



Microbial Functional Foods as a Magic Secret to Healthy Life Style

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Abstract

Functional foods are foods with a physiological function for body in addition to their role in nutrition and satiation. With the increase in immune and emerging diseases, related to unhealthy nutrition, as it is strongly linked to digestive system diseases, which result in most other diseases. Therefore, it is incumbent upon us, each in his specialization, to point out the critical importance of functional nutrition in general, and fermented foods as one of the broadest sectors of functional foods especially; as microbial metabolism products after fermentation contribute to the production of many chemical compounds with important physiological functions.

Using fermented foods has been known since ancient civilizations, folklore and some festive seasons, either because of its distinctive flavor or to increase the duration of preservation, or for its health importance, and this is in both animal and vegetable sources, and for being a special food as a religious custom or for vegetarians.

Conclusion: This article aims to point out the importance of fermented foods and mention some of their sensitive functions, which may contribute to the advancement of humanity and take its hand to return to nature and a healthy life style.

Keywords: Fermented foods; brain-gut axis; immunity-enhancing; anti-microbial; anti-oxidants; anti-inflammatory and traditional folklore.

1. Introduction

Functional foods are nutrients that besides their original function (nutrition and satiation) provide other health benefits to the consumer by providing physiological functions (physical condition) ruling the protecting mechanisms, avoidance of getting old, avoidance and medical management the diet related diseases. From a practical approach, purposeful food may be: (1) natural food, some enriched component by different cultivation conditions, (2) food with added favorable components, (3) food with removed respective components to decrease harmful healthiness impact, (4) foodstuff with chemically modified nature of one or more constituents to scope better absorption of the valuable constituent, and (5) mixture of the aforementioned options [1].

Breast milk is the first functional food for the infant, and it is also his first line of defense, in the neonate and has a main effect on intestinal homeostasis. A lot of immunological constituents are existing in breast milk, which provides several biological functions including defense against both

viral and bacterial infections [2], such as antibodies (i.e. immunoglobulins (Igs)), which transmitted from the mother to the neonate with extra antibodies in the principal 6–12 months after natal. Antibodies are created based on the mother's past experience to infectious pathogens and may inhibit similar infectious agents colonizing the infant [3]. In addition to immunologic antibodies, human milk provides a collection of broad-spectrum constituents which have wide antimicrobial effects containing nucleotides, oligosaccharides and proteins such as α -lactalbumin and lactoferrin. Among others breast-fed infants are famous to have a lower frequency of infection containing respiratory tract infection, gastrointestinal infections accompanying diarrhea, otitis media and additional extra-intestinal infections comparing to their formula-fed peers [4].

Numerous constituents of breast milk have exhibited both antiviral and antimicrobial activity *in vitro*, though their combination into infant formula is partial due to the absence of clinical trials [5], such as fatty acids namely, docosahexaenoic acid (DHA) and

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Received date 03 May 2023; revised date 07 July 2023; accepted date 30 July 2023

DOI: 10.21608/ejchem.2023.202051.7926

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arachidonic acid, oligosaccharides, nucleotides, lutein, taurine, natural vitamin E and an alteration to the whey: casein ratio [6].

Nearly all living organisms have progressive a defense mechanism that destroys undesirable microbes upon entry or prevents their entry of them into their body. This protection mechanism of the body which helps to fight off annoying invaders is known as immunity. In human beings, the immune system is made up of complicated network of cells, proteins, and tissues, which cooperatively defend the body against infections.

Our immune system has numerous roles in the defense of the body, in the following means, 1. It acts by way of a barrier, inhibiting the entry of undesirable external entities. 2. It supports the body in identifying the self (body's own nucleic acid, cell, tissue, protein, etc.) from the non-self (nucleic acid, cell, proteins, etc.) from the attacking germs. 3. It stands as an immune reply to eliminate or deactivate germs overall. 4. It clears up the body's own malfunctioning dead or infected cells. 5. Immunity is the basic body system to resist in opposition to infectious means, established via huge achievements of vaccination concerning removing sickness. Thought about vaccines are mainly operative ways of avoiding infectivity is fully recognized, equally by the public and public-health authorities. **Daniel Davis** inscribed, the public is attracted by the relations among lifestyle selections and immunity that there may be practical inferences for what it proceeds to be healthy. Particularly, public curiosity is about growing immune resistance simply. Possibly, mainly common confidence is on the subject of using vit. C headed for avoid infectivity, a thought widespread subsequent to chain of scientific articles by **Linus Pauling**, who encouraged the consumption of more quantities more than the suggested at that era. Acceptance, amongst lay persons, of this conception is such that, the body's immune system improving is the maximum goal for consuming dietary complement. Market immune enhancers include antioxidants, minerals, vitamins, functional foods, probiotics, other alternative and complementary medication advance [7].

Furthermore, the physical barrier is the principal line of defense, it has consisted of microorganisms that are hosted in the body and populated outside the epithelial cells of gastrointestinal system and the skin. These microorganism populations are termed as the microbiota. The microorganisms' genetic material that makes up the microbiota is named the microbiome. Gut microbiota, or intestinal microbiota which are the intestinal flora of our bodies, have an important role in human health, principally in the development of regulation of metabolic events and the host immune system [8]. The microbiome contains

the microorganisms (viruses, archaea, protists, fungi and bacteria), their genomes, and their immediate environment, including oral mucosa, respiratory systems, the gastrointestinal tract, urogenital and the skin surface. The principal groups of microorganisms which construct the microbiome are bacteria. It is valued that their amount in whole human body is similar to human cells number.

Most bacteria exist inside the guts. Because of their enormous figure and diversity, they could considerably influence ordinary physiology and change human body's vulnerability to illness. Many functions of gut bacteria contain immune system maintenance, digestion, vitamins synthesis, sharing in the production of short-chain fatty acids, and effect on the mucosal barrier permeability. Furthermore, other management of probiotic bacteria may enhance the host health.

