

Review

Fermented Foods and Beverages in Human Diet and Their Influence on Gut Microbiota and Health

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Abstract: Dietary changes have accompanied the evolution of humanity and is proven to be fundamental in human evolution and well-being. Nutrition is essential for survival and as a matter of health and equilibrium of the human body. About 1/3 of the human diet is composed by fermented foods and beverages, which are widely distributed and consumed in different societies around the world, no matter the culture and lifestyle. Fermented foods are derived from the fermentation process of different substrates by microorganisms, and more importantly to humans, by those with beneficial characteristics, due to the positive impact on health. Food is transformed in the gut, gaining new properties, and increasing its value to the organism. The effects of fermented foods and beverages can be assessed by its influence at the gut microbiota level. Recent studies show the major importance of the gut microbiota role in modulating the organism homeostasis and homeorhesis. More crosslinks between health, gut microbiota and diet are being established especially in the gut–brain axis field. Therefore, the benefits of diet, in particularly of fermented foods and beverages, should be studied and pursued in order to promote a good health status.

Keywords: fermented foods; probiotics; gut microbiota; gut-brain axis

1. Introduction

History of man has many branches, but all of them take in consideration progress, alongside with evolution, equilibrium, and the well-being of the human kind. The evolution of nutrition is one of the ways that has shown how diet can impact on health.

Around the world, each culture has its own distinctiveness in terms of food culture and heritage, where fermented foods are included. Naturally fermented foods and beverages contain both functional and non-functional microorganisms, and from these, 90% are still made with traditional techniques/methods [1].

The consumption of fermented foods can bring many advantages to the human organism, nevertheless some disadvantages are known from the consumption of specific fermented foods [1,2]. There is a lack of references for some fermented foods, probably because they do not have a history of use in a particular country or they are made at home instead of being commercialised.

However, this lack of information should not be interpreted as absence of beneficial effects [2]. The importance of fermented foods has gained considerable attention since 1907, when Nobel Prize laureate Elie Metchnikoff, assessed the beneficial effects of fermented milks on the longevity of Bulgarian populations and introduced the concept of probiotics [3,4].

Although clinical trials in humans are still scarce, the most recent studies have opened paths which link nutrition, fermented foods and probiotics, to the role and modulation of the gut microbiota, the maintenance of vital functions in the organisms and to the state of well-being, from immunity to mental health. Studies have linked a healthy gut microbiota and traditional dietary patterns, where fermented foods and beverages are included, to lower risks of anxiety or depression, thus showing the connection to mental health [5,6].

This review introduces these themes, by establishing connections between the consumption of fermented foods and beverages and their beneficial role to human health, mainly on the gut-brain axis.

2. Nutrition and Human Evolution

Since the existence of mankind, foodstuffs and nutrition has played a large role in its evolution. Since 1770, Antoine Lavoisier, the “Father of Nutrition and Chemistry”, discovered the actual process by which food is metabolized. However, nutrition as an independent science from human medicine only occurs on the middle of the 20th century. Food, in its most varied forms, is fundamental to humans. Through food of quality, humans obtain nutrients, micronutrients and energy, which covers their requirements and promotes and secures growth, movement, work, thought and most important of them all, their health and well-being.

Such steps lead to the improvement of the human condition, and to the development of physical and psychological traits, that accompanied the evolution of man. Studies of human ancient civilization show that harvesting food from cultivated land, and its processing, helped them to overcome hunger and disease, allowing at same time increase in population. However, these same practices led to a surprising relative reduction in the diversity of nutritional intake [7,8].

In the past, changes in food availability and in diet composition, for humans, created selective pressures on multiple biological processes such as metabolism, brain activity, digestive system, feeding habits and even in appetite. Metabolic pathways, through enzymatic and hormonal control, have an important role in all type of dietary regimes, and when people focus on a particular diet some pathways and reactions become critical [8]. Different cultures, overtime, embrace different heritages by mixing several flavours such as salty, spicy, sour, sweet and bitter in foods, and has become a portal into culture itself.

3. Fermented Foods on Society

Fermented foods and beverages are made through controlled microbial growth and enzymatic conversions of major and minor food components [9].

Food fermentation is characterized by the primary metabolites, microorganisms and substrates involved in the fermentation processes [2,9,10]. This type of foods is the hub of microorganism’s consortia. These can be present either as natural indigenous microbiota in the substrates, or as added started cultures, containing functional activity that change biochemically and organoleptically the substrates into a different product during the fermentation. This provides an enrichment of the nutritional value in these products, unique flavours, textures and health-benefits to the consumers [2,11].

