European Journal of Molecular & Clinical Medicine
ISSN 2515-8260 Volume 07, Issue 01, 2020

# ROLE OF DIETARY POLYPHENOLS IN THE MANAGEMENT OF PEPTIC ULCER

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**ABSTRACT:**

Peptic ulcer disease is a multifactorial and complex disease involving gastric and duodenal ulcers. Despite medical advances, the management of peptic ulcer and its complications remains a challenge. An accumulating body of evidence suggests that, among a broad reach of natural molecules, dietary polyphenols with multiple biological mechanisms of action play a pivotal part in the management of gastric and duodenal ulcers. The current review confirmed that dietary polyphenols possess protective and therapeutic potential in peptic ulcer mediated by: improving cytoprotection, re-epithelialization, neovascularization, and angiogenesis; up-regulating tissue growth factors and prostaglandins; down-regulating anti-angiogenic factors; enhancing endothelial nitric oxide synthase-derived NO; suppressing oxidative mucosal damage; amplifying antioxidant performance, antacid, and anti-secretory activity; increasing endogenous mucosal defensive agents; and blocking helicobacter pylori colonization associated gastric morphological changes and gastroduodenal inflammation and ulceration. In addition, anti-inflammatory activity due to down-regulation of proinflammatory cytokines and cellular and intercellular adhesion agents, suppressing leukocyte-endothelium interaction, inhibiting nuclear signaling pathways of inflammatory process, and modulating intracellular transduction and transcription pathways have key roles in the anti-ulcer action of dietary polyphenols.Polyphenols ubiquitously present in vegetables and fruits are progressively viewed as natural dietary ingredients vital for a balanced diet. Administration of a sufficient amount of dietary polyphenols in the human diet can result in perfect prevention and treatment of peptic ulcer. In conclusion, administration of a significant amount of dietary polyphenols in the human diet or as part of dietary supplementation along with conventional treatment can result in perfect security and treatment of peptic ulcer. Further well-designed preclinical and clinical tests are recommended in order to recognize higher levels of evidence for the confirmation of bioefficacy and safety of dietary polyphenols in the management of peptic ulcer
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**KEYWORDS:** Anti-inflammatory, H.pylori, Inflammatory cytokines, Natural medicine, NSAID, Peptic ulcer, Polyphenols,

## INTRODUCTION

Peptic ulcer unwellness may be a complex and complicated unwellness involving stomachic and small intestine ulcers(Malfertheiner, Chan and McColl, 2009). For several years, ulcer was thought-about one in every of the most reasons for activity duct surgery, attributable to its high prevalence of morbidity and mortality. ulcer unwellness affects a large vary of individuals worldwide, and is one in every of the foremost common diseases of the ordinal century(O'malley, 2003).Peptic ulcer results from a pathological condition within which the biological balance between defensive and offensive factors within the epithelial duct is disturbed. stomachic acid, pepsin, reactive free radicals and oxidants, leukotrienes, refluxed gall, and endothelins are among the most endogenous aggressive factors(Repetto and Llesuy, 2002). Additionally, stomachic secretion barrier, carbonate, tissue layer blood flow, surface active phospholipids, prostaglandins (PG), gas (NO), likewise as protein and non-enzymatic inhibitor performance are thought-about defensive factors(Cryer, 2001). the precise pathological process of organic process ulcers isn't clear, however various factors, together with consumption of non-steroidal anti-inflammatory drug medication (NSAIDs) and corticosteroids, nerve-racking style, alcohol consumption, Helicobacter pylori (H. pylori) infection, smoking, and case history ar thought-about as risk factors within the pathological process of organic process ulcer(Bandyopadhyay *et al.*, 2001).

