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Influence of Probiotic Fermented Fruit and Vegetables on Human Health and the Related Industrial Development Trend

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A B S T R A C T

The paper briefly discusses the relationship between chronic diseases and gut health, and points out that an imbalance of intestinal microflora and an inadequate intake of dietary fiber are two important causes of chronic diseases. This paper also summarizes the research status of probiotic fermented fruit and vegetables, and discusses the main achievements of our group in this field and future developments of the related industry. The application of fermentation technology to fruit and vegetable processing and the development of a series of probiotic fermented fruit and vegetable products not only increase the added value of fruit and vegetables, but also organically combine probiotics and their active metabolites with prebiotics (dietary fiber, etc.), thereby promoting intestinal health as well as preventing and relieving chronic diseases. Fermentation technology provides a new approach to the study of the effect of probiotics on human health, and will have a revolutionary influence on probiotic application and on the fruit and vegetable processing industry. Thus, fruit and vegetable fermentation technology has excellent market potential.

1. Introduction

Chronic diseases such as cardia-cerebrovascular disease, cancer, diabetes, and hypertension are a serious threat to human health. A report by the World Health Organization on 19 January 2015 [1] stated that 38 million people died of chronic diseases worldwide in 2012, of which more than 40% (nearly 16 million people) died a premature death; this rate was higher than that in 2000 (14.6 million). The China National Health and Nutrition Big Data Report in 2018 [2] indicated that the number of people with chronic diseases in China has exceeded 260 million, and that the fatality rate for these diseases accounts for approximately 85% of all population deaths. In addition, chronic diseases are exhibiting increasing incidence and a younger age of onset.

In the early 20th century, Nobel laureate Ilya Mechnikov studied the human intestinal flora and developed a theory that senility was due to poisoning of the body with the products of certain bacteria, which coincided with the concept of "dung poisons enter the bloodstream and all diseases emerge" in traditional Chinese medicine. At Washington University in the United States, Turnbaugh et al. [3,4] and Ridaura et al. [5] reported a complex relationship between human and intestinal microflora through long-term research, and found that intestinal dysbacteriosis is closely related to malnutrition, obesity, diabetes, and other diseases; these findings provided a new perspective on the delicate relationship between intestinal flora and human health. In fact, intestinal dysbacteriosis may contribute to the development of insulin resistance and chronic inflammation, leading to chronic diseases such as metabolic syndrome, obesity, diabetes, and even cancer [6–10]. Inadequate dietary fiber intake is another major cause of chronic diseases. Taking the United States as an example, the recommended daily intake of fiber is 38 g for adult men and 25 g for adult women. Nevertheless, the actual average intake is only approximately half: 18.7 g for men and 15.6 g for women. Similarly, Chinese residents only consume 8–10 g of dietary fiber per day, which is far below the recommended daily dietary fiber intake of 25–35 g. Inadequate dietary fiber intake can directly lead to the disappearance of some intestinal microbes, which can subsequently result in various chronic diseases [11]. More seriously, the intestinal dysbacteriosis and other health problems caused by a lack of dietary fiber are likely to be "genetic"; that is,

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if dietary fiber intake is persistently insufficient, intestinal microbes may irreversibly disappear [12].

The improvement of people's physical fitness is inseparable from the support of the healthy food industry. The Chinese government issued and implemented the "Healthy China 2030" Plan Outline on 25 October 2016, thereby raising the physical and mental health issues of the population to the level of a national initiative. With the introduction of the "Outline," the public also became increasingly concerned about the impact of food nutrition—especially daily foods—on intestinal health. The intestine, where more than 70% of the body's mucosal immunity occurs, is one of the most important organs in the human body. Moreover, the intestine is closely related to various parts of the body through complex immune mechanisms. Therefore, considerable attention must be paid to intestinal health in order to achieve a healthy population.

