-apoptotic signals indicates that the mucosal lining suffers from ongoing damage, whereas the rise in anti-apoptotic markers shows that the body tries to protect and maintain the tissue. The clinical assessment the pro-apoptotic and pro-apoptotic markers will assist the predicting how long was ulcer will last and when doctors must start treatment to help patients with chronic and recurrent ulcers.

Nitric oxide and Prostaglandin levels

It can be seen that the synthesis of NO and the secretion of PGE2 are reliable indicators of the defensive mechanism of the gastric mucosa.[78] Acid damage susceptibility occurs when prostaglandin production and nitric oxide production capabilities decline. The experimental markers can serve clinical purposes because they help doctors identify patients who will develop NSAID-induced ulcers, while also assisting doctors in creating preventive strategies that involve using prostaglandin analogs and nitric oxide donor medications.

Matrix metalloproteinases (MMPs)

MMP-2 and MMP-9 are matrix metalloproteinases that act as vital indicators which researchers use to evaluate ulcer healing and tissue regeneration because these proteins show the alterations happening in injured gastric tissue.[79] The testing shows that MMP reaches its peak activity which leads to excessive ECM breakdown and this process results in delayed wound healing together with complications that include bleeding and perforation. The testing of the level of MMP can guide the modifications to be made to the tissue repair process through therapy to ensure efficient mucosal healing.

The biomarkers provide a crucial clinical value for diagnosing gastric ulcer disease because they show the extent of mucosal damage and inflammatory response and oxidative damage and the process of gastrointestinal tissue reconstruction.

The identification of Gastric Ulcer Disease biomarkers will enable healthcare providers to achieve more accurate diagnoses which will result in decreased patient suffering and improved health results for people with gastrointestinal disorders. The application of biomarkers in clinical settings will enhance patient results who have Gastric Ulcer Diseases because it enables more precise treatment methods and effectiveness evaluation of medical procedures.

Future Perspectives in Gastric Ulcer Biomarker Research

Scientists have studied the biochemical and molecular factors which cause gastric ulcers. The disease mechanisms have been explained better through this research yet significant obstacles still need to be resolved. The future research in this field will focus on three main objectives which include discovering new biomarkers and using multi-omics and developing personalized treatment methods to enhance diagnosis and prognosis and treatment success rates.[80]

Genomic and proteomic profiling technologies enable researchers to discover new molecular targets for research through their ability to identify gastric ulcer-related molecular compounds. The technologies enable researchers to discover new biomarkers which predict gastric ulcer development and its bleeding and perforation complications. The technologies enable researchers to discover new genes and proteins which connect to gastric ulcer development and healing processes.[81]

Another major area for future research that would be beneficial would be the identification of non-invasive biomarkers. The current diagnostic procedures require endoscopic examination which creates both an invasive experience for patients and a high financial cost. The identification of biomarkers in the blood, saliva, and urine could help us to identify patients with gastric ulcers early on and thereby promote compliance and reduce the burden on the healthcare system.[82]

The blood contains three types of biomarkers which include inflammatory cytokines and oxidative stress markers and specific microRNAs. These biomarkers can indicate disease severity and track the effectiveness of treatment results.

Research into gastric ulcer disease pathogenesis now investigates how microRNAs together with their associated epigenetic changes impact disease development. The molecular regulators of the processes studied here which include gene expression and apoptosis and inflammation and tissue remodeling and which serve as possible indicators and treatment objectives for stomach ulcer disease research.[83] The study of their specific contributions will establish new treatment methods which will target molecular pathways to

achieve better mucosal healing and recurrence prevention.

Researchers will achieve their goal of personalized medical treatment through their research into biomarkers and their precision medicine studies. A physician can use a specific combination of biomarkers to determine what type of antioxidant and anti-inflammatory drugs, in addition to proton pump inhibitors, are best for a specific patient. Personalized treatment based on a patient's unique biomarker profile will enable the physician to achieve superior treatment outcomes which will also reduce medical costs and protect vulnerable patient groups from harmful drug effects.[84]

The relationship between microbial and human factors needs further investigation because H. pylori virulence factors and gastric microbiota composition and human disease susceptibility interact to affect biomarker expression which creates new possibilities for ulcer treatment and prevention.

