

The Benefits of Fermented Food on Metabolism, Gut Immune Homeostasis, and Psychology

Jue Wang

Tianjin Xinhua High School, China

Abstract

The benefits of fermented food across all categories are being more and more recognized today. Fermented food, as a kind of probiotics, is shown to have a multitude of interplays with human physiology and psychology systems. Fermented food could help maintain proper homeostasis achieve some weight loss effects of the metabolic process through unique ingredients and certain strains of bacteria. Other than metabolic homeostasis, fermented food could also regulate the homeostasis of the immune system of the GI tract and thereby can potentially relieve the conditions of the bowel diseases. Fermented food can affect behavior of mice with early life stress-induced depression and/or anxiety through gut-brain axis (GBA) and improve certain conditions related to the psychological wellbeing of the mice. Overall, fermented food could play significant role in the regulation human mental and physical health.

Keywords

Fermented food; Metabolism; Gut immune homeostasis; Gut microbiota; Gut-brain axis; probiotics.

1. Introduction

Fermented food played a crucial part in human life. Bread, yogurt, cheese, pickles, etc. are all products of fermentation. It has a long history--recent research suggested that the earliest form of fermentation could trace back to 13,000 years ago[1]. Notable examples of microbes used in fermentation are *Lactobacillus Plantarum* and *Saccharomyces cerevisiae* (a.k.a. yeast.) In contemporary society, people make use of fermented food mainly as a part of their usual diet as a complementary source of energy, while other people also reap additional benefits of fermented food on human gut microbiota and metabolism. As recent papers point out, phenolic compounds in alcohol free fermented blueberry have the potential to reduce obesity in mice caused by high-fat diet [2], and a strain of *Lactobacillus* has similar effect in weight loss [3; 4]. The compounds produced by fermenting bacteria can exert numerous benefits, including the antioxidant, anti-microbial, opioid antagonist, anti-allergenic, and blood pressure lowering effects to human body. [5]

When considering the effect of probiotics on human wellbeing, the role played by gut microbiota cannot be overlooked. As early as the birth of a child, a number of bacterial, archaeal, viral, fungal, and protozoal microorganism communities begin to colonize the baby's intestines. In 1-2 years, the composition of the microbiota would stabilize, but its exact makeup would be largely based on the environmental factors. The environmental factors continue to shape the composition of gut microbiota in the adulthood, subject to the antibiotics, the lifestyle of the host, the diet, the hygiene, etc., which also exerts effects on the host itself. [6,7]. In the past decade, a plethora of researches has been published on their impact on their host's physiology. The microbiota is shown to promote the formation of intestinal vessel, promote increased vascularization, influence the host's nervous system, facilitate energy harvest from the diet, and regulate homeostasis [7]. In fact, some probiotics benefit human health by leveraging the gut microbiota community.

Not only can they modulate the physiology of the host, but the gut microbiota also has a crucial role in the immune system and are involved in both the inhibition and promotion of inflammatory diseases. It has been realized that the intestinal microbiota has a key role in guiding several aspects in the

development and regulation of the host's immune tissues, immune cell populations, and immune mediators.

It has been proved that the germs are essential to the mice's gut development. In an experiment in which germ-free mice and control are compared in terms of the development of their bowel tissues, it has been shown that the germ-free mice have longer and thinner villi in their intestinal linings (which decreases the absorbance efficiency), less complex vascular network, very few isolated lymphoid follicles, immature Peyer's patches, and immature mesenteric lymph nodes (MLNs) [7]. All these traits can finally lead to curtailed immune ability. Therefore, the gut microbiota is clearly essential to the immune system.

The gut microbiota can not only alter the physiology of the host, but also play a major part in the modulation of nervous systems, serving as part of a system of gut-brain axis (GBA). The gut and the central neural system (CNS) submit and receive signals in either direction, influencing each other in different ways. For example, the CNS control of food ingestion can alter the gut microbiota's composition by impacting availability of nutrients. In addition, the brain can synthesize most of the satiation-signaling peptide such as peptide YY (PYY) to exert control over the GI tract. On the other hand, the microbiome can also influence the performance of CNS. Alterations in psychological activities (such as anxiety and depression) are found in patients both before and after inflammatory bowel disease (IBD) diagnosis.

2. Fermented food reduces obesity by treating metabolic impairment and readjusting the homeostasis of gut microbiota after ingestion of disruptive diet

Several researches have indicated that fermented food does have positive effects on human metabolism. Because it contains anthocyanin, a chemical that can enhance heart health, protect against obesity, and ward off cancer, the alcohol-free fermented blueberry-blackberry beverage (AFFB) is shown to help mice lose weight, even under forced high-fat diet. At the end of the 3-week-long high fat diet, all the groups, regardless of their feed, are hyperglycemic. However, mice consuming 1X and 2X post-amberlite extract (PAE) had significantly lower fasting blood glucose than the water and the sitagliptin groups. The mice receiving the phenolic compound treatment are observed to have smaller pancreatic islets, lower staining of the glucagons, and smaller adipocytes; on the other hand, significantly increased liver weights coincide with unexpected periportal hepatic lipidosis. The AFFB protected the mice against the HFD-induced midzonal lipid deposition, suggesting there may be an unidentified compound in the AFFB masking the negative effects in the PAE groups at the provided doses. In regards of gene expression, the PAE treatments 0.1X, 1X and 2X caused differential gene expression of networks related to cell proliferation and carbohydrate and protein metabolism.[2]