Studies have confirmed lower levels of blood harmful fats and cholesterol when probiotics and prebiotics are consumed together. Possibly by improving the diversity of the gut microbiota community, that reinforces the importance of more clinical research on individual cases [9].

Among many diverse of psycho-biotic and probiotics bacterial strains have a valuable consequence upon cerebral healthiness after swallowed in enough quantities. These bacteria have an important effect on Central Nervous System task and metabolism, accordingly affecting cerebral healthiness, cheers to Brain-Gut-Microbiome Axis via endocrine, neuronal and immune-mechanism. Prebiotics can also promote the impact of probiotics on human neuro-metabolism, which motivates the suitable probiotic bacteria augmentation and could enhance the Gut-Brain Interaction. Additionally, new investigations show sharing of postbiotics into Brain-Gut-Microbiome axis modulation [10].

Food fermentation was discovered fortuitously thousands of years ago. The importance of microbes in food fermentation came more lately, through Van Leeuwenhoek and Hooke in 1665. Then, microorganisms have been practical for food production as unique economic method of food storage and processing. Several food substrates can be used in fermentation processes, as well as milk, seafood, meat, cereal grains, vegetables, fruits, root crops, and additional miscellaneous food compounds. The nutritional and medicinal properties of fermented foods promoted as an approach to improve food functionality [11]. Nowadays, consumers are deciding on foods with functional properties to enhance their health. These opinions of consumers to healthy foods have developed from the concept of "functional foods" [12].

Therefore, we aspire in this scientific presentation to promote the idea of increasing nutritional

awareness towards fermented foods as one of the most important and oldest functional foods developed by humans, and we can name them from the point of view of microbiologists, microbial functional foods to distinguish them from other types of functional foods prepared by humans.

It is worth noting that we should not overlook the role of breast milk in strengthening the immunity of a person throughout his life, because breastfeeding is not only considered the first functional nutrition in a person's life, but it is the nucleus on which his vital and immune functions will be built for life.

Therefore, it should be noted, without further details, about the importance of feeding the children on breast milk, especially in the first six months after birth.

2. Microbial Functional Nutrients

Microbial functional nutrients are nutrients fermented naturally or by incubation to convert the unprocessed resources to fermented-products by some microbial enzymes actions. Microbial functional foods are whichever plant-origin or animal-origin relying upon initial unprocessed stuff. The most common and earliest animal-origin microbial functional foods which produced for thousands of years are fermented dairy products. nevertheless, healthiness effects of fermented dairy products as yogurt, cultured-cream, cultured milk, *cheese*, *kefir* and *leben* [13], have been known in 1917 through Metchnikoff who showed fitness profits related to eating fermented dairy foods in the middle of some people in East Europe [14].

Fermented foods vary around the world and in different civilizations and times. One study indicates that the number of fermented foods may exceed 5,000 types worldwide [15]. There are many laboratory studies that prove the production of microbes for metabolites known for their vital activity as anti-inflammatories, antioxidants, antimicrobials, etc. However, it is necessary to prove these laboratory studies with clinical studies to confirm their importance and effectiveness within the living body [16].

2.1. Microbial Functional Nutrients from animal sources

2.1.1. Microbial functional foods from meat

Fermentation of beef was usually applied to prolong meat's shelf-life and advance exclusive flavor in novel manufactured goods. Fermented meat products in the company of difference for additives and process are additional usual inside Europe, U.S.A. and Northern Africa, [17]. The LAB is the major micro flora of fermented meat products

particularly *Lactobacillus* spp. containing *pentosus*, *alimentarius*, *versmoldensis* and *plantarum*, followed by *Pediococcus* spp. *pentosaceus* and *acidilactici* [13]. Majority of famous fermented-meat products contain fermented sausages, salami and jerky which could set-uped from mutton, pork and beef. *Basterma* is arranged by normal fermentation via combination of salt, garlic and seasonings that is stuffed in cow intestines with the minced meat and kept 1-2 weeks at room temperature. *Nem chua* is prepared by fermentation of crushed little-fat pork got ready in the company of diverse spices and kept for three-four days at room temperature; Lactic Acid Bacteria are the principal microbes discovered in last product [18].

2.1.2. Microbial functional foods from milk

Fermented milk is considered one of the main items on the daily table of most peoples of the world, as it is characterized by its distinctive and beloved flavors, in addition to its health value enhanced with probiotics, in addition to its technological properties that make it longer than raw milk [19]. Fermented-milk foods are further usual in diets within Europe, North America, North Africa and Middle East [20]. Hence, various Asian goods are created like kumis (Mongolia), dahi (India) and dadiah (Indonesia) [21]. The fermented-milk products include great variety of microbes containing yeast, fungi and bacteria [22]. Traditional fermented-milk products are a gorgeous resource of bio-active composites containing peptides, *amino-acids*, minerals and vitamins [18]. Cultured-milk is a right common product got ready by spontaneous fermentation of sheep and cow-milk [17].

2.1.2.1. Yogurt

Easiest fermented milk product is Yogurt that is produced by two recognized Lactic Acid Bacteria strains; specifically *Streptococcus thermophiles* and *Lactobacillus delbrueckii* subsp. *Bulgaricus* [23]. Yoghurt fortified with fish oil nano-emulsions was prepared; it was characterized by fairly good physical, chemical and sensory properties, as well as high oxidative stability [24].

2.1.2.2. Cheese

Also, cheese with approximately 1400 varieties is an olden fermented milk product [25]. Diverse cheese kinds are created by diverse inoculum cultures like bacteria (*Siciliano* – *Majorero* – Feta - Pecorino), yeast (Romano - Parmesan – Gouda - Cheddar) and molds (Monterey-Jack - Gruyere – blue-cheese) [18]. Nevertheless, Lactic Acid Bacteria “LAB” is the main microbes for producing fermented-milk products and their chief function is to use lactose-producing L.A. [26]. It was found that the use of resistant potato starch as a prebiotic enhances the amount of probiotics in low-fat cheese, and it also

has a qualitative effect on the sensory properties of cheese and improves the smoothness of low-fat cheese [27]. Completing this study, it was found that mixing inulin prebiotics with probiotics in low-fat head cheese had a positive effect on manufacturing costs [28].

