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Application Progress and Optimization of Probiotics and Prebiotics in Chronic Diseases

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Abstract:

The increasing prevalence of chronic illnesses can be attributed to modern unhealthy lifestyle habits, sparking significant interest in the role of probiotics in supporting gut health. Research has demonstrated the potential of probiotics to balance gut microbiota, leading to their application in functional foods. However, challenges remain, including ensuring the probiotics' survival through the gastrointestinal tract and their absorption once they reach the gut. This article explores the relationship between probiotics and the human gut microbiome, with a focus on how dietary habits influence gut health. Furthermore, it discusses the mutagenesis of Lactobacillus plantarum and the application of these mutant probiotics in the treatment of hyperuricemia (HUA) and gout. A phenol high-throughput screening method is presented for identifying mutant probiotics, offering insights into more effective probiotic mutagenesis and screening techniques. Future research should aim to verify the success of probiotic mutations and focus on improving methodologies for probiotic development and delivery.

Keywords: Probiotics; chronic illnesses; gut microorganisms; Lactobacillus plantarum; phenol high-throughput screening.

1. Introduction

With the standard of people's living level rise, people's daily diet has changed. In recent years. This article aims to review the connections between probiotics and human bodies. From the 19th century, when scientists began to explore the relationship between gut bacteria and human health, to the recent development of new concepts such as the „intestinal-brain" and the „gut-X axis, „the important impact of gut bacteria on human health has long been a well-established fact. The influence of intestinal flora on human health has long been an indisputable fact.[1] In the last decade, the incidence of chronic diseases has risen. Analysis of chronic disease monitoring data in recent years shows that the prevalence rate of HUA in adults in China has increased by 14%, 24.5% for males, and 3.6% for females, the age of onset

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is gradually younger, and the incidence of gout is rising, making HUA the „fourth high“ after hyperglycemia, hyperlipidemia and hypertension [2]. Probiotics are playing a more and more important role in curing chronic diseases. Equally, labs are searching for some new methods to discover beneficial probiotics. Like the UV mutagenesis is a genetic experimental technique used to trigger mutations in DNA [3]. It is based on the effect of ultraviolet (UV) radiation on DNA molecules, which causes base damage in DNA, leading to mutations [4]. UV energy causes the hydrogen bonds between DNA single strands to break, causing the DNA double strands to separate. Then, the DNA single strands are recombined into new DNA double strands. According to some research, the mutant is unstable and difficult to control. To sum up, microorganisms play an important role in chronic disease prevention. The probiotics can manage the equilibrium of gut flora to enhance the functioning of the intestine. Currently, two primary techniques exist for modifying gut flora: using probiotics to enhance bacterial growth and probiotics to support bacterial growth [5]. Prebiotics refer to substances that can selectively promote the growth and reproduction of one or several beneficial bacteria in the intestinal tract of the host and are not digested by the host and inhibit the growth of harmful bacteria through the multiplication of beneficial bacteria, so as to achieve the purpose of adjusting intestinal flora and promoting body health. Consuming probiotics and prebiotics leads to the regulation of gut flora balance, enhancement of intestinal performance, increased nutrient uptake, vitamin synthesis, and maintenance of liver health [6]. The article proposes to find out the connection between gut microorganisms and people's daily diet and the application of probiotics in chronic illnesses, and look for some effective ways to screen the beneficial mutant strain.

2. Connections between Microorganisms and Human Metabolism

Hosting 100 trillion microorganisms, the human intestine is vital for preserving the host‘s ecological equilibrium due to its varied and abundant microbiota [7], affected by factors such as diet, illness, etc. Changes in gut microbiota, known as intestinal dysbiosis, involve disturbances in gut microbiota makeup and disorders of intestinal function. So, microorganisms are playing more and more important role in people's health. People's diets are really important role in health.

As the result, humans' bad diet would break the balance of the gut microorganisms and it would lead to some illnesses. Research by Afzaal et al. indicates that gut microbiota, residing in the gut, significantly influence host health via both direct and indirect routes, namely the „gut-X“ axis [8]. A multifaceted web of neural, endocrine, and immune networks forms the gut-brain axis, linking the brain to the digestive system. The system facilitates bidirectional interaction between the gut and brain via multiple signaling pathways, encompassing nerve conduction, hormone release, and immune cell regulation. The gut‘s microbial population (gut flora) impacts brain activity and emotional conditions through the generation of metabolites and signaling entities, which in turn alter neurotransmission and immune reactions.

