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AN OVERVIEW ON THERAPEUTIC ROLE OF COMBINATION OF PROBIOTICS IN TREATING PEPTIC ULCER

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ABSTRACT

Peptic ulcer is a chronic gastrointestinal disorder characterised by localised erosion in the stomach lining those results in to abdominal pain, hyper acidity, bleeding, nausea, bloating or diarrhoea. The most common cause of peptic ulcer is infection due to Helicobacter pylori or prolonged use of Non-Steroidal Anti-Inflammatory (NSAID) drugs. This review aims to provide an overview on the combination of different strands of Lactic Acid Bacteria (LAB) and bifidobacterial involving mechanisms that protects the gastric mucosal layer, helps in upregulation of prostaglandin for improving stomach lining, anti-inflammatory property of probiotics in peptic ulcer caused due to pro-inflammatory cytokines.

INTRODUCTION

Peptic ulcer is an acid-induced lesion of the digestive tract that is usually located in the stomach or proximal duodenum, and is characterized by denuded mucosa with the defect extending into the submucosa or muscularis propria[1]. The estimated prevalence of peptic ulcer disease in the general population is 5-10% [2], but recent epidemiological studies have shown a decrease in the incidence, rates of hospital admissions, and mortality associated with peptic ulcer [3,4]. This is most likely secondary to the introduction of new therapies and improved hygiene, which resulted in a decline in Helicobacter pylori (H. pylori) infections.

Traditionally, mucosal disruption in patients with the acid peptic disease is considered to be a result of a hypersecretory acidic environment together with dietary factors or stress. Risk factors for developing peptic ulcer include H. pylori infection, alcohol and tobacco consumption, non-steroidal anti-inflammatory drugs (NSAIDs) use, and Zollinger-Ellison syndrome[5]. The main risk factors for both gastric and duodenal ulcers are H. pylori infection and NSAID use[6]. However, only a small proportion of people affected with H. pylori or using NSAIDs develop peptic ulcer disease, meaning that individual susceptibility is important in the beginning of mucosal damage. Functional polymorphisms in different cytokine genes are associatedwith peptic ulcers. For example, polymorphisms of interleukin 1 beta (IL1B) affect mucosal interleukin 1β production, causing H. pylori-associated gastroduodenal diseases [7].

On the other hand, the risk of complications of peptic ulcer is increased four times in NSAID users, and two times in aspirin users[8]. The concomitant use of NSAIDs oraspirin with anticoagulants, corticosteroids, and selective serotonin reuptake inhibitors increase the risk of upper gastrointestinal bleeding[9]. Although many people who use NSAIDs or aspirin have concurrent H. pylori infection, their interaction in the pathogenesis of peptic ulcer disease remains controversial. A meta-analysis of observational studies resulted in a conclusion that NSAIDs, aspirin use, and H. pylori infection increase the risk of peptic ulcer disease independently[10].

H. pylori-negative, NSAID-negative, and aspirin-negative peptic ulcer disease, which is classified as an idiopathic ulcer, can be diagnosed in about one-fifth of cases[11]. It is caused by the imbalance between factors that contribute to mucosal integrity and aggressive insults, but the pathogenic mechanisms behind the development of idiopathic peptic ulcer are still unknown[5]. A Danish study showed that psychological stress could increase the incidence of peptic ulcer[12]. Other etiologies include ischemia, drugs (steroids, chemotherapeutic agents) and radiotherapy, viruses, histamine, eosinophilic infiltration, gastric bypass surgery, and metabolic disturbances[13].

Probiotics

Probiotics are defined as live microorganisms that can confer beneficial properties for health when consumed by individuals [14,15,16]. To be considered as probiotics, microorganisms must meet several requirements, including functional and safety aspects [17,18]. Probiotic bacteria must be non-pathogenic and should produce antibacterial substances to successfully compete with pathogens[19,20]. They should also be tolerant to gastric acid and bile salts, and should be able to colonize and persist in the gastrointestinal epithelium[21,22,23]. In addition, potential probiotic bacteria should meet safety aspects,

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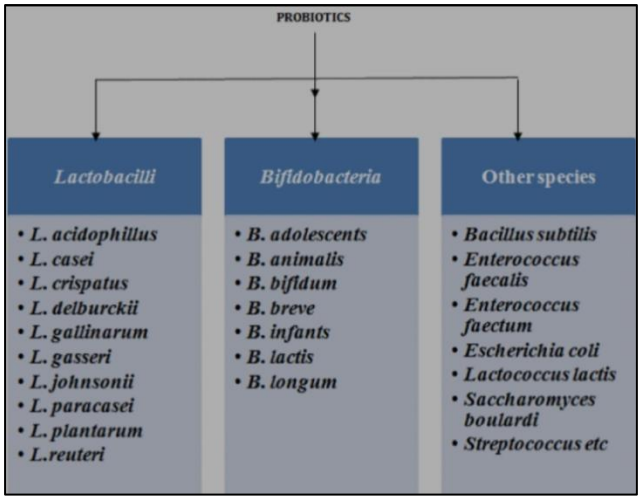
including the absence of transmissible antibiotic-resistance genes [24] and the capacity to synthesize haemolysin or other toxic compounds such as nocive biogenic amines (histamine, tyramine, putrescine, cadaverine phenylethylamine or tryptamine) [25].