Some of these fermentative bacteria containing functional activity have been referred as probiotics when they fulfil the definition establish by the Food and Agriculture Organization of the United Nations (FAO) and by the World Health Organization (WHO): “live microorganisms which, when administered in adequate amounts, confer a health benefit on the host” [1,2,12]. Probiotics used in foods must have the capacity to survive and resist the gastric juices and bile, also being able to proliferate and to colonise the digestive tract [13]. The oral consumption of ingested strains from fermented foods and probiotics are between 10^8 and 10^{12} CFU per day [4,14]. However, the application

of probiotics is controversial since the European Food Safety Authority (EFSA) rejected all submitted health claims related to the term “probiotic” while in Japan, the Ministry of Health, Labour, and Welfare approves foods or ingredients that have enough scientific evidence for health claim substantiation and use a Foods for Specific Health Use (FOSHU) label to identify them. In the case of Food and Drug Administration (FDA), it has allowed nutritional supplements of *Saccharomyces boulardii* to be sold with the following information in the label: (1) maintains the balance of the intestinal flora; (2) keeps intestines functioning well; and (3) promotes intestinal health [15–17].

The most commonly used and applied microorganisms to produce fermented foods and beverages from plant and animal origin are lactic acid bacteria (LAB) [11,14]. Additionally, the most commonly used probiotics are LAB belonging to the genus *Lactobacillus* and *Enterococcus* along with bacteria of the genus *Bifidobacterium* [1,14]. Recently, yeasts and other microbes (e.g., *Bacillus*) have been developed as potential probiotics [1].

The matrix of some fermented foods supports the delivery of high numbers of microorganisms to the gastrointestinal tract having a beneficial impact on the human gut microbiota [9]. One example of fermented foods as good matrices to delivering probiotics to the host are table olives, an important food commodity of the Mediterranean diet and one of the most important agricultural products that are consumed fermented, which at the same time do not contain lactose and cholesterol. Table olives are generally fermented by natural indigenous LAB and/or by some yeasts present in the olives [18,19].

Fermented foods and beverages are estimated to make up 1/3 of human diet, and have been a part of diets for approximately 10,000 years ago, dating back to the same period of agriculture and animal husbandry introduction [4,6,14]. Food fermentation was used, in ancient times, as a technique to prevent food spoilage.

In the early days of the use of fermentation, people were not aware of the existence of microorganisms or their role in the fermentation process; therefore, they applied artisanal methods to make fermented foods and beverages. It was only in the middle of the 19th century that a development in the concept of fermentative processes and knowledge about food fermentation happened, thanks to the emergence of microbiology as a science and to the industrial revolution. The advances in microbiology have made possible to understand the basic biological concepts behind food fermentation [10]. These advances resulted in an increase of variety of microorganisms and their combinations (e.g., bacteria and yeast) which created thousands of different types of fermented foods and beverages consumed worldwide [9].

Nowadays, different fermented foods and beverages (~3500) are being processed and consumed by billions of people in the world [10,11]. The different fermented foods and beverages are classified within 9 major groups based on substrates used from animal/plant sources: (1) fermented cereals, (2) fermented vegetables and bamboo shoots, (3) fermented legumes, (4) fermented roots/tubers, (5) fermented milk products, (6) fermented and preserved meat products, (7) fermented, dried and smoked fish products, (8) miscellaneous fermented products, and (9) alcoholic beverages [11].

The present review will not focus on the effect of individual groups of fermented foods but instead will focus on the general effect of fermented foods on the gut microbiota.

The main focus, at the moment, is to prove their functionality, meaning they still have to demonstrate improvements in target functions in the human body leading to health and well-being. Nevertheless, numerous food market options, from milks and yogurts to fermented soy products, cereals, vegetables and juices are already available [20]. Human studies will have to be carried out to validate the potential benefits already shown in *in vitro* and rats/mice studies up to now.