2.1.2.3. Milk beverage

The production of fermented milk drink rich in probiotics, especially *Lactobacillus helveticus*, supported with cereal extracts and with a shelf life of up to two weeks, is recommended in the diets of special groups, as it is considered a Synbiotic product rich in antioxidants and with distinctive physical properties [29]. Functional milk drink fortified with 1% whey and 10% coconut extract, recommended for school children and the elderly; Coconut extract contains L-arginine that boosts immunity, is an antioxidant and anti-inflammatory, and these drinks also contain biologically active lactoferrin [30].

2.1.3. Microbial Functional Nutrients from aquatic sources

2.1.3.1. Fish sauce

Budu is a sauce of brown-fish made via combination of convinced kinds of fish for example *Sardinella* and *Stolephorus* species plus salt, and then fermented [31]. On the other hand, *Budu* has many names in Asian nations containing *nam pla* (Thailand), *terasi* (Indonesia), *patis* (Philippines), *nước mắm* (Vietnam) and *teuk trei* (Cambodia). Aquatic-based fermented products prepared by spontaneous fermentation because of the existence of wide variety of microorganisms on their surface. Though, the application of inoculum-culture was suggested to make sure protection of the products from pathogenic bacteria as a result of presence of anti-microbial substances like bacteriocins, organic-acids, bioactive peptides and fatty-acids [32].

2.1.3.2. Fermented fish

Moreover, fish sauce and fermented fish prepared by natural fermentation process are famous in Asian nations comprising Malaysia, Japan, China, Thailand, Philippine and Indonesia. The fermentation is to conserve fish, and guarantee pathogenic microbes' nonexistence. Fermentation procedure includes large variety of microbes that are in nature originated on the fish exterior and in stomach, and the gut-linings [33]. *kapi* (*Belacan*) is shrimp-paste impulsively fermented in the attendance of inhabitant microbes of shrimps and salt [34].

2.2. Microbial Functional Nutrients from plant sources

Microbial functional foods from plant sources

containing fermented vegetables, cereals, legumes and fruits are quickly rising owing to numerous issues as claims of health benefits, the low price of raw materials and diversity of the raw materials. As well, elevated commands from vegans and vegetarians caused the growth in novelty for microbial functional foods from plant sources. **Farouk et al.** [35] used yoghurt starters and baker's yeast as inoculating starters for the production of pickles within the framework of limited experience and infrastructure; while taking advantage of the benefits of probiotics in the final product in terms of sensory and color characteristics. They were distinguished from the traditional pickled product with salt and vinegar in terms of safety and probiotic properties.

2.2.1. Fermented cereals

Fermented glutinous rice (*tapai pulut*), *kimchi* distributed in South Korea, tapioca (*tapai ubi*) in Malaysia and *natto* in Japan [18].

2.2.2. Fermented legumes

Fermented legumes are mostly those of black gram (*Vigna mungo*), soybean (*Glycine max*), mung beans (*Vigna radiata*) and chickpea (*Cicer arietinum*) [36]. Soybean is widely used for fermented foods preparation containing *doenjang*, *tempeh*, *doubanjiang*, *natto* and *miso*. Their main modifications are microorganisms, additives and the fermentation process. Also, natural flavors such as butter and cheese flavor and fruity aroma were produced by fermentation of Basil wastes [37]. As research has found that extracts of broccoli, red cabbage and ginger -whether in the traditional form or in nano capsules- are rich in antioxidants and can replace industrial antioxidants and the ball mill method of extraction before encapsulation increases the amount of antioxidants by about double, and boosted immunity when used as food additives in the manufacture of lentil soup [38].

2.2.3. Fermented vegetables

Fermented-vegetables contain wide variety of unprocessed materials; for example olives, *cucumber*, pepper, mustard, onion, *radish*, cabbage and ginger [13]. Though, *Sauerkraut* (Germany) and *Kimchi* (Korea) are internationally known got ready by cabbage and special fermentation-procedure for every product [39]. *Kimchi* is got ready by cutting the cabbage into small pieces and addition of seven to fifteen % salt to decrease water content and create environment for augmentation of needed microbes. Treated cabbage is packed in last containers for 2–3 days at 28±2°C. Alternatively, sauerkraut is settled through chopping the cabbage into exact lesser strips, mixed by salt (one to five %) and fermented for two

to three days at 15°C [40]. *Sauerkraut* and *Kimchi* have been projected as “functional-foods” advised by numerous researches acquiring wide variety benefits as improve immune system function, anti-constipation, anticancer and antiobesity [18]. Functional-activities have been established to be in parallel with the ordinary microorganisms mostly probiotics and the bioactive composites as vitamins, phenolics, peptides and amino-acids.

2.2.4. Fermented herbs and fruits

Conversely, fermented plant-based beverages for example vinegar and kombucha (fermented sugared tea) have wonderfully health benefits and documented preparation methods. Vinegars are prepared by diversity of fruits for instance apple, grape and date. Their healthiness benefits containing antihypertensive, anti-oxidant, anti-microbial, antiobesity and anti-diabetic were lately sound acknowledged [41]. Oppositely, kombucha is an earliest drink prepared from sweetened tea by symbiotic-culture of yeast and bacteria [42]. Its healthiness profits contain anti-oxidant, anticancer and antimicrobial. Beverages and fermented plants are frequently addicted in Africa and Asia with fewer common at West nations wherever milk-based fermented-foods are the main [20]. Nevertheless, enlarged wakefulness concerning their healthiness benefits along the current **Covid-19** plague have directed to augment request for beverages and microbial functional foods [43]. *Moringa oleifera* is considered a functional food in itself, because it contains a high percentage of calcium, but the fermentation of *Moringa oleifera* leaves with lactic acid bacteria supported the bioavailability of calcium, both at the in vitro and in vivo level to rats, through a marked increase in the weight, density and thickness of the bone cortex, and body weight of rats, indicating improved calcium bioavailability by fermentation of *Moringa oleifera* leaves [44].