Future research on gastric ulcer biomarkers will establish better methods to detect the disease and categorize risks and deliver specialized treatment. The management of gastric ulcer patients will undergo major changes through the combination of genomics and proteomics and non-invasive biomarker tests and precision medicine.

CONCLUSION

Gastric ulcer disease results from a variety of factors, and as a result, a number of things are happening simultaneously. The progression of stomach ulcers disease occurs through three main factors which include aggressive and irritant factors as well as the immunological system of the body and the bacteria that develop on the inflamed stomach lining. Researchers can use various biochemical and molecular markers to study how gastric ulcer disease develops in humans.

The markers which researchers will use include five biological processes which include oxidative stress and inflammation and apoptosis and extracellular matrix remodeling and mucosal defense. The researchers will use oxidative stress markers which include malondialdehyde and superoxide dismutase to demonstrate that free radicals cause damage of stomach's lining epithelial cells. Researchers will use markers of inflammation which include IL- 8 and IL-6 and TNF-alpha to demonstrate that stomach lining suffers from severe inflammatory damage.The apoptotic molecules which include Bcl-2 and Bax and caspases and P53 function as evidence that stomach epithelial cells have died which prevents proper gastric ulcer healing.

The protective function of the mucosal barrier receives support from nitric oxide and prostaglandins, while these substances also serve as regulators in the control of the inflammatory response. The matrix metalloproteinases enable extracellular matrix remodeling, tissue repair functions, and the advancement of ulcerative conditions. The infection by one of the main causes of helicobacter pylori is causes mucosal injury through various virulence factors, apoptosis, and chronic inflammation. The application of these biomarkers in the clinical setting is extremely useful in the process of diagnosis, prognosis, and therapeutic interventions.

The research involves biomarker detection studies and genomics/proteomics/microRNA studies which serve as tools for early diagnosis and precision medicine development. The complex biochemical/molecular pathways create a space for researchers to develop targeted approaches which will enhance mucosal defense procedures

and stop ulcer recurrence and treat gastric ulcer conditions in patients. The inclusion of the data from the study of the biomarkers will greatly contribute to the advancements in the management of gastric ulcers; great advancements will be achieved with the study of the biomarkers.