Increasing research indicates that targeting gut microbiota could be a viable for the prevention and treatment of various human illnesses, chronic conditions included.

Nowadays, people's diets are changing. People are more likely to consume high-fat and high-oil food.[9] Prolonged consumption of a high-fat diet results in fat build-up in different human organs and also leads to disturbances in gut microbiota [9]. The study [9] indicates that germ-free (GF) mice fed a high-fat diet avoided obesity, hinting at the significant role of gut microbiota in obesity caused by a high-fat diet. A multitude of research indicates that consuming a diet high in fat modifies the amount and makeup of mice‘s gut microbiota, causing a disruption in gut microbial populations and consequently leading to gastrointestinal inflammation [9].

Moreover, Modern people, due to work stress and other reasons, are not very inclined to exercise. One of the key factors that can help improve metabolic disorders is exercise [10], which is utilized as an effective method for prevention and intervention to provide health benefits [10]. Exercise is effective in lowering blood sugar levels in diabetic patients [10] and can improve and prevent obesity and metabolic syndrome [10]. Additionally, it has been reported to alleviate symptoms in patients with colorectal cancer, irritable bowel syndrome (IBS), and IBD [11–13]. To improve and prevent metabolic disorders through regular exercise, the American College of Sports Medicine (ACSM) recommends moderate-intensity aerobic exercise for at least 30 min a day, five days a week, or a total of 150 min per week, or vigorous-intensity aerobic exercise for at least 20 min a day, three days a week [14].

The gut microorganisms are associated with metabolic disorders, it can lead to physiological change and increase the risk of obesity, diabetes, cardiovascular disease, liver disease, as well as conditions related to gut health such as colorectal cancer and irritable bowel syndrome [10].

3. The Application of Probiotics

3.1 The Application of Probiotics in Chronic Illness

Gout is a crystal-associated arthropathy caused by the deposition of monosodium urate (MSU), and the biochemical basis of its causation is usually considered to be hyperuricemia (HUA). Nowadays, more and more people are suffering from chronic illnesses, like it. People are becoming more and more interested in how to treat it. In gout treatment, traditional medicine like Allopurinol, is found it related to the undesirable Skin Reactions [15]. And benzbromarone, due to its severe hepatotoxicity, it's banned in most European countries although it is still commonly used in several Asian countries [16]. In recent years, scientist have been trying to use probiotics product to prevention and treat chronic illness. Lactobacillus plantarum is a type of lactic acid bacteria that is widely distributed in nature and has extensive applications in the food industry [17]. It has a variety of health effects with fewer side effects and higher market acceptance. Lactobacillus plantarum LP03 and LP20 contain purine nucleoside phosphorylase gene. Because Lactobacillus plantarum has high purine nucleoside phosphorylase activity, it can convert the guanine nucleoside and adenine nucleoside accumulated in the intestinal tract of gout patients due to eating into guanine and hypoxanthine, which can be further absorbed and utilized by probiotics efficiently, so as to reduce the absorption of purine by the intestinal cells of the human body and lower the rate of uric acid formation and reduce the deposition of urate. The rate of uric acid formation reduces urate deposition and plays a role in relieving gout. Moreover, the short chain bifidobacteria DSM 16604 and Lactobacillus plantarum LMG P-21021 are used to cure constipation, they can improve the consistency of their stool. In addition, short-chain fatty acids such as acetic acid and butyric acid produced by Bifidobacterium bifidum CCFM16 can change the intestinal microenvironment and stimulate intestinal peristalsis [18]. Additionally, the treatments for chronic illness still have some issues. First, the price of that is expensive. Second, Low market acceptance. Third, the technology is not mature enough, and some of them may have side effects.

3.2 Functional Food

Recently, probiotics have been used in some functional foods. Probiotics are alive microorganisms, when it used in food, they can provide some benefits to humans. It can prevent gut illnesses and hyperuricemia (HUA).