At present, it is generally acknowledged that probiotics and prebiotics are beneficial to intestinal health, and research on probiotics and prebiotics has become a hotspot in many fields, including food science, microbiology, medicine, nutrition, immunology, and intestinal health science. Hence, the effects of probiotics, prebiotics, and probiotic fermented foods on intestinal health and their interaction mechanisms must be studied. In recent years, probiotic products have become popular around the world. Statistics indicate that there are more than 380 kinds of probiotic products worldwide, including probiotic fermented yogurt, probiotic capsules, and probiotic powders. Among these, the proportion of probiotic fermented dairy products is as high as 80%, while probiotic fermented fruit and vegetable products are very rare in the market today. The main reason for this may be a lack of specialized strains for fruit and vegetable fermentation and outdated agent preparation technology.

2. Research status of probiotics and their fermentation technology

Since Tissier discovered the first probiotic strain (*Bifidobacterium*) in 1899 [13], scientists around the world have not stopped exploring the relationship between probiotics and human health. Numerous scientific studies have confirmed that oral probiotics help to prevent or cure gastroenteritis, antibiotic-associated diarrhea, travel diarrhea, constipation, and intestinal infections. Moreover, probiotics can inhibit the colonization of pathogenic bacteria in the intestinal tract of the host, and have good preventive and therapeutic effects on intestine-related diseases such as irritable bowel syndrome, inflammatory bowel disease, and colon cancer [14–17]. Large-scale dairy groups and lactic acid bacteria (LAB) preparation companies in Japan, Europe, and the United States have developed their own brands of internationally renowned strains, as well as product brands, and have conducted many clinical trials on the probiotic functions of these strains. For example, the *Bifidobacterium lactis* BB-12 strain developed by Chr. Hansen (Denmark) is the most thoroughly studied *Bifidobacterium* strain in the world [18,19]. It has been described in over 300 scientific publications, of which more than 130 are related to human clinical studies. Another example is the *Lactobacillus casei* strain Shirota [19] of the Yakult Company (Japan). In the past 80 years, this strain has undergone a large number of scientific studies and clinical trials. By the end of May 2015, its survival, effectiveness, and safety in the intestine had been scientifically verified in the United Kingdom, Japan, Thailand, China, and other countries and regions [20–25].

In recent years, further domestic studies on the promotion of intestinal health using probiotics have been conducted. Zhang [26] from Inner Mongolia Agricultural University conducted thorough studies on the probiotic function of *Lactobacillus casei* Zhang, which was selected from traditional fermented sour milk in Inner Mongolia. This strain has many excellent probiotic properties, including lipid-lowering, immunity-regulating, and antioxidant properties; furthermore, it inhibits the growth of intestinal pathogens and tumor cells. To establish a functional screening model for LAB, Chen [27] from Jiangnan University, China, conducted in-depth studies on the probiotic function of *L. plantarum* ST-III. This strain can effectively colonize the intestine and regulate intestinal flora; it also has excellent probiotic properties in terms of lowering cholesterol and regulating blood lipids. In addition, many reports on the promotion of intestinal health by probiotic and fermented dairy products are available. Many authoritative journals, including the *American Journal of Clinical Nutrition*, have reported that the daily ingestion of fermented milk improves immune function, while reducing allergies and the incidence of inflammatory bowel disease and bladder and colon cancers [28–32]. The efficacy of various commercial probiotic fermented dairy products, such as Yakult and Weiquan, has now been clinically proven [33–36].

Compared with probiotic fermented dairy products, few studies have reported on the effects of fermented fruit and vegetable products on human health. As the "first dish" of Korea, the nutrient composition and health benefits of kimchi have been fully studied. The benefits of kimchi toward weight loss, tumor reduction, and lowering cholesterol and blood fat have been reported by Korean scholars [37]. However, few studies on the health effects of self-produced probiotic fermented juices have been reported. Klewicka et al. [38,39] from the Technical University of Lodz conducted a systematic study on the efficacy of laboratory-made fermented beet juice in improving the intestinal flora and antioxidant activity of rats. Chu et al. [40] and Guan et al. [41,42] from Chongqing Medical University, China, studied the effects of mixed fruit and vegetable juice fermented by *Bifidobacterium* on immune regulation and anti-fatigue effect in mice. All of these results confirmed that fermented juice has a beneficial effect in promoting the health of rats and mice.