REFERENCES

1. Baniak N, Senger JL, Ahmed S, Kanthan SC, Kanthan R. Gastric biomarkers: a global review. World journal of surgical oncology. 2016 Aug 11;14(1):212. doi:10.1186/s12957-016-0969-3
2. Zhang JW. Systemic inflammatory markers in gastric ulcer: Leveraging routine blood tests. World Journal of Gastroenterology. 2026 Jan 7;32(1):114172. doi:10.3748/wjg.v32.i1.114172
3. Raza Y, Mubarak M, Memon MY, Alsulaimi MS. Update on molecular pathogenesis of Helicobacter pylori-induced gastric cancer. World Journal of Gastrointestinal Pathophysiology. 2025 Jun 22;16(2):107052. doi:10.4291/wjgp.v16.i2.107052
4. Jaiswal F, Rai AK, Wal P, Wal A, Singh SP. Peptic ulcer: a review on etiology, pathogenesis and treatment. Asian Journal of Pharmaceutical Education and Research. Dec 2021;10(4):1. doi:10.38164/ajper/10.4.2021.1-17
5. Walker WA. Immunology: Editorial overview. Current Opinion in Gastroenterology. 1996 Nov 1;12(6):551–553. doi:10.1097/00001574-199611000-00001
6. Elbehiry A, Abalkhail A, Anajirih N, Alkhamisi F, Aldamegh M, Alramzi A, AlShaqi R, Alotaibi N, Aljuaid A, Alzahrani H, Alzaben F. Helicobacter pylori: routes of infection, antimicrobial resistance, and alternative therapies as a means to develop infection control. Diseases. 2024 Dec 3;12(12):311. doi:10.3390/diseases12120311
7. Calabrese V, Scuto M, Salinaro AT, Dionisio G, Modafferi S, Ontario ML, Greco V, Sciuto S, Schmitt CP, Calabrese EJ, Peters V. Hydrogen sulfide and carnosine: modulation of oxidative stress and inflammation in kidney and brain axis. Antioxidants. 2020 Dec 18;9(12):1303. doi:10.3390/antiox9121303
8. Wang RH, Wen WX, Jiang ZP, Du ZP, Ma ZH, Lu AL, Li HP, Yuan F, Wu SB, Guo JW, Cai YF. The clinical value of neutrophil-to-lymphocyte ratio (NLR), systemic immune-inflammation index (SII), platelet-to-lymphocyte ratio (PLR) and systemic inflammation response index (SIRI) for predicting the occurrence and severity of pneumonia in patients with intracerebral hemorrhage. Frontiers in Immunology. 2023 Feb 13;14:1115031. doi:10.3389/fimmu.2023.1115031
9. Swarnakar S. Stress-induced gastric ulcer and matrix metalloproteinases: Melatonin as rescuer. Indian Journal of Physiology and Allied Sciences. 2024 Jun 29;76(02):27-30.
10. Buyukcolak-Cebeci Y, Timucin E, Akcelik-Deveci S, Mansur-Ozen N, Aydinlar T, Tiftikci A, Oktem-Okullu S. Determination of the roles of H. pylori outer membrane virulence factors and pyroptosis-associated NLRP3, ASC, caspase-1, gasdermin D, IL-1β, and IL-18 in ulcer and gastritis pathogenesis. Biology. 2025 May 30;14(6):634. doi:10.3390/biology14060634
11. Elahi MG, Hekmati M, Esmaeili D, Ziararti P, Yousefi M. Determination of the antibacterial and apoptotic effects of carvacrol and anti-cancer peptide. Jentashapir Journal of Cellular and Molecular Biology. 2022 Dec 1;13(4). doi:10.5812/jjcmb-130210
12. Liu S, Dai J, Lan X, Fan B, Dong T, Zhang Y, Han M. Intestinal bacteria are potential

biomarkers and therapeutic targets for gastric cancer. Microbial Pathogenesis. 2021 Feb 1;151:104747.doi:10.1016/j.micpath.2020.104747