### Oxidative damage

The polar role of antioxidants within the hindrance and healing of ulcers has been widely studied in varied investigations. Tissue harm is usually related to intense generation of free radicals like reactive gas species (ROS) that cause aerophilus stress and ulterior tissue layer injury. Likewise, aerophilous tissue layer harm contributes with polymer fragmentation, lowering cellular polymer content, and impairment of supermolecule expression that is mediated by the extraordinary generation of ROS(Ashwini and Anitha, 2017). These free radicals conjointly disturb the cellular inhibitor accelerator that acts as a very important cellular defense against aerophilus stress, that results in aggravated tissue harm throughout gastroduodenal ulceration. Leukocytes (particularly neutrophils) include a nicotinamide A dinucleotide phosphate (NADPH) enzyme, that has associate aerophilus action(Rajeshkumar, Agarwal, *et al.*, 2018); reduction of molecular gas to anion radical, one in every of the most style of ROS(Sen *et al.*, 2013). Free radicals initiate microvascular porousness, resulting in additional infiltration of plasma cells and macrophages to stomachic epithelium cells(Ashwini, Ezhilarasan and Anitha, 2017). Varied endogenous anti-oxidative agents like sulfhydryl (SH) non-protein compounds, protein antioxidants [including enzyme (SOD) and enzyme (CAT)], likewise as non-enzymatic proteins like glutathione (GSH) block biological production of ROS and ensuant tissue damage(Tandon *et al.*, 2004)

### Helicobacter pylori

Chronic infection of stomachic membrane with H. pylori is mostly related to stomachic lesions. H. pylori may be a current human microorganism with an associated incidence of ninetieth in some developing countries. H. pylori undergoes symptomless stomachic colonisation in just about seventieth of the population, with a 10%-20% status of developing into organic process ulcer(Lakshmi *et al.*, 2015).The pathological process and pattern of H.pylori -induced rubor is extremely related to the morbidity of tissue layer atrophy and duodenal/gastric ulcers. destruction of H. pylori from the stomachic membrane of infected patients is taken into account to be the simplest therapeutic approach for complete remission of H. pylori associated rubor and its ensuant ulcers(Wang, 2014).H. pylori infection stimulates overexpression of pro-inflammatory cytokines [e.g., lymphokine (IL)-1β, IL-6, growth mortification issue (TNF)-α, and IL-8] in stomachic animal tissue cells, that act as neutrophil-activating chemokines and cause white blood cell infiltration(Ezhilarasan *et al.*, 2017). It's attainable that H. pylori-associated IL-8 activation leads to worrisome tissue layer integrity thanks to generation of ROS, likewise because the activation of chemical process enzymes(Zaidi *et al.*, 2009). varied factors are concerned within the severity of H. pylori-associated unwellness, like age of acquisition, host

system, and microorganism strain(Sharma *et al.*, 2019). Strains of H. pylori that carry the Cag-PAI (Cag Pathogenicity Island) show a strenuous inflammatory and chemoattractant response than people who are Cag-negative(Ezhilarasan, Sokal and Najimi, 2018). This early and severe response of Cag-positive strains is mediated by activating protein-1, likewise as nuclear transcriptional factors(Crabtree *et al.*, 1995).

**Health benefits of polyphenol**

Polyphenols are one in every of the most important secondary plant metabolites ubiquitously given in fruits associated vegetables thought-about an integral part of the human diet(Perumalsamy *et al.*, 2018). Polyphenols are characterised by the presence of various numbers of phenolic resin rings, beside 2 or a lot of group substitutions. Polyphenols comprises a large sort of chemical structures supporting the substitutions of the essential chemical structure of polyphenols, chemical action, and also the degree of oxidation. Polyphenols are classified as flavonoids and non-flavonoids, supporting their chemical structure. Flavonoids are composed of 2 aromatic hydrocarbon rings connected by a linear three-carbon chain, that type associate aerated heterocycle(Lakshmi *et al.*, 2017). Flavonoid-type polyphenols ar divided into totally different subclasses per the oxidation number of the central pyran ring, together with anthocyanins, anthocyanidins, flavones, flavanols, catechins, isoflavones, flavanones, and flavonols. Non-flavonoids are stilbenes, phenolic resin acids, lignans, and hydroxycinnamic acids(Farzaei, Abdollahi and Rahimi, 2015). Their basic phenolic resin structure, called "aglycone", may be connected with totally different carbohydrates and organic acids to make "glycine" structures, likewise like varied polyphenols to make "polymers". phenolic resin compounds with pharmaceutical interest ar straightforward phenolic resin compounds like acid, ellagic acid, catechin, eugenol, vanillin, caffeic acid, ferulic acid, apigenin, quercetin, gingerol, kaempferol, myricetin, resveratrol, rutin, naringenin, and cyanidin(Antolovich *et al.*, 2000).Mounting proof suggests that polyphenols ar health promoting phytochemicals(Lakshmi *et al.*, 2017).an outsized range of human studies have shown that polyphenol intake is related to a reduced risk of assorted chronic illnesses, together with disorder, neurodegenerative disorders, diabetes, cancers, degenerative arthritis, and duct diseases. The biological activities of polyphenols vary thanks to varied parameters, like food process ways, metabolism, absorption, bioavailability, derived compounds, and bioefficacy(Farzaei *et al.*, 2014). At the cellular and molecular levels, a large vary of pharmacologic functions are confirmed for polyphenols, together with as associate inhibitor, anti-apoptotic, anti-carcinogenic, anti-aging, antiviral, anti-allergic, antiplatelet, anti-estrogenic, anticarcinogenic, anti-inflammatory drug, and anti-proliferative properties(Menon *et al.*, 2018). These therapeutic helpful effects of polyphenols ar related to molecular mechanisms of action on intercellular communication pathways; regulation of NFκB, mitogen-activated supermolecule kinases (MAPKs), living thing signal-regulated enzyme (ERK), c-Jun N-terminal enzyme (JNK), and signal transduction pathway interference [e.g., toll-like receptor four (TLR4)]. The inhibitor potential of polyphenols ar performed by their dissent on radical scavenging, breaking of radical chain reactions, peroxide reduction, and metal chelating properties, or indirectly by interacting with definite proteins of aerophilous stress communication pathways and by activating anti-oxidative enzymes like CAT and SOD(Cardona *et al.*, 2013).