3. An overview of the development of probiotic fermented fruit and vegetable technology

The combination of probiotics with fruit and vegetables can simultaneously provide the probiotics and dietary fiber the body needs, indicating an important development direction for the probiotics industry in the future. The combination of "probiotics + fruit and vegetables" has various forms; of these, directly adding probiotics to existing traditional fruit and vegetable products is the simplest way. For example, probiotic powder or a certain amount of probiotic fermented milk can be directly added to cold preserved juice and processed into a viable (or non-viable) beverage. However, for vegetables such as carrots, bitter gourds, and celery, and for other nutritious but poorly flavored vegetable materials, the simple addition of probiotics cannot improve the inferior flavor of the vegetable product itself. Consequently, the best approach is to ferment fruit and vegetable raw materials using probiotic strains. Fermentation can diminish most of the olefinic substances in vegetables (i.e., the sources of undesirable flavor) while producing organic acids, amino acids, and various aromatic compounds that can intensify the desirable taste of the products. Moreover, large amounts of active substances, such as short-chain fatty acids, viscous polysaccharides, and peptides, are produced by fermentation, which can reduce constipation, relieve colitis, and prevent and treat digestive tract inflammation.

Although a great deal of research has been done in the field of fermented fruit and vegetables, the industrial production of fermentation technology is still in its infancy, and there has been no emergence of relevant products with excellent brand quality in domestic or foreign markets. This is because the following bottlenecks have not been solved in the core technologies related to this field.

First, there is a lack of specific strains for fruit and vegetable fermentation. It is well known that *Lactobacillus bulgaricus* and *Streptococcus thermophilus* are used for yogurt fermentation, but the specific species used for the pure fermentation of fruit and vegetables are as yet unclear. Plant-derived LAB such as *L. plantarum* [43–45] and *L. acidophilus* [46–48] have gradually come into use for the pure fermentation of fruit-vegetable juices, but no single species can be used to ferment all fruits and vegetables due to the diversity of the raw materials. It is therefore necessary to extensively screen excellent strains for the fermentation of different fruit and vegetable raw materials. Second, there is a lack of high-density culture technology for fruit and vegetable fermentation strains suitable for industrial production. Previous studies on the high-density culture technology of LAB have mostly focused on membrane filtration dialysis culture [49,50], ion exchange [51], cell cycle culture [52,53], and so forth. However, these technologies are confined to the laboratory level, making it difficult to achieve industrialized mass production, even though the high-density enrichment of cells can be achieved [54]. In recent years, the method of optimizing the medium composition in combination with batch culture or fed-batch culture has mainly been used to achieve the high-density culture of LAB, and the density of the obtained LAB is generally 1×10^9–1×10^{10} CFU·mL^{-1} (CFU: colony forming unit) [55,56]. Furthermore, the technology for the large-scale preparation of high-activity engineered microbial agents that are specific for fruit and vegetable fermentation is backward. Vacuum freeze-drying technology is generally used for the preparation of microbial agents in the existing literature, but the activity of lyophilized powders such as LAB prepared by this method is not high enough, and the live bacteria content is typically about 1×10^{10}–1×10^{11} CFU·g^{-1} [57–59].

4. Innovative developments by our team on the key technologies and industrial applications of probiotic fermented fruit and vegetables

For the first time, we have introduced fermentation technology into fruit and vegetable processing and have developed an innovative technological system to solve the problems in the fruit and vegetable fermentation industry, such as the lack of bacterial strains specific for fruit and vegetable fermentation, the underdeveloped technology of bacterial agent preparation, and the limited types of fruit and vegetable fermentation products. This system comprises upstream, midstream, and downstream industrial chains, which have broken through the technology bottleneck of high-density culture and industrial agent preparation (Fig. 1). Using this technology, a series of safe, nutritious, tasty, and convenient fermentation products have been developed, thereby spawning the establishment of an entirely new industry of fruit and vegetable fermentation. The effect of these probiotics and their fermented fruit and vegetable products on intestinal health is under preliminary study, and progress has been made.