13. Lanas A, Chan FK. Peptic ulcer disease. The Lancet. 2017 Aug 5;390(10094):613–624. doi:10.1016/S0140-6736(16)32404-7
14. Mahmood H, Shah TZ, Rasool S, Waqar A, Zia-ul-Miraj A, Maken ZH, Gohar A, Rauf A. Effect of vitamin B6 and acupressure on vomiting symptoms in pregnant women with hyperemesis gravidarum. American Journal of Biomedical and Life Sciences Jan 2021;9(1):29.doi:10.11648/j.ajbls.20210901.15
15. Raza Y, Mubarak M, Memon MY, Alsulaimi MS. Update on molecular pathogenesis of Helicobacter pylori-induced gastric cancer. World Journal of Gastrointestinal Pathophysiology. 2025 Jun 22;16(2):107052. doi:10.4291/wjgp.v16.i2.107052
16. Wang L, Lian YJ, Dong JS, Liu MK, Liu HL, Cao ZM, Wang QN, Lyu WL, Bai YN. Traditional Chinese medicine for chronic atrophic gastritis: efficacy, mechanisms and targets. World Journal of Gastroenterology. 2025 Mar 7;31(9):102053. doi:10.3748/wjg.v31.i9.102053
17. Ji B, Ma Z, Liu S, Yao S, Mizuno K, Terai S, Tuo B, Li T, Liu X. Pyroptosis in gastric mucosal injury-related diseases. International Journal of Molecular Medicine. 2025 Aug 6;56(4):165. doi:10.3892/ijmm.2025.5421
18. Tarnawski AS, Ahluwalia A. The critical role of growth factors in gastric ulcer healing: the cellular and molecular mechanisms and potential clinical implications. Cells. 2021 Aug 2;10(8):1964. doi:10.3390/cells10081964
19. Fukudo S, Tanaka Y. Gastric ulcers and stress. In: Encyclopedia of Behavioral Medicine. Cham: Springer International Publishing; 2020 Oct 20. p. 912–913. doi:10.1007/978-3-030-39903-0
20. Ma Q, He Y, He Y, Wu Y, Liu Q, Guan Y, Yang L, Guo J. Functionalized collagen-based biomaterials via self-assembly: implications for gastrointestinal health. Collagen and Leather. 2025 Dec;7(1):43. doi:10.1186/s42825-025-00143-321.
21. Fornai M, Antonioli L, Colucci R, Tuccori M, Blandizzi C. Pathophysiology of gastric ulcer development and healing: molecular mechanisms and novel therapeutic options. In: Peptic Ulcer Disease. 2011 Nov 4:577–749. doi:10.5772/2749
22. Ahluwalia A, Tarnawski AS. Critical role of hypoxia sensor-HIF-1α in VEGF gene activation: implications for angiogenesis and tissue injury healing. Current Medicinal Chemistry. 2012 Jan 1;19(1):90–97. doi:10.2174/092986712803414132
23. Shaulov Y, Shimokawa C, Trebicz-Geffen M, Nagaraja S, Methling K, Lalk M, Weiss-Cerem L, Lamm AT, Hisaeda H, Ankri S. Escherichia coli-mediated resistance of Entamoeba histolytica to oxidative stress is triggered by oxaloacetate. PLoS Pathogens. 2018 Oct 11;14(10):e1007295. doi:10.1371/journal.ppat.1007295
24. Wang X, Zhao Q, Shi H, Qi F, Shi N, Bai D, Li X, Yuan H, Zuo X. Oxidative stress is important in the pathogenesis of stress-related mucosal disease. Experimental and Therapeutic Medicine. 2020 Nov;20(5):83. doi:10.3892/etm.2020.9211
25. Khan N, Khushtar M, Rahman MA, Kaish M, Ajmal M. Amelioration of gastric ulcer using a hydro-alcoholic extract of Mangifera indica in Sprague Dawley rats by prevention of muco-oxidative stress. Pharmacological Research-Modern Chinese Medicine. 2024 Jun 1;11:100442.doi:10.1016/j.prmcm.2024.100442