4. Health Benefits of Fermented Foods and Beverages

The reference to fermented foods as being health-promoting is common, and health benefits are often perceived by folk beliefs, nonetheless scientific foundations of such claims are not that solid and perspectives for product innovations and impact studies have yet to be made in especially more controlled *in vivo* studies [20]. However, studies have shown until now that the two main effects of

the daily consumption of fermented foods are upon the immune system and metabolic function. It has been suggested that these foods can reduce incidence and duration of respiratory infections, bring improvements to bone, liver, body mass, and blood pressure indices, to the prevention of diarrhoea and constipation, and even skin health [2,21–29]. Some studies have shown safety and effectiveness from the use of probiotic foods to aid recovery from organ transplant and abdominal surgery, to provide benefits on the managing of some cardiovascular risk factors and the possibility to reduce the load of pathogens by the intake of LAB [2,9]. Fermented foods and beverages have also been shown to possess the potential to influence brain health, stress relief, memory enhancement, and to have beneficial immune and neuroprotective effects [1,5,6,9]. Still, further studies are required in these prominent fields.

It has been argued that the fermented foods and beverages may influence positively the mental health of humans, alleviate inflammation, control oxidative stress that can lead to cognitive dysfunction and neurodegenerative diseases (e.g., Alzheimer's disease), and even lower the risk of anxiety or depression [5,6]. Preventive effects of the administration of fermented food, as red mould rice, which is common on Asian foods, were found on neurodegenerative diseases as Parkinson's and on behavioural dysfunctions [5,30].

Other studies have tried to explain the influence of diet in mood, by the establishing a link to the production of neurotransmitters and validating the role of the non-essential dietary components in the antioxidant defence system, as well as to the ability to provide anti-inflammatory support [6]. As an example, supplementation with *Bifidobacterium*, bacteria genera that can be found on several fermented foods and beverages, may attenuate exaggerated stress responses and maintain adequate levels of neuropeptide brain-derived neurotrophic factor, which are known to be low in depression. This supplementation is also expected to provide systemic protection against lipid peroxidation and decrease brain monoamine oxidase activity, that will potentially increase intersynaptic neurotransmitter levels [31,32]. Another case is the one of *Lactobacillus plantarum*, present in traditional Chinese fermented food, which showed strong antioxidant activity in animals [33].

In traditional diets, the fermentation of fibre-rich components has shown the capacity of producing beneficial immune, glycemic, and anti-inflammatory activity [6,34–37].

Findings have linked fermented foods and beverages to positive influences on the gut microbiota with long-term impact gut-brain communication. Moreover, the most recent advances in gut microbiota studies have been able to establish the concept of the gut-brain axis, showing the modulatory effect of the gut microbiota composition on the brain and the central nervous system in interaction. Therefore, a link can be established between diet, as an influencer on the gut microbiota composition and consequently on the brain and furthermore on the homeostasis of the organism [5,38–40].

Although it is possible to find many studies showing the beneficial effects of different fermented foods, most of them are tested in in vitro or in rats/mice models. There are still few studies involving the impact of fermented foods on humans. More studies are needed to be conducted in humans to prove the results verified in the other studied models. Examples of fermented food and beverage impact studies on humans can be seen in Table 1.

Table 1. Examples of the impact studies of fermented foods on humans.

Fermented Food	Microorganism Present	Beneficial Effect Associate	Study Group	Reference
Yogurt	<i>Lactobacillus delbrueckii</i> ssp. <i>bulgaricus</i> and <i>Streptococcus thermophilus</i>	Lower risk of T2D	Non-diabetic human volunteers, N = 194,458	[41]
Fermented milk	<i>Lactobacillus casei</i> Shirota	Normalization of bowel movement and infection control	Elderly human volunteers, N = 72	[42]
Fermented milk	<i>Lactobacillus casei</i> DN-114 001	Reduction of respiratory infection	Elderly human volunteers, N = 1072	[21]
Chungkookjang (Korean fermented soybean paste)	<i>Bacillus licheniformis</i>	Improvement of body composition in overweight and obese adults	Overweight/obese human volunteers, N = 120	[43]
Kimchi (Korean fermented and salted vegetables)	<i>Lactobacillus plantarum</i> , <i>Lactobacillus brevis</i> , <i>Pediococcus cerevisiae</i> , <i>Enterococcus faecalis</i> and <i>Leuconostoc mesenteroides</i>	Reduction of body weight	Overweight/obese human volunteers, N = 22	[44]
Ancient grain bread	<i>Saccharomyces cerevisiae</i>	Reduction of cardiovascular risk factors	Healthy human volunteers, N = 45	[45]

N—number of participants.