3. Microbial Functional Foods Distribution in Egypt, Africa and the Arab world

3.1. Microbial Functional foods in Egypt and the Arab world

Fesikh comes at the top of the traditional folk dishes to celebrate Sham El-Nessim since the time of the ancient Egyptians. It is the fermentation of whole mullet (Tobara) by natural or industrial methods (in modern times), and fesikh has a very distinctive flavor and aroma. **Amin et al.** [45] were able to control the degree of salting and industrial fermentation, and the role of lactic acid bacteria was shown in reducing the microbial load in general and preventing the growth of coliforms in particular, in addition to the superiority of industrial fermentation than natural in color, texture, flavor and smell, which resulted in

high quality fesikh in a short time. **El-Gendy** [46] referred in detail in his research article to most of the fermented foods in Egypt and the Arab world, and their names differed from one country to another and even from one region to another within the same country. The article focused on the details of traditional manufacturing, which was explained that it did not differ from industrial methods in more developed countries. Of them for example: Rayeb or Laban Matared, Karish cheese, Mish cheese, Laban Zeer (Laban Khad), Kishk, Zabady, Shamsy and Balady bread and an overview of some Sudanese fermented foods. It is remarkable the variation in the chemical composition of the nutritional components of these foods before and after microbial fermentation. Here are some recent pictures of some fermented foods of traditional Egyptian heritage, as shown in the illustrated **Fig. 1**.



Fig. 1. Some traditional Egyptian fermented foods.

3.2. Microbial Functional foods in Africa

Fermented foods vary in African folklore, for example, Fufu, Lafun and Gari from tuber based foods, Ogi, Burukutu, Kunnu-zaki and Pito from cereal based, Iru or Dawadawa, Ogiri and Ugba from legume based, Emu and Oguro from beverage based, Fura, Nunu and Wara-kishi from milk based products [47].

4. Suggested mode of action of physiological function of microbial functional foods

Fermented foods health benefits suggested due to direct and indirect pathways, because of diverse active-substances that were formed through probiotic growth and were not native component naturally found in their ordinary equivalents for example exopolysaccharides, organic-fatty and amino-acids, bacteriocins, peptides, and vitamins [48]. The disease prevention and health-benefits of microbial functional nutrients are owing to amplified formation of bio-active composites as vitamins, peptides, polyphenols, linoleic acid and amino butyric [49]. Effective composites are from two dissimilar

resources containing products produced from unprocessed materials because of elevated acidic pH and hydrolytic enzymes released by probiotics [36].

Fermented foods with animal-based are generally related to health-promoting constituents with alleviation of lactose intolerance, anti-radical, antioxidant and anti-hypertensive activity that are mainly or partly caused by actions of short chains fatty acids and bioactive peptides produced by milk or meat products fermentation. One of the mainly public bio-active peptides which are produced via fermented-meat, milk and oysters are the inhibitory peptides of Angiotensin Converting Enzyme Inhibitory (ACE-I) peptides [50]. Those peptides produced through fermentation of milk by *Lactobacillus* are active against hypertensive (high blood pressure) outcome because of inhibition of angiotensin creation [51]. Other bio-activities published include anti-mutagenic, anti-inflammatory, antihemolytic, and antimicrobial properties [18].

Sausage was stated to excrete ACE-I, anti-thrombotic, anti-microbial, anti-oxidative and immune-modulating activities when *Staphylococcus carnosus* and *Lactobacillus pentosus* were used as an inoculum [52]. Additional report that peptide production with higher ACE-I activity by fermenting *Ruditapes philippinarum* clams with *Bacillus natto* that as well applies anti-cancer activity [53]. Excluding ACE-I production, SCFAs production through human gut microflora fermentation was exposed when investigating the probable health properties of probiotic salami using dietary fibre [54]. **Bartkiene and others** [55] showed that fermentation of meat by *Lactobacillus* can enhance its nutritional and security values because of the creation of numerous anti-microbial composites and degrading toxins naturally existing in meat. **Laranjo et al.** [56] reported that meat toxins which can cause thoughtful health risk containing biogenic amines and polycyclic aromatic hydrocarbons were significantly decreased through the fermentation by LAB starter cultures.

Healthiness-promoting components against hypertension, cancer, oxidation, microbial activities and diabetes because of fermentation of plant sources and plant bio-active composites formatted by pre-handling of unprocessed materials by microbial treatment or via carrying out microbial treatment to the total nutrient product [18]. Probiotic microorganisms and fermented plants have healthiness profits such as; fermented rice bran was exposed to have anticancer properties. Research use dissimilar rice cultivars bran and comparing its metabolites composition with bran composition after fermentation which have significant improvement [57]. **Muhalidin and others** [18] reported that the rice brans have diverse composition and consequently different bio-active compounds structure of fermented rice

bran.

Camellia sinensis after fermentation called “Fu Zhuan” consumption exposed to have both anti-microbial and anti-obesity activities [58]. Tea leaves were fermented with *Eurotium cristatum* fungus displayed augmented quantity of linoleamide, dodecanamide, epicatechin gallate, and stearamide more than tea leaves before fermentation [59]. Ginseng Roots symbolize extra plant including bioactive compounds containing nonsaponins and saponins (ginsenosides), with about fifty ginsenosides recognized to date that offer probable profits to controlling insulin levels and blood sugar glucose [60]. Saponins content of Ginseng roots exceeded by fermentation and exhibit anti-adipogenic, anti-inflammatory, anti-oxidant and anti-diabetic properties [61].

Soybean Fermented foods yield bio-active peptides that indicates healthiness profits as ACE inhibitory and anti-diabetic prosperities. Additional conventionally microbial functional foods as the sauerkraut, *babroo*, *idli* and *kimchi* have also been verified to get anti-microbial, anti-oxidant and probiotic activities.