4.1. Mechanism of metabolic regulation in co-fermentation by multi-microorganism during the fermentation of fruit and vegetables

We studied the microbiology community structure and the dynamic changes that occur in various types of traditional fermented fruit and vegetables during natural fermentation in

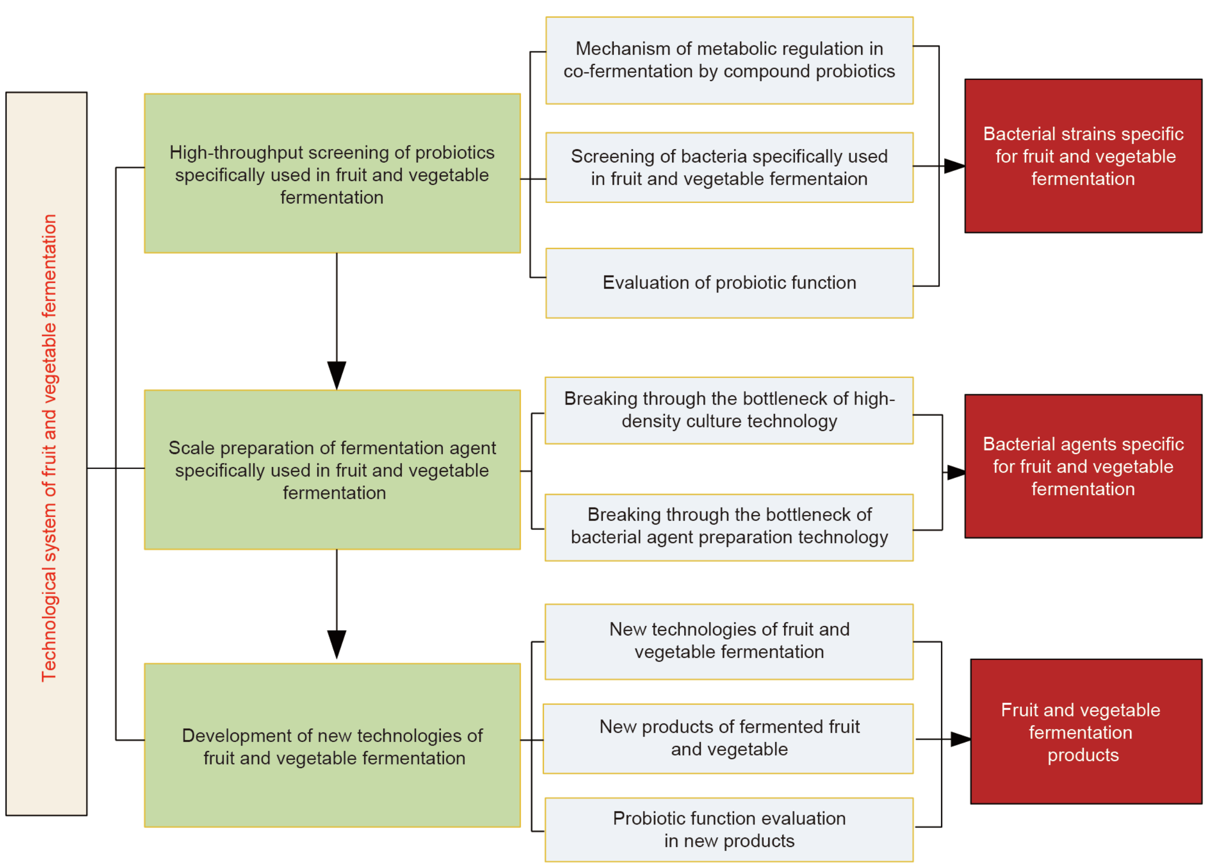

Fig. 1. A key technological innovation system for probiotic fermented fruit and vegetables, comprising upstream, midstream, and downstream industrial chains.

China, and revealed the interactions between the main strains, as well as their metabolites and substrates in the fermentation process. We clarified the metabolic regulation mechanism of multi-strain co-fermentation, thereby laying a solid theoretical foundation for the study of high-throughput screening of good strains, agent preparation, and the fruit and vegetable fermentation process [60–67].

4.2. High-throughput screening of probiotics specific for fruit and vegetable fermentation

On this theoretical basis, we have collected nearly 1000 samples of traditional fermented fruit and vegetables at home and abroad, and have fully explored and standardized the traditional techniques and microbial resources. We have preserved more than 6000 strains, including 56 species (Table 1) of LAB, and established the first dedicated strain library with independent intellectual property rights for fruit and vegetable fermentation. This library includes 335 strains with both excellent fermentation performance and good probiotic properties, such as strong acid and bile salt tolerance, good intestinal adhesion, regulation of intestinal microecological balance, ability to ease constipation, and regulation of immunity [68–78].