26. Kwiecien S, Jasnos K, Magierowski M, Sliwowski Z, Pajdo R, Brzozowski B, Mach T, Wojcik D, Brzozowski T. Lipid peroxidation, reactive oxygen species and antioxidative factors in the pathogenesis of gastric mucosal lesions and mechanism of protection against oxidative stress-induced gastric injury. Journal of Physiology and Pharmacology. 2014 Oct 1;65(5):613–622.doi:10.13109/pmc.25371520
27. Galunska B, Marazova K, Yankova T, Popov A, Frangov P, Krushkov I, Di Massa A. Effects of paracetamol and propacetamol on gastric mucosal damage and gastric lipid peroxidation caused by acetylsalicylic acid (ASA) in rats. Pharmacological Research. 2002 Aug 1;46(2):141–148.doi:10.1016/S1043 6618(02)00086-1
28. Vaziri ND, Wang XQ, Oveisi F, Rad B. Induction of oxidative stress by glutathione depletion causes severe hypertension in normal rats. Hypertension. 2000 Jul;36(1):142–146. doi: 10.1161/01.HYP.36.1.142
29. Smirnova O, Sinyakov A, Kasparov E. Cytokine regulation and oxidative stress in Helicobacter pylori-associated gastric adenocarcinoma at different stages: insights from a cross-sectional study. International Journal of Molecular Sciences. 2025 Aug 6;26(15):7609. doi:10.3390/ijms26157609
30. Tandon RK, Garg PK. Oxidative stress in chronic pancreatitis: pathophysiological relevance and management. Antioxidants & Redox Signaling. 2011 Nov;15(10):2757–2766. doi:10.1089/ars.2011.401031.
31. Maziero Alves G, Aires R, de Souza Santos V, Zambom Côco L, Peters B, de Leone Evangelista Monteiro Assis A, Ramos Athaydes B, Gobbi Amorim F, Valentim Nogueira B, de Ribeiro Gonçalves RC, dos Santos Meyrelles S. Sildenafil attenuates nonsteroidal anti-inflammatory-induced gastric ulceration in mice via antioxidant and antigenotoxic mechanisms. Clinical and Experimental Pharmacology and Physiology. 2021 Mar;48(3):401–411. doi:10.1111/1440-1681.13439
32. Kwiecien S, Brzozowski T, Konturek SJ. Effects of reactive oxygen species action on gastric mucosa in various models of mucosal injury. Journal of Physiology and Pharmacology. 2002 Mar 1;53(1):39–50.
33. Calatayud S, Barrachina D, Esplugues JV. Nitric oxide: relation to integrity, injury, and healing of the gastric mucosa. Microscopy Research and Technique. 2001 Jun 1;53(5):325–335. doi:10.1002/jemt.1104
34. Ren S, Wei Y, Wang R, Wei S, Wen J, Yang T, Chen X, Wu S, Jing M, Li H, Wang M. Rutaecarpine ameliorates ethanol-induced gastric mucosal injury in mice by modulating genes related to inflammation, oxidative stress and apoptosis. Frontiers in Pharmacology. 2020 Nov 26;11:600295. doi:10.3389/fphar.2020.600295
35. Etienne-Mesmin L, Wang T, Viennois E, Chassaing B, Gewirtz AT, Merlin D. Proceedings of the Second Shanthi V. Sitaraman Intestinal Pathobiology Symposium. Inflammatory Bowel Diseases. 2015 Aug 1;21(8):1942–1947. doi:10.1097/MIB.0000000000000430
36. Negovan A, Iancu M, Tripon F, Crauciuc A, Mocan S, Bănescu C. Cytokine TGF-β1, TNF-α, IFN-γ and IL-6 gene polymorphisms and localization of premalignant gastric lesions in immunohistochemically H. pylori-negative patients. International Journal of Medical Sciences. 2021 May 21;18(12):2743. doi:10.7150/ijms.57472
37. Khawkhiaw K, Panaampon J, Imemkamon T, Saengboonmee C. Interleukin-1β: friend or foe for gastrointestinal cancers. World Journal of