Historically, the concept of probiotics began around 1900 by the Nobel laureate Elie Metchnikoff who discovered that the consumption of live bacteria (Lactobacillus bulgaricus) in yogurt or fermented milk improves the biological features of the gastrointestinal tract[26,27]. The Food and Agriculture Organization and the International Scientific Association for Probiotics and Prebiotics define probiotics as live microorganisms which, when administered in adequate amounts, confer a health benefit on the host [28]

The gut microbiota includes ~30 species of Bifidobacterium, 52 species of Lactobacillus, and others, such as Streptococcus and Enterococcus[29]. The most extensively studied probiotics for treating and/or preventing gastrointestinal diseases are lactic acid bacteria, namely Lactobacillus and Bifidobacterium species.While these species are non-pathogenic, they can resist the harsh luminal environment of the gastrointestinal tract [30]

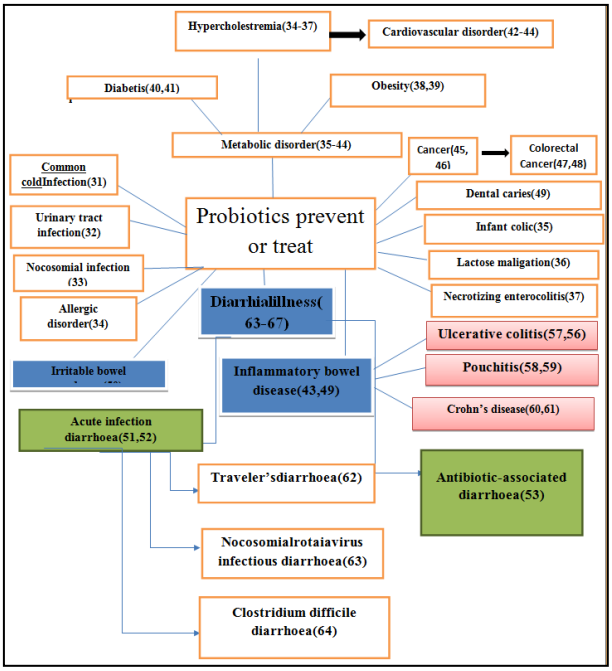
Strains of Probiotics:-



The need of Combination of Probiotics

As with all antibiotics, H. pylori medications often cause diarrhoea, nausea, and vomiting, which lead to poor tolerance and ultimately decreased patient compliance, the single most important factor in H. pylori eradication.[65,66] Graham *et al*[67] reported H. pylori eradication rates of 96% in high medication-compliant patients (taking ≥60% of the prescribed antibiotics), while only 69% eradication rates were observed among low medication-compliant patients (taking <60% of prescribed antibiotics). With the decline in H. pylori eradication rates, novel therapeutic alternatives are being studied and evaluated. Eradication rates are highest during the early phase of treatment when antibiotic sensitivity and patient compliance are greatest. Early treatment failure results in elevated risk of secondary antibiotic resistance due to the need for additional, less effective antibiotics used over longer periods of time with the possibility of additional medication side effects, thereby perpetuating the increase in antibiotic resistance and decreased medication compliance cycle.[68]

Gong *et al*[69] reported lower odds of H. pylori eradication with triple therapy alone, compared to triple therapy with probiotic supplementation (odds ratio [OR] 0.58; 95% confidence interval [CI], 0.50-0.68; **P**<0.05). Significant reductions in side effects, including nausea, vomiting, bloating, epigastric pain, diarrhoea, constipation, taste distortion, and skin rash, were also observed.[70]



Lactobacillus and Bifidobacterium are resistant to low pH and tolerant to a wide range of temperatures as well as can promote gut maturation and integrity, protect against pathogens, and modulate the immune system[71]. In our paper, the study group was supplemented with live combined Bifidobacterium, Lactobacillus, and Enterococcus capsules, and this combination has been reported in treatment of irritable bowel syndrome [72]. Hp is difficult to be treated since it acquires resistance to common antibiotics. Probiotics combined with antibiotics are currently used to eradicate Hp. Probiotics are useful in treating intestinal diseases such as diarrhea[73].

It has been documented that probiotics combined with triple therapy for treating peptic ulcer infected by Hp can greatly improve the eradication rate of Hp and increase recovery rate of patients, with less adverse reaction [74]. Several studies reveal the favorable effect of probiotics against Hp via different mechanisms including strength of mucosal barrier, competition for adhesion, and immunomodulatory mechanisms [74,75].

Probiotics can also inhibit TNF-α expression, generating an immunosuppressant and anti-inflammatory effect as a response; this has been frequently reported in recent studies and is the focus of the present study.[76]

CONCLUSION

The aim of this review was to summarize existing evidence on the mechanisms through which probiotics may exert an anti-ulcer activity and be used in case of gastric/peptic ulcer condition. The combination form of probiotics is preferable for better treatment and to prevent relapse of the disease like peptic ulcer.

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