Similarly, as a research team from Jiangsu University notes, *Lactobacillus Plantarum*-fermented barley (LFB) has similar effect in slowing the weight growth in mice under high-fat diet. Moreover, the mice fed with *Lactobacillus*-fermented barley exhibit more oral tolerance of glucose than those under normal diet. More specifically, after fermentation with *Lactobacillus Plantarum*, the amount of crude protein, beta-glucan, and phenolic compounds (such as phenolic acids like gallic acid) in barley increased. Both beta-glucan and polyphenolic substances are associated with anti-obesity effects. Additionally, the LFB group saw a decline of factors associated with inflammation and weight gain and incline of the factors with opposite functions: compared to high-fat diet group, the LFB group showed a significant reduction in plasma levels of TNF-, IL-1 and IL-6 and an increase in plasma levels of IL-10. LFB supplementation improves glucose intolerance and insulin resistance, too, making the LFB-fed group secreting the least amount of insulin to balance the blood sugar. The study also shows that *Lactobacillus*-fermented barley can decrease the levels of TG (Triglycerides) and TC (Total Cholesterol) to maintain normal blood lipid levels in HFD-induced obese rats. In regards of the cytokine mechanism, the paper points out that the LFB prevents insulin resistance in adipose

tissue of obese rats, possibly by inhibiting the activation of upstream mediators of inflammation such as p-JNK1, p-P38 or NF-kB. [4]

Other researches yield similar results. In one study, the mechanism of the anti-obesity effect of *Lactobacillus Plantarum* is further explored, the effect of which is later accredited to the inhibition of *Enterobacter cloacae* in the intestine of mice. *Enterobacter cloacae* is often thought to be pathogenic in the gut. Out of 230 lactic acid bacteria isolated during the investigation, the strain of *L. Plantarum* LMT1-48 exhibited maximal inhibition of *E. Cloacae*. To induce obesity, *E. Cloacae* induced high-fat diet fed mice obesity model is employed as the previously introduced experiment. The administration of *E. Cloacae* causes a decrease in abdominal fat volume in *E. cloacae*-induced HFD-fed mice and reduced leptin and TC levels in plasma, both of which indicate an anti-obesity effect caused by the *Lactobacillus Plantarum*. [9]

The beneficial effects summarized above can confirm that probiotics play an important role in regulating the immune system and thereby improving the physique by reducing obesity of the administered subject. (See Figure 1)

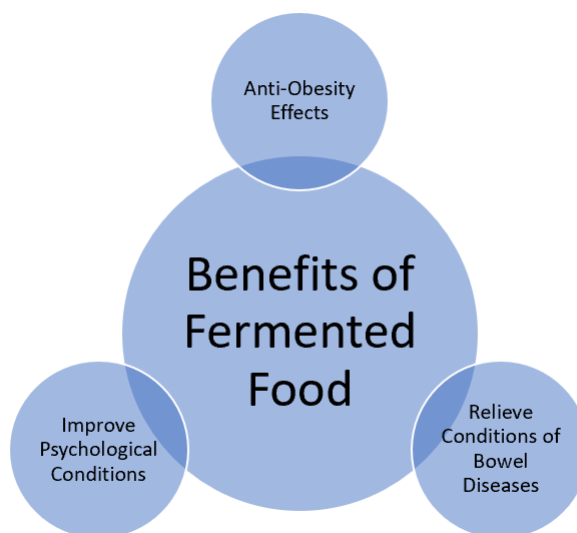


Figure 1. Fermented food and its role in human health

3. Probiotics enhance immune systems by providing protection of the gut microbiota against disruption and inflammatory diseases

One of the probiotics that demonstrates therapeutic abilities is the fermented vegetable extract under the brand of OM-X®. A recent paper shows that the consumption of OM-X® is safe to the rats. Although oral infection by *C. Rodentium* induced a significant colitis at the histological level, inflammatory lesions were prone to be less serious in mice treated with OM-X®; however, statistically speaking, this protective effect was not significant. In addition, OM-X® exerts a protective effect against bacterial translocation from the intestinal lumen to the mesenteric lymph nodes (MLN) and the systemic blood circulation, which indicates a decrease of permeability of the intestinal barrier. What's more, the treatment up-regulated the production of IL-10 (an anti-inflammatory factor) and expression of FoxP3, which is expressed in anti-inflammatory T regulatory (Treg) cells. Reinforced intestinal barrier and induced proliferation of epithelial cells, as evidenced by PCNA staining, are also observed from the treatment. Another interesting result drawn from the research is that the ingestion of OM-X® could favor the growth of specific commensal bacteria species in mice like *Faecalibacterium*, *Roseburia*, *Eubacterium*, *Acidaminococcus*, heavy producers of butyrate, a short-chain fatty acid (SCFA) acting as an essential source of energy for colonocytes, stimulating their proliferation, and exerting anti-inflammatory effects. [10]