Table 1
The 56 species of LAB isolated and preserved by our team.

No.	LAB	No.	LAB
1	*Lactobacillus plantarum*	29	*Lactobacillus nodensis*
2	*Lactobacillus brevis*	30	*Lactobacillus silagei*
3	*Lactobacillus fermentum*	31	*Lactobacillus oligofermentans*
4	*Lactobacillus coryniformis*	32	*Lactobacillus diolivorans*
5	*Lactobacillus curvatus*	33	*Lactobacillus harbinensis*
6	*Lactobacillus sakei*	34	*Lactobacillus rapi*
7	*Lactobacillus buchneri*	35	*Lactobacillus versmoldensis*
8	*Lactobacillus alimentarius*	36	*Lactobacillus tucceti*
9	*Lactobacillus parabrevis*	37	*Lactobacillus rossiae*
10	*Lactobacillus koreensis*	38	*Lactobacillus acidipiscis*
11	*Lactobacillus delbrueckii*	39	*Lactobacillus fabifermentans*
12	*Lactobacillus yonginensis*	40	*Weissella hellenica strain*
13	*Lactobacillus parabuchneri*	41	*Weissella paramesenteroides*
14	*Lactobacillus parafarraginis*	42	*Weissella viridescens partial*
15	*Lactobacillus paracasei*	43	*Weissella confusa*
16	*Lactobacillus xiangfangensis*	44	*Weissella cibaria*
17	*Lactobacillus casei*	45	*Weissella koreensis*
18	*Lactobacillus paralimentarius*	46	*Leuconostoc mesenteroides*
19	*Lactobacillus nagelii*	47	*Leuconostoc pseudomesenteroides*
20	*Lactobacillus amylolyticus*	48	*Leuconostoc citreum*
21	*Lactobacillus heilongjiangensis*	49	*Leuconostoc fallax*
22	*Lactobacillus sunkii*	50	*Pediococcus parvulus*
23	*Lactobacillus paraplantarum*	51	*Pediococcus ethanolidurans*
24	*Lactobacillus pentosus*	52	*Pediococcus pentosaceus*
25	*Lactobacillus hammesii*	53	*Lactococcus lactis*
26	*Lactobacillus namurensis*	54	*Pediococcus inopinatus*
27	*Lactobacillus senmaizukei*	55	*Enterococcus durans*
28	*Lactobacillus fuchuensis*	56	*Pediococcus damnosus*

In addition, the probiotic *L. plantarum* NCU116, which was derived from traditional Chinese sauerkraut, was sequenced using third-generation sequencing technology (SMRT); it was shown to survive gastrointestinal stress *in vitro* and to lower the blood sugar, lipid, and cholesterol indexes *in vivo*, while its laxative effects were confirmed by a constipation model. Due to its strong ability for fruit and vegetable fermentation, this probiotic was used as a starter strain, especially for plant-associated substrates.

According to genome-wide and comparative analyses of *L. plantarum* NCU116, the genome of *L. plantarum* NCU116 shares high homology with complete genome-sequenced strains, including the *L. plantarum* strains WCFS1, ST-III, and JDM1. However, *L. plantarum* NCU116 possesses a large number of genes related to carbohydrate metabolism and transport (e.g., *ldh*, fumarate hydratase, and phosphoenol-pyruvate carboxykinase) and multiple metabolic pathways found in pyruvate metabolism, indicating that *L. plantarum* NCU116 can transport and catalyze monosaccharides, oligosaccharides, and sugar alcohols [79]. Furthermore, the two-component regulation and ABC transport systems found in the genome of *L. plantarum* NCU116 correspond with the phenotype of acid and osmotic tolerance. Most of all, no virulence gene was detected in the genome of *L. plantarum* NCU116, which aligns with the results of the animal experiments and indicates that *L. plantarum* NCU116 is a safe and reliable probiotic.