5. Fermentation Benefits and Risks

Fermented foods and beverages are products that went through a fermentation process which is an economical process that helps to prevent food spoilage by microorganisms. This process not only retains shelf-life time, but it also promotes the safe consumption of products [2]. Fermentation, in most cases, leads to detoxification and destruction of undesirable substances that are common in raw foods, like toxic components and anti-nutritive factors (e.g., phytates, tannins, and polyphenols) [2,10]. In addition, most of the times, the fermentation process enhances the bio-availability of nutrients and enriches the sensory quality of food [1,10]. Fermentation, in this way, becomes a food safety practice.

Despite the existence of positive effects related to fermented foods and beverages, there are also negative effects related to the consumption of specific fermented foods. Adverse effects associated with fermented foods and probiotics consumption may be under-reported [46]. Pathogen contaminant microorganisms present in fermented foods are a biological risk for human health. An example can be *Escherichia coli* or *Clostridium botulinum*, which can cause poisoning in fermented foods and turning them hazardous in fermented milk and meat products [47–49]. Another shared concern are the viruses present in fermented foods, which can affect and influence the human gut microbiota, but their impact and prevalence is still limitedly studied [50].

The presence of biogenic amines is one of the most important health risks associated with fermented foods consumption [1]. Biogenic amines are low molecular weight organic molecules, formed by microbial decarboxylation of their precursor amino acids or by transamination of aldehydes and ketones by amino acid transaminases [1,51,52]. These organic compounds are present in some fermented foods (e.g., sauerkraut, fish products, cheese) [1,51,53,54].

Nevertheless, the consumption of food with low levels of biogenic amines is not considered a serious health risk since, under normal physiological conditions, biogenic amines are degraded in the gut lumen by monoamine oxidase and diamine oxidase enzymes. However, the intake of high levels of biogenic amines (>100 mg/kg) from diet, or pathological alterations of the detoxification system, can induce several human health disorders [1,52–54].

6. The Role of Gut Microbiota

The gut microbiota is the microbial population living in the gut, especially in the colon. This microbial population is diverse and abundant (10^{14} cells) and consists of bacteria, archaea, and eukaryotes that live in an intimate relationship with the host [5,14].

At the bacterial level, the main phyla found in the human gut are Firmicutes and Bacteroidetes, and in a smaller representation the Proteobacteria and Actinobacteria. These phyla, together, constitute 93.5–98% of gut microbiota. Some of the most common bacteria genera found in gut are *Bifidobacterium*, *Lactobacillus*, *Bacteroides*, *Clostridium*, *Escherichia*, *Streptococcus* and *Ruminococcus* [55–58]. These bacteria are important for the well-being of their host, as in the case of disease, or in the maintenance of the immunological activity, energy consumption and even the brain activity (e.g., stress response), having an impact on host health [5,14,55,59,60].

Diet has an important role in shaping the composition and the activity of the complex microbial population in the gut, providing macronutrients such as carbohydrates, proteins, and fats [14,55]. Diet is not the only factor that can affect gut microbiota, but it is one of the most important which can provoke dysbiosis, i.e., any compositional change of the resident commensal bacteria in the gut, compared to the one found in healthy individuals.

Obesity and type II diabetes are disease states associated with gut microbiota composition and compositional changes [3,61,62]. In addition, studies show that dysbiosis is associated with anxiety and depression while the administration of probiotics produces anxiolytic- and antidepressant-like activity in animal studies [5,40,63,64]. Diet has influence over the composition and function of the human gut microbiota, crucial for the extraction of energy from food and even the maintenance of the immune system. Furthermore, diets rich in probiotics (prepared either naturally or with industrial processes) showed positive results on stress relief and memory enhancement, possibly by via gut microbiota

improvement. Other studies indicate that fermented dairy products may also have neuroprotective effects [5,65].

Our diet has effect on the composition and activity of gut microbiota, therefore, in short-chain fatty acids (SCFA) production [66–68]. The production of SCFA (e.g., acetate, propionate, and butyrate) is one of the functions of the gut microbiota and several bacteria may also produce them during fermentation of food matrices. The fermentation and SCFA production, in the colon or in the food, inhibit the growth of pathogens by reducing the local pH. The SCFA are produced in the gut through colonic fermentation, in a complex process involving the interactions of many microbial species in anaerobic conditions leading to a breakdown or conversion of dietary fibre, protein, and peptides into different end products [68–71]. The most abundant SCFA in the colon are acetate, propionate and butyrate and are normally present in molar ratio ranging from 3:1:1 to 10:2:1 [68,70–72]. Their production in the gut promote directly the growth of symbionts, which decrease the peptide degradation and the production of toxic compounds (e.g., ammonia, amines) [71,73,74].