Critical functions for microorganisms related to plant-based foods contain involvement to advance the resistance actions of immune system. Fermentation works to pre-adapt useful microorganisms native to garden-fresh vegetables to acidic pH and extraordinary lactic-acid contents representative of the colon and to the metabolism of nutritional fiber, principally pectins naturally existing in the gut and the plant material. The microbial treatment improves the adaptation between gut microbes and food microbes in the surrounding environment due to the pH resulting from lactic acid formed in the colon to metabolize dietary fibers, especially pectin, which is naturally present in plants and the colon [54]. Excessive figures of investigations established in the literatures verified healthy effects of plant-based, aquatic-based and animal-based fermented products [13].

Healthiness effects of Microbial functional foods are related to the bio-active components which existing at low concentration or not present in the initial unprocessed materials. Thus, the selection of the starter cultures and the raw resources are identical serious for making of bio-active composites of positive health profits. Hence, the adjustment of the fermentation process must have or not have minimum impact on the user favorite mainly for conventional beverages and microbial functional foods [18].

5. Probable health profits of some microbial functional foods

Microbial treatment develops aroma and flavor of raw materials. Furthermore, fermented foods believed

to offer healthy profits for customer. They improve content of probiotic-bacteria; thus enhance of metabolic-functions available and needed for gastrointestinal tract for resilience anabolism in personality healthiness. Probable healthy profits of microbial functional foods which discovered recently in investigations were based on a wide body of subjective information, and involved such profits as: blood glucose-lowering benefits, antihypertensive activity, anti-diarrheal, and antithrombotic properties [18].

6. Importance of fermented foods

Fermented food spreads from the east to the west, and the main reason for its use is its health benefits, especially for the digestive system. There are several pathways through which fermented food benefits health, such as:

- 1- They contain probiotic organisms such as lactic acid bacteria, and one gram contains at least one million microbial cells, with different concentrations according to the region, age and timing of samples analysis. It has physiological benefits for the intestine through its by-products as immune regulators, through its competition with pathogenic bacteria.
- 2- Health benefits of metabolites resulting from microbial fermentation, for example lactic acid bacteria produce peptides and polyamines that have a healthy effect on the heart, immunity and metabolism.
- 3- Fermentation may convert some compounds into bioactive metabolic compounds. Lactic acid bacteria may convert some phenolic compounds such as flavonoids into bioactive compounds.
- 4- In addition to the benefits of the same fermented food components as prebiotics and vitamins.
- 5- Microbial fermentation can reduce food toxins, soybean fermentation lowers the concentration of phytic acid, and carbohydrate fermentation reduces the sensitivity of some patients with metabolic disorders.

It is worth noting the lack of research on humans to confirm the importance of fermented foods for human health in general and the digestive system in particular, with the exception of kefir, which has received many of your research, so we recommend paying attention to this type of research in light of the global trend of sustainable development for healthy nutrition [62].

7. The relationship between the immune system and fermented foods

Vald'es *et al.* [63] showed that the Immune-system is the most important organ for fighting viruses in their early stages. It has a protocol to deal with various pathogenic viruses as shown in Fig.2. The

human immune system is divided into two main systems: a fast, non-specialized system, and a slow but specialized system. Where they put together successive priorities to improve the condition of the body against viral infection and then respond quickly to remove pathogens by destroying them directly [64].

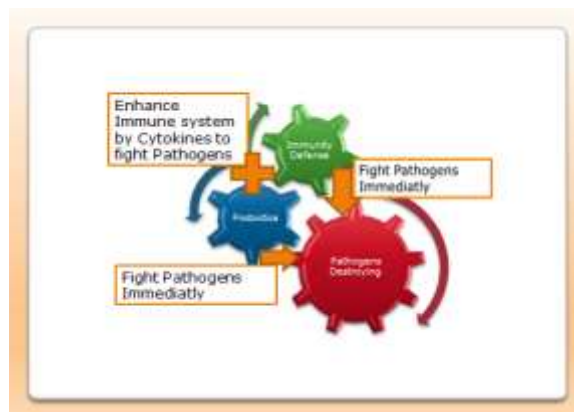


Fig.2. Probiotics Molecular Mechanism to Enrich Immunity Reply

Numerous investigations stated that microbial functional foods probiotics enhanced immunity. On the word of Nishihira *et al.* [65], the probiotics molecular mechanism to enrich immunity reply is by the interaction with T-cells, dendritic-cells and epithelial cells that cause the stimulation of many cytokines containing TGF- β , IL-6, IL-10. Improving immunity response is due to microbial functional foods probiotics activity to produce active metabolites like butyric acid, bacteriocins and extracellular polysaccharides [66]. N'acher-V'azquez *et al.* [67] reported that, dextran (extracellular-polysaccharide) produced by definite probiotic strains established anti-viral properties against infectious hematopoietic necrosis virus. The mechanism of inhibiting the progression of viral cell replication suggested was by the interaction of dextran and the surface of virus cells.

Additionally Fanning *et al.* [68] showed that, the effects on the immune response of the surface exopolysaccharides biosynthesised by *Bifidobacterium breve* UCC2003 were assessed in *in vivo* investigation. The results showed weighty high concentrations of cytokines (one of the initiators of inflammation) as an outcome of pre-using polysaccharides. Immunity mode of action was owing to exopolysaccharides. Conversely, eating probiotics in/ and microbial functional foods are considered as new pioneer to enhance immunity and reducing gastrointestinal diseases. NKC (natural killer cells) are portion of immunity against antigen, inside tumor development and extraneous pathogens [69].

8. Mode of action of probiotics antimicrobial activity

Additionally, microbial functional foods and their probiotics enhance intestinal microorganisms to the approval of healthiness microbes especially *Bifidobacteria* and *Lactobacillus* [70].