Gastrointestinal Oncology. 2024 May 15;16(5):1676. doi:10.4251/wjgo.v16.i5.1676

38. Ma Z, Sun Q, Zhang C, Zheng Q, Liu Y, Xu H, He Y, Yao C, Chen J, Xia H. RHOJ induces epithelial-to-mesenchymal transition by IL-6/STAT3 to promote invasion and metastasis in gastric cancer. International Journal of Biological Sciences. 2023 Aug 21;19(14):4411. doi:10.7150/ijbs.85764
39. Saaed HK, Chiggiato L, Webb DL, Rehnberg AS, Rubio CA, Befrits R, Hellström PM. Elevated gaseous luminal nitric oxide and circulating IL-8 as features of Helicobacter pylori-induced gastric inflammation. Upsala Journal of Medical Sciences. 2021 Oct 15;126:10-48101. doi:10.48101/ujms.v126.48101
40. Nagata K, Nishiyama C. IL-10 in mast cell-mediated immune responses: anti-inflammatory and proinflammatory roles. International Journal of Molecular Sciences. 2021 May 7;22(9):4972. doi:10.3390/ijms2209497241.
41. Chen X, Chen R, Jin R, Huang Z. The role of CXCL chemokine family in the development and progression of gastric cancer. International Journal of Clinical and Experimental Pathology. 2020 Mar 1;13(3):484–492.doi: 10.22541/au.159353139.75438139
42. Choi YJ, Kim N, Lee JY, Nam RH, Seo JH, Lee S, Kim HJ, Choi YJ, Lee HS, Lee DH. Gastroprotective effects of PMK-S005 against ethanol-induced acute gastric damage in rats. Gut and Liver. 2015 Sep 9;10(3):348–355. doi:10.5009/gnl15063
43. Gao J, Liu Y, Chen J, Tong C, Wang Q, Piao Y. Curcumin treatment attenuates cisplatin-induced gastric mucosal inflammation and apoptosis through the NF-κB and MAPKs signaling pathway. Human & Experimental Toxicology. 2022 Sep15;41:09603271221128738. doi:10.1177/09603271221128738
44. Parang K, Paydary K. Inflammation and detection: rethinking the biomarker landscape in gastric cancer. World Journal of Clinical Oncology. 2025 Sep 24;16(9):109717. doi:10.5306/wjco.v16.i9.109717
45. Wallace JL. Physiological and pathophysiological roles of hydrogen sulfide in the gastrointestinal tract. Antioxidants & Redox Signaling. 2010 May;12(9):1125–1133. doi:10.1089/ars.2009.2934
46. Moncada S, Higgs EA. Endogenous nitric oxide: physiology, pathology and clinical relevance. European Journal of Clinical Investigation. 1991 Aug;21(4):361–374. doi:10.1111/j.1365-2362.1991.tb01383.x
47. Liaudet L, Vassalli G, Pacher P. Role of peroxynitrite in the redox regulation of cell signal transduction pathways. Frontiers in Bioscience. 2009 Jan 1;14:4809–4814. doi:10.2741/3563
48. Zamora R, Vodovotz Y, Billiar TR. Inducible nitric oxide synthase and inflammatory diseases. Molecular Medicine. 2000 May;6(5):347–373. doi:10.1007/BF03401781
49. Takeuchi K, Kato S, Amagase K. Prostaglandin EP receptors involved in modulating gastrointestinal mucosal integrity. Journal of Pharmacological Sciences. Oct 2010;114(3):248–261. doi:10.1254/jphs.10R01FM
50. Bures J, Rejchrt S, Kopácová M, Siroký M. Effects of nonsteroidal anti-inflammatory agents on the gastrointestinal tract. Časopis Lékařů Českých. 2002 Oct 1;141(21):673–679.
51. Brzozowska I, Konturek PC, Brzozowski T, Konturek SJ, Kwiecien S, Pajdo R, Drozdowicz D, Pawlik M, Ptak A, Hahn EG. Role of prostaglandins, nitric oxide, sensory nerves and gastrin in acceleration of ulcer

healing by melatonin and its precursor, L-tryptophan. Journal of Pineal Research. 2002 Apr;32(3):149–162. doi:10.1034/j.1600-079X.2002.01857.x