4.3. Large-scale preparation technology of probiotics agent

Through the integration of techniques, including exponential addition, fuzzy logic control, feedback control, and lifted cell suspension culture, the concentration of live bacteria in the fermentation broth at the factory level was greatly improved [80–82]. We have invented a two-step drying method for the production of high-activity LAB agent, as well as its large-scale production technology. Based on these achievements, we developed a probiotic agent product with high activity for fruit and vegetable fermentation. The number of viable cells in the agent is as high as 1×10^{12} CFU·g^{-1} [83]. This technology fills the gap in the production of special agents for fruit and vegetable fermentation.

4.4. An innovative technology of fruit and vegetable fermentation by probiotics

We have constructed new technology for the direct production of probiotic fermented fruit and vegetables, and developed a series of new products, including probiotic fermented fruit and vegetable purees, beverages, and jelly. These products not only have good flavor and mouth-feel [84], but also contain a large number of active substances, such as short-chain fatty acids, sticky polysaccharides, and peptides, which are beneficial to human health [85].

4.5. Evaluation of the biological function of probiotics and their fermented fruit and vegetable products

We have established animal models of diseases, such as constipation, immunosuppression, hyperlipidemia, fatty liver, colitis, and diabetes, to evaluate the functional properties of the strains preserved in our library and of their fermented products that we developed. Taking *L. plantarum* NCU116 as an example, evaluation of this strain and its fermented carrot products showed that both have good probiotic characteristics in mice for improving immunity, improving intestinal mucosal structure, relieving constipation, relieving diabetes and colitis, alleviating hyperlipidemia, and regulating intestinal flora [85–96].

5. Challenges and future development trends in the probiotic fermented fruit and vegetable industry

Although the technology of probiotic fermented fruit and vegetables has now achieved a key breakthrough, the development of the related industry still faces a series of key scientific and technological issues. For one thing, the probiotic fermented products we developed only involved carrots, mangoes, pears, pumpkins, and other ordinary fruits and vegetables, because in our previous research, we only isolated strains with excellent fermentation performance for materials that were available in large quantities. However, there are many kinds of fruits and vegetables, each with its own uniqueness. Thus, more strains with excellent fermentation performance are required to develop more varieties of probiotic fermented fruit and vegetable products. However, for certain special materials, such as hawthorn, which has a particularly high acidity, it is extremely challenging to screen good strains that are suitable for fermentation because few strains can tolerate such high acidity. Furthermore, the safety and functional evaluations of probiotic fermented fruit and vegetable products were only carried out in related animal experiments, and no systematic clinical trials have been done. Thus, a more comprehensive nutrition function and safety evaluation system for probiotic strains and their fermented fruit and vegetable products must be constructed in order to confirm the probiotic function of fermented fruit and vegetable products. In addition, more advanced large-scale production technology for the agents of fruit and vegetable fermentation must be developed. Finally, the effects of prebiotics, probiotics, and fermented fruit and vegetable products on human health, in addition to their mechanisms of action, must be further clarified. If these problems can be solved effectively, research and industries in the field of probiotic fermented fruit and vegetables will have greater opportunities for development.

6. Conclusions

In recent years, the traditional beverage industry has shown an irreversible declining trend. Probiotic fermented fruit and vegetable beverages not only cater well to consumers' demand for safe, nutritious, delicious, and healthy drinks, but also meet the development trend of the health industry. Therefore, healthy products based on probiotic fermented fruit and vegetables will have an important impact on the fruit, vegetable, and fermented food industries. This review presented the view that an imbalance of intestinal microflora and an inadequate intake of dietary fiber are two important causes of chronic disease, and described the research status of key technologies related to probiotic fermented fruit and vegetables, recent development of the screening of special strains for the fermentation of fruit and vegetables, the scale preparation of fermentation agent, and the development of new technologies and products in this field. The challenges and development trends in probiotic fermented fruit and vegetable technology were also discussed from various viewpoints. In the future, an increasing number of probiotic fermented fruit and vegetable products with the distinctive characteristics of being safe, nutritious, delicious, and healthy will provide consumers with an increasing amount of and high-quality fruit and vegetable products.

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Compliance with ethics guidelines

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