The gut microbiota acts actual important part in immunity because of prevent colonization of enteropathogenic, antibodies, natural killer cells cytotoxicity, enhance less inflammations and toxins detoxification [71]. Microbial functional foods are amusing resource of bio-attainable compounds enhance immunity by generating new cells of different organs [72].

Well-adjusted food composition support immunity. Additionally to immune deficiencies diseases, malnutrition principally decreases immunity reply. Consistent with **Calder and Kew** [73] limited consumptions of one or further of these nutrients containing essential fatty acid, essential amino acids, linoleic acid, folic acid, vitamins (A, B6, C, B12 and E), Fe, Cu, Se and Zn affected all types of immunity cells. Fit people generally have enough innate immunity constituent dissimilar in definite collections for example elderly, infants, immune deficiency diseases, patients, undergoing surgery and stressed individuals, these groups are at huge danger of infections because of permanent or temporary weakened immunity [74].

Though, probable healthiness properties of microbial functional foods are restricted to decrease both signs and viral infections. Fermented foods and their bio-active composites were recommended to be shared with traditional treatment to decrease the hospitalization stage for the patients [18].

9. Antiviral activity of fermented foods

Viral infection development in the human body involves many steps containing virus attachment to cell-surface then the delivery of the viral genome to replication location. Accordingly, viral penetration into the cell surface is the most important stage of viral infection [75].

One of the most important causes of common viral infections is respiratory viruses, which usually entails entering the air at a speed of about six liters of air per minute, causing the entry of viruses and foreign bodies as well, in addition to daily habits such as eating and drinking, which may cause the entry of the virus.

Though, virus invasion needs numerous causes for example the absence of the immune system response, accessibility to the infection cite and presence of sufficient viral genome. To prevent the entry of viruses to human body there are numerous defense mechanisms as simplified in **Fig.3**.

9.1. Mechanical mechanism

Through the mechanical union of the respiratory tract body with mucus involving sub-epithelial mucous-secreting glands, mucous-secreting goblet cells and ciliated cells. The viruses entering through upper respiratory tract or the nasal cavity stuck within secretion, passed to the end of the throat, and swell.

It is also worth mentioning the role of the lower part of the respiratory system, whether the mechanical movement to expel mucus and foreign particles or the presence of the macrophage, which also fights viruses and foreign particles alike. Alternatively, the alimentary tract is obviously protected due to bile detergents, protease enzymes, pH and the secretion that could inhibit the access of viruses and inhibit infections [76].

Furthermore, the ciliary act in the lower respiratory tract show significant task to eliminate any particles stuck in the lung-mucus to the throat. The lowest portions of the respiratory tract have macrophages covering the alveoli ingest and terminate particles containing viruses.

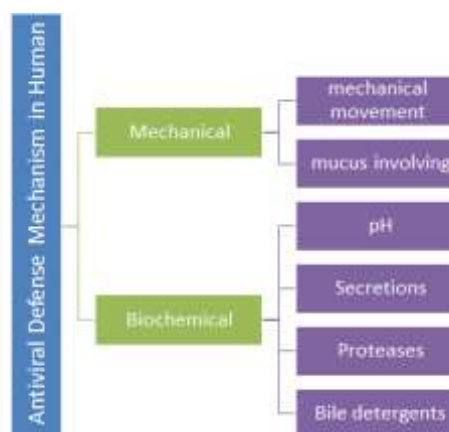


Fig.3. Antiviral Defense Mechanism in Human.

This calls for reference regarding nutrition and the coronavirus pandemic, enteric viruses and their access to the digestive system through eating foods, and one of the most important points that require discussion is their incomprehensible ability to live within these difficult conditions in the digestive system. [77].

Studies have proven that consuming lactic acid bacteria (leading in the field of fermented foods) shows significant viral resistance to micro-viridae viruses, bearing in mind that vaccination is the traditional factor in viral resistance. Yet, viral infections contain a wider range of virus sub-types not known by the long-term immune response. The life round of viruses containing their attachment, replication and separation is completely happened in the host cells cytoplasm [18].

Therefore, numerous advanced of medications against viruses. Medications are aiming enzymes of virus containing integrase, protein hydrolase and polymerase. Additional collection of anti-viral medications goals host cell factors and/or the viral proteins to prevent viral replication in the cells [78]. Nitazoxanide maturing hem agglutinin of the virus is reported to have high anti-influenza probable [79]. Furthermore, definite medications for example MBX-300 cooperate with receptors immunity and inhibit attachment between virus and cell surface. But, antiviral drugs have side effects containing diarrhoea and nausea, and can cause severe side effects as liver injury and kidney problems. In addition, extreme use of anti-viral drugs affected emerging of virus resistance because of mutations. So, high demand saw for unconventional anti-viral means that could decrease the severity and risk of pathogenicity by virus.

Lately, probiotic bacteria were broadly considered for their wide variety of anti-viral action. Mainstream of probiotics because of lactic acid bacteria (LAB) with usually observed as immune-modulatory actions and safe status. These probiotics are great plentiful within numerous ordinary microbial functional foods from animal source or plant source. Furthermore, the probiotics with wide range of anti-microbial prosperities was proposed to be involved in the conventional Microbial functional foods to improve their properties containing anti-viral [18].

10. Antiviral activity of probiotics of microbial functional foods

Alternatively, the bioactive substances of the microbial function foods that are produced by the probiotics bacteria act a vital function to increase the antiviral-activity. Hence, the probiotics have been renamed to "Immunobiotics" because of their antiviral activity [80]. Lactobacilli excite immunity response by complement activation, rising lysozyme, increasing the formation of super-oxide and phagocytic activity [81].

Anti-viral activity mechanism is actual indistinct if it is because of the probiotic bio-active compounds, the probiotic cells and/or the mix of bioactive compounds and cells. The fermented foods anti-viral mechanism is not fit identified because of constricted clinical investigations texted everyday intake for extended period [82].