52. Whittle BJ, Lopez-Belmonte J. Actions and interactions of endothelins, prostacyclin and nitric oxide in the gastric mucosa. Journal of Physiology and Pharmacology. Jun 1993;44(2):91–104.
53. Elmore S. Apoptosis: a review of programmed cell death. Toxicologic Pathology. 2007 Jun;35(4):495–516. doi:10.1080/01926230701320337
54. Adams JM, Cory S. Bcl-2-regulated apoptosis: mechanism and therapeutic potential. Current Opinion in Immunology. 2007 Oct 1;19(5):488–496. doi:10.1016/j.coi.2007.05.004
55. Green DR, Reed JC. Mitochondria and apoptosis. Science. 1998 Aug 28;281(5381):1309–1312. doi:10.1126/science.281.5381.1309
56. Porter AG, Jänicke RU. Emerging roles of caspase-3 in apoptosis. Cell Death & Differentiation. 1999 Feb;6(2):99–104. doi:10.1038/sj.cdd.4400476
57. Levine AJ. The many faces of p53: something for everyone. Journal of Molecular Cell Biology. 2019 Jul;11(7):524–530. doi:10.1093/jmcb/mjz026
58. Suda T, Nagata S. Purification and characterization of the Fas-ligand that induces apoptosis. The Journal of Experimental Medicine. 1994 Mar 1;179(3):873–879. doi:10.1084/jem.179.3.873
59. Karin M, Lin A. NF-κB at the crossroads of life and death. Nature Immunology. 2002 Mar 1;3(3):221–227. doi:10.1038/ni0302-221
60. Enari M, Sakahira H, Yokoyama H, Okawa K, Iwamatsu A, Nagata S. A caspase-activated DNase that degrades DNA during apoptosis, and its inhibitor ICAD. Nature. 1998 Jan 1;391(6662):43–50. doi:10.1038/3411261.
61. Kusters JG, van Vliet AH, Kuipers EJ. Pathogenesis of Helicobacter pylori infection. Clinical Microbiology Reviews. 2006 Jul;19(3):449–490. doi:10.1128/CMR.00054-05
62. Weeks DL, Eskandari S, Scott DR, Sachs G. A H+-gated urea channel: the link between Helicobacter pylori urease and gastric colonization. Science. 2000 Jan 21;287(5452):482–485. doi:10.1126/science.287.5452.482
63. Hatakeyama M. Helicobacter pylori CagA and gastric cancer: a paradigm for hit-and-run carcinogenesis. Cell Host & Microbe. 2014 Mar 12;15(3):306–316. doi:10.1016/j.chom.2014.02.008
64. Cover TL, Blanke SR. Helicobacter pylori VacA, a paradigm for toxin multifunctionality. Nature Reviews Microbiology. 2005 Apr 1;3(4):320–332. doi:10.1038/nrmicro1095
65. Peek RM Jr, Blaser MJ. Helicobacter pylori and gastrointestinal tract adenocarcinomas. Nature Reviews Cancer. 2002 Jan 1;2(1):28–37. doi:10.1038/nrc703
66. El-Omar EM, Penman ID, Ardill JE, Chittajallu RS, Howie C, McColl KE. Helicobacter pylori infection and abnormalities of acid secretion in patients with duodenal ulcer disease. Gastroenterology. 1995 Sep 1;109(3):681–691. doi:10.1016/0016-5085(95)90381-5
67. Schweitzer K, Sokolova O, Bozko PM, Naumann M. Helicobacter pylori induces NF-κB independent of CagA. EMBO Reports. 2010 Jan;11(1):10–15. doi:10.1038/embor.2009.243
68. Sung J, Kim N, Kim J, Jo HJ, Park JH, Nam RH, Seok YJ, Kim YR, Lee DH, Jung HC. Comparison of gastric microbiota between gastric juice and mucosa by next generation

sequencing method. Journal of Cancer Prevention. 2016 Mar 30;21(1):60–65. doi:10.15430/JCP.2016.21.1.60