SCFA are important to the normal function of the gut and the human body [75]. SCFA regulate the metabolism of glucose and lipids, promote mineral absorption, stimulate proliferation and differentiation of intestinal enterocytes, reduce the prevalence of inflammatory diseases and antioxidative functions. Additionally, it was found that SCFA positively influence the host metabolism and have a crucial role in the functions of the central nervous system [5,40,60,76].

The overall lack of quantitative data on actual fluxes of SCFA and metabolic processes regulated by SCFA and, thus, the influence of the gut microbiota is a key research subject.

7. Gut Microbiota, Fermented Foods, and Beverages

Several studies have been conducted to assess the role, importance and impact of the gut microbiota [58,59,77–81]. Some models can be established in different ways, providing a wide range of data on the researched topics.

The analysis of the impact of different foods on the gut microbiota can be done in model studies in vivo (e.g., human studies) or in vitro. The utilization of in vitro gut microbiota simulation models, used to reduce the use of in vivo models, are more useful to setup and explore different conditions and compositions for the study, thus enabling the simulation of different gut conditions [82,83]. Simulation models can help to understand the complex relationship between host-gut microbiota-food component. The in vitro fermentation models are used nowadays as essential tools to screen substances, from dietary ingredients to pathogens and to assess how they alter or are altered by gastrointestinal environments and microbial populations. These models allow to cultivate complex gut bacteria, in controlled conditions adjusted according to the aim of each study, to study their metabolism. Although the advantages of the use of in vitro models, the utilization of the in vivo models are still important and crucial to be done and to analyse the “real” effect of food ingredients in human health. In vitro models are models that attempt to mimic closely in vivo conditions and even simulate physicochemical and physiological events on the digestive tract, allowing the studies of structural changes, bioavailability, and digestibility of foods when they arrive on the gut microbiota. However, these models cannot correspond totally to what happens in the interior of the human gastrointestinal system [84,85]. For that reason, human studies are still required and necessary to make a claim about the effect of a food ingredient on human health.

Experimental works, mainly on mice, have been developed to explore the contribution of the microbiota in modulating the gut-brain axis, recurring to the use of germ-free animals, probiotics, antibiotics, and infection studies [38,39,86]. Studies with rats and mice suggest that gut microbiota interact with the brain. In animals, changes in the gut microbiota can modulate peripheral and central nervous systems, resulting in altered brain functions, and as these systems interact with the immune system thus having changes at this level. Still, this influence on the central nervous systems and on behaviour has very little evidence on humans, correlating the microbiota to the brain. Further studies

with probiotics, fermented foods and beverages and their effect on the gut microbiota, especially in humans can open path to new diet therapies [3,40,86].

Diet has a very large impact on gut microbiota, and the composition of such diet is known to modulate gut microbiota, with a wide range of effects on the organism, affecting intestinal permeability, mucosal immune function, intestinal motility and sensitivity and also the activity in the enteric nervous system (Figure 1) [38,39,86,87].