Instead, probiotics mechanism has been conventional by numerous fine planned clinical investigations that suggested necessary doses daily [83]. Influenza virus is the most ordinary viruse that can reason severe respiratory tract infection and cause high morbidity and mortality [84]. Consequently, many researches assess probable anti-viral action of some probiotic

isolated from fermented foods against influenza virus [85].

Lactobacillus plantarum YU isolated from Japanese fermented foods has anti-viral activity able to decrease influenza A virus replication because of the development of Th1 immune responses [86]. **Park et al.** [87] reported that the probiotic *Lactobacillus plantarum* DK119 strain isolated from fermented cabbage (kimchi) established full-percentage defense against influenza A viruses.

Covid-19 infection altered the patients gut microorganisms in spite of their age and the clinical data demonstrated considerable growth in pathogenic populations above the friendly bacteria [88]. Rise in the pathogenic populations drive stresses the immune-system and meaningfully decreases its function in Covid-19 resistance [89].

Consequently, probiotics and fermented foods consumption can return and equilibrium intestinal microbes by enhancing probiotics causing decrease immunity stress and increase antiviral activity. The human microbiota refers to the traditional microorganisms that human beings host. The little mortality speed affected by Covid-19 in Middle East, Africa, *Asia* and East-Europe is because of their diets which have wide variety of microbial functional foods. Popular of those conventional fermented foods include elevated quantities of probiotics belong mostly to the genus *Lactobacillus* consumption that is related to healthy profits and protection condition [18]. Thus, outcome of prior investigations established hopeful function of probiotics to decrease the severity of the symptoms or inhibit viral infections. So, there is elevated probability to consume probiotics in arrangement in the company of traditional management would have the prospective to augment the immunity purpose and decrease infection [18].

11. Success Story

It is worth noting that I have an actual experience in this regard, as I'm suffering Rheumatoid Arthritis disease several years ago, which began with severe consecutive attacks until it reached the point of stiffness and swelling of all joints of the body for a whole year, which made me lose the ability to move during that year, which I was taking suggested medications for rheumatoid arthritis, but the condition was getting worse. Then, I read about the importance of lifestyle modification to treat immune diseases, and I went to "Siwa" Oasis for a treatment trip that lasted only ten days, and resulted in a strong and rapid improvement, and I came back from there and could move. Since then, I have been following my body's response to any type of food to avoid developing seizures in the beginning. This method has succeeded in stabilizing my health for more than three years.

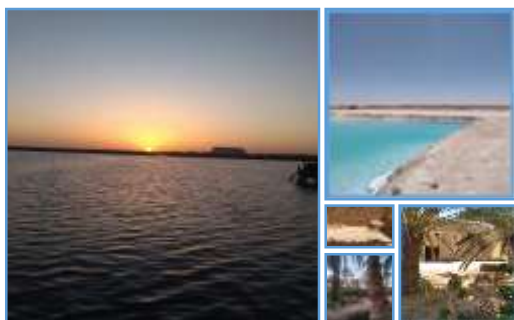


Fig. 4. Siwa Oasis life style.

After my return from Siwa's trip, I went to study the basics of nutrition at the National Institute of Nutrition in Egypt to develop my awareness of a healthy lifestyle, especially the nutritional pattern, I have received a specialized training course in therapeutic nutrition, and I am trying to direct the content of my research in the coming period to nutrition research and its effects, and I will publish my case as a study soon.

Therefore, I advise all healthy people, in the first place before patients, to always monitor their nutrition and life style from birth to life.

12. Conclusions

It seems clear that modifying the lifestyle and reaching the balance of food components, whether from direct feeding without technological treatments for food processing, such as some plant sources of nutrition, or food manufacturing processes for animal and plant sources, or by traditional methods of preserving and processing food such as food fermentation and its impact on stimulating the immune system by affecting the gut microflora.

13. Conflicts of interest

There are no conflicts to declare.

14. References

- [1] Havrlentová, M.; Petrušáková, Z.; Burgárová, A.; Gago, F.; Hlinková, A. and Šturdík, E. (2011) Cereal β -glucans and their Significance for the Preparation of Functional Foods – A Review. *Czech J. Food Sci.*, 29(1): 1–14.
- [2] Walker, W.A. and Iyengar, R.S. (2015) Breast milk, microbiota, and intestinal immune homeostasis. *Pediatric Research*, 77(1–2): 220–228.
- [3] Fouda, G.G.; Martinez, D.R.; Swamy, G.K.; and Permar, S.R. (2018). The Impact of IgG transplacental transfer on early life immunity. *Immunohorizons*, 2(1): 14–25.
- [4] Duijts, L.; Jaddoe, V.W.; Hofman, A. and Moll, H.A. (2010) Prolonged and exclusive breastfeeding reduces the risk of infectious diseases in infancy. *Pediatrics*, 126(1): e18–e25.
- [5] Wada, Y. and Lonnerdal, B. (2020). Bioactive peptides derived from human milk proteins: An update. *Current Opinion in Clinical Nutrition and Metabolic Care*, 23(3): 217–222.
- [6] Victora, C.G.; Bahl, R.; Barros, A.J.; Franca, G.V.; Horton, S. and Krasevec, J. (2016) Lancet Breastfeeding Series, G. Breastfeeding in the 21st century: epidemiology, mechanisms, and lifelong effect. *Lancet*, 387(10017): 475–490.
- [7] Patil, A.P.; Patil, T.M.; Shinde, A.R.; Vakhariya, R.R.; Mohite S.K. and Magdum, C.S. (2021) Nutrition, Lifestyle and Immunity: Maintaining Optimal Immune Function and Boost Our Immunity. *Asian Journal of Pharmaceutical Research and Development*, 9(3): 129–136.
- [8] Yeşilyurt, N.; Yılmaz, B.; Ağagündüz, D. and Capasso, R. (2021) Involvement of Probiotics and Postbiotics in the Immune System Modulation. *Biologies* 2021 (1): 89–110.
- [9] Esmail, Eman A.; Fathy, Hayam M.; Sedik, M. Z. and Mohamed, A. F. (2022). Assessment the effect of prebiotics, probiotics and synbiotics on Hyperlipidemia. *Egypt. J. Chem.* Vol. 65, No. 6 pp. 421 – 432.
- [10] Chudzik, A.; Orzyłowska, A.; Rola, R. and Stanisł, G.J. (2021) Probiotics, Prebiotics and Postbiotics on Mitigation of Depression Symptoms: Modulation of the Brain–Gut–Microbiome Axis. *Biomolecules*, 2021(11): 1000.
- [11] Ganatsios, V.; Nigam, P.; Plessas, S. and Terpou, A. (2021) Kefir as a Functional Beverage Gaining Momentum towards Its Health Promoting Attributes. *Beverages* 2021(7): 48.
- [12] Brown, L.; Caligiuri, S.P.B.; Brown, D. and Pierce, G.N. (2018) Clinical trials using functional foods provide unique challenges. *J. Funct. Foods*, 45: 233–238.
- [13] Tamang, J.P.; Watanabe, K. and Holzapfel, W.H. (2016) Review: Diversity of microorganisms in global fermented foods and beverages. *Frontiers in Microbiology*, 7: 377.
- [14] Anukam, K.C. and Reid, G. (2007) Probiotics: 100 years (1907–2007) after Elie Metchnikoff's observation. *Communicating Current Research and Educational Topics and Trends in Applied Microbiology*, 1: 466–474.
- [15] Leeuwendaal, N. K.; Stanton, C.; O'Toole P. W. and Beresford, T. P. (2022) Fermented Foods, Health and the Gut Microbiome. *Nutrients* 2022, 14, 1527. <https://doi.org/10.3390/nu14071527>.
- [16] Martin, J. G. P. (2022) Methods applied in studies about fermented foods. *J Microbiol Exp.* 2022;10 (2):59–63.
- [17] Delgado, S.; Rachid, C.T.; Fern'andez, E.; Rychlik, T.; Alegría, 'A. and Peixoto, R.S. (2013) Diversity of thermophilic bacteria in raw, pasteurized and selectively cultured milk, as assessed by culturing, PCR-DGGE and pyrosequencing. *Food Microbiology*, 36(1): 103–111.