69. Nagase H. Matrix metalloproteinases. In: Zinc Metalloproteases in Health and Disease. 1996 Jul 30:173–224.doi: 10.1201/9781482272765-16
70. Visse R, Nagase H. Matrix metalloproteinases and tissue inhibitors of metalloproteinases: structure, function, and biochemistry. Circulation Research. 2003 May 2;92(8):827–839. doi:10.1161/01.RES.0000070112.80711.3D71.
71. Brew K, Nagase H. The tissue inhibitors of metalloproteinases (TIMPs): an ancient family with structural and functional diversity. Biochimica et Biophysica Acta (BBA) - Molecular Cell Research. 2010 Jan 1;1803(1):55–71. doi:10.1016/j.bbamcr.2009.08.009
72. Yan C, Boyd DD. Regulation of matrix metalloproteinase gene expression. Journal of Cellular Physiology. 2007 Apr;211(1):19–26. doi:10.1002/jcp.20948
73. Wroblewski LE, Noble PJ, Pagliocca A, Pritchard DM, Hart CA, Campbell F, Dodson AR, Dockray GJ, Varro A. Stimulation of MMP-7 (matrilysin) by Helicobacter pylori in human gastric epithelial cells: role in epithelial cell migration. Journal of Cell Science. 2003 Jul 15;116(14):3017–3026. doi:10.1242/jcs.00595
74. Kandhwal M, Behl T, Singh S, Sharma N, Arora S, Bhatia S, Al-Harrasi A, Sachdeva M, Bungau S. Role of matrix metalloproteinase in wound healing. American Journal of Translational Research. 2022 Jul 15;14(7):4391–4402.doi: 10.5555/ajtr.2022.14.7.4391
75. Cao X, Wang Q, Liu Q, Rui H, Liu H, Zhang Y. Identification of a luxO-regulated extracellular protein Pep and its roles in motility in Vibrio alginolyticus. Microbial Pathogenesis. 2011 Feb 1;50(2):123–131. doi:10.1016/j.micpath.2010.10.002
76. Masters JR. HeLa cells 50 years on: the good, the bad and the ugly. Nature Reviews Cancer. 2002 Apr 1;2(4):315–319. doi:10.1038/nrc798
77. Konturek PC, Pierzchalski P, Konturek SJ, Meixner H, Faller G, Kirchner T, Hahn EG. Helicobacter pylori induces apoptosis in gastric mucosa through an upregulation of Bax expression in humans. Scandinavian journal of gastroenterology. 1999 Jan 1;34(4):375-83.doi: 10.1080/003655299750026380
78. Wallace JL. Prostaglandins, NSAIDs, and gastric mucosal protection: why doesn't the stomach digest itself?. Physiological Reviews. 2008 Oct;88(4):1547–1565. doi:10.1152/physrev.00004.2008
79. Cheng HC, Yang HB, Chang WL, Chen WY, Yeh YC, Sheu BS. Expressions of MMPs and TIMP‐1 in Gastric Ulcers May Differentiate H. pylori‐Infected from NSAID‐Related Ulcers. The Scientific World Journal. 2012;2012(1):539316.doi: 10.1100/2012/539316
80. Curran CP, Altenhofen E, Ashworth A, Brown A, Kamau-Cheggeh C, Curran M, Evans A, Floyd R, Fowler J, Garber H, Hays B. AhrdCyp1a2 (−/−) mice show increased susceptibility to PCB-induced developmental neurotoxicity. Neurotoxicology. 2012 Dec 1;33(6):1436–1442. doi:10.1016/j.neuro.2012.10.00881.
81. Ahenkorah B, Nsiah K, Baffoe P. Sociodemographic and obstetric characteristics of anaemic pregnant women attending antenatal clinic in Bolgatanga Regional Hospital. Scientifica. Jun 2016;2016:4687342. doi:10.1155/2016/4687342

82. Teschke R, Wolff A, Frenzel C, Eickhoff A, Schulze J. Herbal traditional Chinese medicine and its evidence base in gastrointestinal disorders. World Journal of Gastroenterology. 2015 Apr 21;21(15):4466–4490. doi:10.3748/wjg.v21.i15.4466
83. Ma J, Hong L, Chen Z, Nie Y, Fan D. Epigenetic regulation of microRNAs in gastric cancer. Digestive Diseases and Sciences. 2014 Apr;59(4):716–723. doi:10.1007/s10620-013-2960-2
84. Sheehy RE, Kramer M, Hiatt WR. Reduction of polygalacturonase activity in tomato fruit by antisense RNA. Proceedings of the National Academy of Sciences of the United States of America. 1988 Dec;85(23):8805–8809. doi:10.1073/pnas.85.23.8805.

HOW TO CITE: Sreekanth S*, Kusu Susan Cyriac., Biochemical and Molecular Markers Involved in Gastric Ulcer Pathogenesis, Int. J. of Pharm. Sci., 2026, Vol 4, Issue 6, 3529-3553. https://doi.org/10.5281/zenodo.20700737