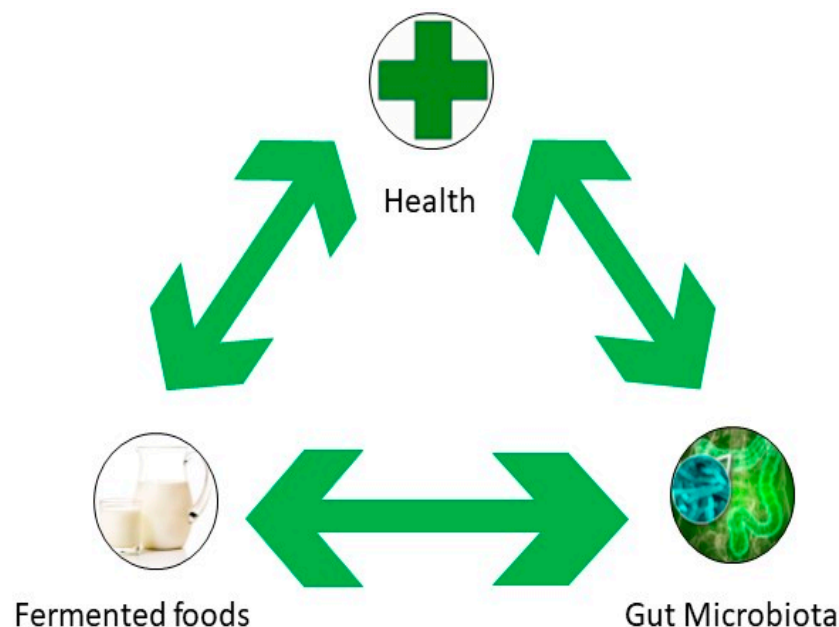


Figure 1. Relationship between fermented foods, gut microbiota, and impact on the human health.

Despite the lack of evidence in humans, preclinical findings identify a key role of gut microbiota on modulating the brain and the gut-brain axis (a bidirectional communication network between the central and the enteric nervous system, which links the emotional and cognitive centres of the brain with peripheral intestinal functions) [38,39,87]. In animals, the absence of a normal gut microbiota has shown significant effects on adult stress responsiveness and such alterations were partially reversed with gut colonization [38].

There are well documented effects of how adverse early life influences on the gut-brain axis, and in animal models, prenatal and postnatal stress can alter the composition and total biomass of the enteric microbiota. The brain and behavioural effects of perinatal stress in rodent models offer a high translational validity for human diseases, including gastrointestinal and psychiatric disorders [38,86]. The microbiota influences interactions between the gut and the brain. Microbiota interacts with the central nervous system by regulating brain chemistry and influencing neuro-endocrine systems associated with stress response. Influences in the central nervous system can affect the microbiota indirectly by altering its environment and directly by signalling molecules [38,39]. The use of fermented foods and beverages, mainly with probiotic bacteria can restore a perturbation of the normal luminal habitat and so change the effects of the central nervous system on the microbiota [5,39,86].

The knowledge of the mechanisms behind the impact of fermented foods and beverages on the gut-brain axis are still relatively scarce, regardless authors have hypothesised that changes in composition and activity of the gut microbiota lead to brain and cognitive health [5,6].

Positive mental health has been linked to the consumption of fermented foods. Controlled fermentation, by amplifying nutrient and phytochemical contents on foods, takes impact on mental health. Changes in the gut microbiota can influence mood and fatigue taking therapeutic value. Agmatine and polyamines in fermented foods and beverages have been related, experimentally, to several benefits related to brain health [6]. Furthermore, evidences show neuroprotective effects

of fermented foods, by preventing neurotoxicity [5]. These ideas lead to the convergence of microbe-nutrition and gut-brain axis researches [5,6,38,39]. The main mechanisms involved show that diet impacts the gut microbiota and the gut microbiota is linked to brain health. From the gut microbiota to brain, processes include production, expression and turnover of neurotransmitters (e.g., serotonin) and neurotrophic factor, the protection of the intestinal barrier, the mucosal immune regulation and the production of bacterial metabolites. From the brain to the gut microbiota, impact is shown by the alteration in mucus and biofilm production, in motility, in the intestinal permeability and on the immune function. Within these perspectives, fermented foods and beverages, by its direct impact and modulation of the gut microbiota and its function, may take action on positive brain and cognitive health [39].

Probiotics have also shown potential health effects on gut microbiota in relation to brain functions and cognitive health promotion. Fermentation modulates chemical constituents improving bioavailability of the food and the incorporation of microbes in natural foods seems to enhance their neuroprotective effects. Probiotics in fermented foods may influence brain function through the gut microbiota. Recent studies show that neurotransmitters are affected by the gut microbiota and so fermented foods can influence cognitive function. Changes in the chemical composition of foods induced by fermentation related to probiotics and homeostasis in the gut microbiota may explain the beneficial effects of fermented foods in human health [5].

8. Conclusions

Fermented food consumed in our diet modulates gut microbiota and the functions of the gut microbiota influence a great number of systems in the human organism. Notably the gut-brain axis, as the bidirectional influence of both (gut and brain), the deriving consequences and most importantly, the benefits of its good maintenance is now acknowledged. A correlation between diet, gut microbiota and health is established as more findings are supporting the established connexions and the modulatory effects in each other. However, more human clinical studies are necessary to corroborate and verify the health benefits and the new possible interactions between the organism's systems, therefore clarifying the links between diet, probiotics, fermented foods and human well-being.

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