**Dietary supplementation of polyphenols:**

There is ample evidence in the literature suggesting the beneficial role of a healthy diet in the prevention and remission of various diseases(Mehta *et al.*, 2019). One of the most sustainable approaches in order to protect against various chronic diseases and alleviate symptoms is removing patients from their habitual diet and providing them with natural dietary agents. As a disorder of the GI tract, pathological conditions in peptic ulcers could be alleviated by nutritional factors(Lakshmi *et al.*, 2017). Dietary consumption of a significant amount of "natural" protective supplements in early life leads to prevention or delayed peptic ulcer. Regarding the wide range of positive biological effects of polyphenols, as well as their crucial role in human health, incorporation of these dietary supplements in a balanced diet is necessary for the prevention and management of diseases. The average daily dietary intake of polyphenols in a balanced diet is estimated at nearly 1 g/d(Ezhilarasan, 2018)

**Polyphenols for the management of peptic ulcer:**

Allylpyrocatechol is a phenolic compound elicited from the leaves of Piper betel (*P. betel*) commonly grows in a tropical humid climate and the leaves are widely-used as a mouth freshener in South East Asia.(Gheena and Ezhilarasan, 2019) Allylpyrocatechol is an excellent antioxidant agent and also possesses anti-inflammatory, antibacterial, and anti-arthritic effects. Various investigations have confirmed the therapeutic potential of allylpyrocatechol for the management of peptic ulcer via different molecular mechanisms(Karthiga, Rajeshkumar and Annadurai, 2018). Yadav et al showed the significant protection of allylpyrocatechol against indomethacin-induced gastric ulcer in an animal model in comparison with that of standard drugs (misoprostol and omeprazole). In a histopathological assay, allylpyrocatechol demonstrated a protective effect on mucosa and submucosa. Indomethacin-induced gastric damage is mediated by a decrease in COX-1 expression, along with simultaneous elevation of COX-2 expression, which is reversed by allylpyrocatechol.(Rajeshkumar, Agarwal, *et al.*, 2018)Prostaglandins have a pivotal role in the prevention and treatment of peptic ulcers. They alleviate indomethacin-induced gastric mucosal damage and promote ulcer healing *via* the enhancement of bicarbonate and mucus secretion, as well as the acceleration of angiogenesis and mucosal blood flow(Rajeshkumar, Venkat Kumar, *et al.*, 2018).

## CONCLUSION

Peptic ulcer unwellness has been a significant threat to human health over the past 2 centuries. Despite medical advances, the management of ulcer and its relevant complications remains a medical challenge, thanks to its high morbidity and mortality.Therefore, there's a growing interest in dietary factors as supplements for the hindrance or remission of rubor and duct ulcers

## AUTHOR CONTRIBUTIONS

Idea and study was conceptualized by Lakshminarayanan Arivarasu, collection of the literature and drafting the manuscript was done by Barani shankar, revising the manuscript for publication was done by Jayalakshmi Somasundaram.

## CONFLICT OF INTEREST

The authors declare no conflict of interest

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