Recently, another group of researchers ascertained another probiotic strain of bacteria, *L. lactis* ML2018, that has beneficial anti-inflammatory properties. Their results show that oral administration

of *L. lactis* ML2018 significantly ameliorated colitis induced by dextran sulfate sodium (DSS), and its detailed effect included preventing a decline in body weight, reduction of the colon length and apoptosis of epithelial cells. Like the effects of OM-X®, the strain *L. lactis* ML2018 can integrate the intestinal epithelial barrier and boost the concentrations of short-chain fatty acids (SCFAs). Furthermore, not unlike the findings with *Lactobacillus*-fermented barley, the activation of NF- κ B signaling pathways by the strain *L. lactis* ML2018 could also ward off inflammation [11]. Previous data also report that a Caucasian fermented milk drink, kefir, also has effects in both lactose malabsorption and *Helicobacter pylori* eradication in the GI tract. However, as the same data set reveals, the effectiveness of gastronomical benefits of other fermented foods like kombucha, sauerkraut, fermented soy products (tempeh, natto, miso), kimchi, and sourdough bread has yet to be scientifically confirmed. [12]

Also, it has been found that *L. Rhamnosus*-fermented soymilk administration has potentially health-promoting effects and may provide protection against gut microbiota disruption caused by antibiotics, as well as improving fecal enzyme activity. Specifically, the fecal activity of the enzyme beta-glucosidase is improved even when the antibiotics are simultaneously administered. Moreover, the administration of soy milk is also related with less decrease in bacterial taxa. [13]

By activating largely similar cellular pathways, the probiotic bacteria from fermented food exert influence on the regulation of gut microbiota and hence the immune system. (See Figure 1) The factors upregulated in the cases, such as NF- κ B and IL-10, do not vary significantly between different probiotic bacterial species and exhibit similar, effective results throughout the experiments.

Therefore, the practicability of administering fermented food to treat intestinal disease is substantiated by various case studies, and it can be inferred that more than one species are responsible for the beneficial effects. Further studies should focus on which strains of which species of bacteria have the most pronounced effect and cost-effective when applied to pharmaceutical, industrial usage.

4. Fermented food ameliorates symptoms of mental disorders through GBA

As per the development of the field of psychology and physiology, it has been realized that mental disorders like depression and anxiety are often coincidental with physiological symptoms like digestive and bowel disorders. This leads to the establishment of the concept of gut-brain-axis (GBA), a communicative and regulatory system that involves brain and central nervous system and the enteric environment of the gut in either direction. [14] Also, as advanced in one of the field's papers, it is suggested that the clinicians of the patients with inflammatory bowel disease should address the negative psychological attributes such as stress and depression as well as the negative physiological ones, for fear that these sentiments may aggravate the inflammatory bowel disease's course. [3]

Though still in its infancy, the field of psychobiotics, probiotics that produce health benefits in patients suffering from psychiatric illnesses, has seen major developments in recent years along with relevant scientific research.

It has been known that adverse early life events are linked with a flawed stress response system, raising the probability of increasing the vulnerability to disease in later life. Studies have shown that the maternal separation (MS) form of early life stress (ELS) has solid effect on the GBA in the model of mice.[15] Recent data evaluate the psychotropic effects of a potential psychobiotic bacterium, *Lactobacillus plantarum* strain PS128 (PS128), on mice subjected to early life stress and on naïve adult mice. The researchers used maternal separation as a model to bring about early life stress, which conveys negative effects on brain development and causes behavioral changes in adulthood.

Behavioral tests were utilized to evaluate the effects of PS128 on the reduction and improvement of depression-like and anxiety-like behaviors. The behavioral tests were conducted starting from the least stressful to the most stressful test in the following order: Sucrose Preference Test (SPT), Open Field Test (OFT), Elevated Plus Maze (EPM), and Forced Swimming Test (FST). In regards to the ELS mice, the results reveal increased locomotor activities in OFT, reduced depression-like behaviors in the other three tests, and reduced anxiety-like behaviors in SPT and FST.

Also, PS128 was observed to normalize ELS-induced exaggerated corticosterone release, decrease inflammation (characterized by a decrease of pro-inflammatory factors and an increase of anti-inflammatory factors), and promote serotonergic and dopaminergic activities. [16]

Overall, the administration of probiotics manifestly improves the psychological conditions on mice, and this implication has already been observed in humans as well, despite limited cases application. Because this field is still in its nascence, further researches are needed to draw definite, comprehensive conclusions on the mental-health benefits fermented food brings about and set the groundwork for realistic pharmaceutical applications to take place.

5. Summary

Fermented food has proved to ameliorate human health in various ways (Figure 1), and the field of research on this subject matter is still growing. This paper categorizes three ways in which fermented food helps human maintain a good health condition. The field of fermented food, especially that of psychobiotics, is rapidly developing, and further research should be done in order to fully understand the functionalities, nuances, and combinational implications of different kinds of fermented food.

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