Tan and others. extracted *Lactobacillus plantarum* HFY11 (LP-HFY11) from yak yogurt fermented naturally and examined its impact on colitis caused by oxazolone in mice [19]. The study revealed that LP-HFY11 markedly reduced symptoms of colitis and controlled inflammation along with immune-related elements in the colon and blood [20].

In China, there is a typical functional probiotics yogurt named Yakult. The research shows that yogurt is beneficial for H.pylori patients. The probiotics exert both immediate and secondary suppressive impacts on H.pylori disease. The Yakult, an active lactic acid bacterial beverage akin to a standard diet, poses no major strain on the patient. Within this group, lactic acid bacteria are part of a category of probiotics known for their resistance to various antimicrobial medications. Concurrently, they exhibit robust resistance, a high tolerance to acid, and proliferate rapidly, playing a pivotal role in sustaining the stomach's microecological equilibrium. Furthermore, it may impede the growth of H. pylori within the body through the generation of organic acids, bacteriocins, and various agents that harm H. pylori's cell wall or membrane, or by disturbing the surrounding alkaline milieu [21].

4. The Methods of Screening the Probiotics in The Treatment of HUA

4.1 Phenol high throughput screening plate

In the treatment of HUA. Because the probiotics have high PNPase activity. It can convert guanosine and adenine nucleosides, which accumulate in the gut of HUA patients due to food intake, into guanine and hypoxanthine. Then, effective absorption and utilization of probiotics can reduce the body's absorption of purine and the rate of uric acid formation, thus alleviating HUA.

When the purine is degrading, the inosine can be catalyzed by PNPase to hypoxanthine; Then, it can be oxidized by XOD and converted to uric acid. Hydrogen peroxide generated during the period will degrade the phenol in the medium. Thus the bacteria with high pnpase activity can survive and grow in the medium.

4.2 Fully Automatic Growth Curve

Growth factors in the microbial culture solution (e.g. nutrients produced by the bacteria) affect the light absorption values in the sample. So use a fully automated growth curve to determine the steady-state biomass. Keep focus on the change in absorbance in the sample. then can plot a growth curve of the microorganisms The growth curve reflects the growth rate and growth pattern of the microbial population at different points in time. Usually, the growth curve of microorganisms can be divided into four phases:

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delayed, logarithmic, stabilization, and death. So can use this to monitor and analyze the growth status of mutant probiotics strain communities in real-time. It can help us to screen the mutant probiotics.

4.3 High-Performance Liquid Chromatography (HPLC)

HPLC is a method for separating and analyzing compounds based on the difference in partition coefficients of a sample in solution between a stationary phase (solid particles packed in a column) and a mobile phase (a continuous flow of solvent through the column). Compounds can be analyzed qualitatively and quantitatively by measuring the retention time of components in the column at different time points. By HPLC, can know the guanosine and inosine concentrations. So it can analyze the concentration in each sample to know the ability of the mutagenic strain to process purine. It also helps us to screen mutant probiotics.

5. Conclusion

This article aims to explore the relationship between probiotics and human health, with a particular focus on the role of probiotics in the prevention and treatment of chronic illnesses, which are often exacerbated by modern lifestyle habits. The study highlights the significance of Lactobacillus plantarum in addressing HUA and other chronic diseases. Additionally, the paper discusses the potential of probiotics with high PNPase activity to degrade uric acid, thereby offering therapeutic benefits.

The article also explores methods for inducing mutagenesis in probiotics to enhance their efficacy for human health. The phenol lethal plate method is identified as an effective approach for screening mutant probiotic strains, particularly by utilizing hydrogen peroxide—a byproduct of purine metabolism—as a screening marker. However, the practical application of this method remains unclear, and further studies are necessary to comprehensively evaluate its effectiveness.

The conclusion emphasizes the need for more efficient probiotic mutagenesis and screening techniques. Future research should also focus on enhancing the survivability of probiotics in the human gastrointestinal tract to ensure their effective colonization and functional impact. In addition, it is important to consider potential side effects on human health, as the development of more functional foods with health-promoting properties continues.

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