- [18] Muhialdin, B.J.;Zawawi, N.;Abdull-Razis, A.F.;Bakar, J. and Zarei, M. (2021) Antiviral activity of fermented foods and their probiotics bacteria towards respiratory and alimentary tracts viruses. *Food Control*, 127: 108140.
- [19] El-Sayed, A. S.; Ibrahim, H. and Farag, M. A. (2022) Detection of Potential Microbial Contaminants and Their Toxins in Fermented Dairy Products: a Comprehensive Review. *Food Analytical Methods* (2022) 15:1880–1898. <https://doi.org/10.1007/s12161-022-02253-y>.
- [20] Tamang, J.P.; Cotter, P.D.; Endo, A.; Han, N.S., Kort, R.; Liu, S.Q. and Hutkins, R. (2020) Fermented foods in a global age: East meets West. *Comprehensive Reviews in Food Science and Food Safety*, 19(1): 184–217.
- [21] Tesfaye, W.; Suarez-Lepe, J.A.;Loira, I.;Palomero, F. andMorata, A. (2019) Dairy and nondairy-based beverages as a vehicle for probiotics, prebiotics, and symbiotics: Alternatives to health versus disease binomial approach through food. In *Milk-based beverages* (pp. 473–520).Woodhead Publishing.
- [22] Wouters, J.T.; Ayad, E.H.;Hugenholtz, J.andSmit, G. (2002)Microbes from raw milk for fermented dairy products.*International Dairy Journal*, 12(2–3): 91–109.
- [23] Delavenne, E.; Ismail, R.; Pawtowski, A.; Mounier, J.; Barbier, G.; and Le-Blay, G. (2013) Assessment of lactobacilli strains as yogurt bioprotective cultures. *Food Control*, 30(1): 206–213.
- [24] Hamed, S.F.; Soliman, T. N.; Hassan, L.K. and Abo-Elwafa, Ghada.A. (2019). Preparation of Functional Yoghurt Fortified with Fish Oil-In-Water Nanoemulsion. *Egypt.J.Chem. Vol. 62*, Special Issue (Part 1), pp. 301 – 314.
- [25] McSweeney, P.L.H.;Ottogalli, G. and Fox, P.F. (2004) Diversity of cheese varieties: An overview. *Cheese: Chemistry, Physics and Microbiology*, 2:1–23.
- [26] Muhialdin, B.J. andAlgoory, H.L. (2018) Identification of low molecular weight antimicrobial peptides from Iraqi camel milk fermented with *Lactobacillus plantarum*.*PharmaNutrition*, 6(2): 69–73.
- [27] El- Rhmany, Amira S.; El- Dardiry, Amal; Abdelazez, A. and Khalil, O. S. F. (2022). Functional low-fat labneh fortified with resistant potato starch as prebiotic and assessed physicochemical, microbiological, and sensory properties during storage. *Egypt. J. Chem. Vol. 65*, No. 12 pp. 555 – 568.
- [28] Khalil, O. S. F.; Abdelazez, A. and El-Dardiry Amal (2022). Combination of Prebiotic Inulin and Probiotics intervention on the Physicochemical, Microbiological, and Sensory Properties of an Innovative Synbiotic Ras Cheese. *Egypt. J. Chem. Vol. 65*, No. SI:13B pp. 629–639.
- [29] Abd El-masked, Fatma S.; El-Gendy, Marwa H.; Metwally, A. M. and El Nawawy, M. A. (2023). Properties of Fermented Permeate Beverages Enriched With Barley, Oat and Black Rice Extract. *Egypt. J. Chem. Vol. 66*, No. 7 pp. 319 – 327.
- [30] Hassan, Fatma, A. M.; Hussein, A. M. S.; Abd El-Gawad, Mona A. M.; Enab, A. K.; Bayoumi, Hala M. and Mabrouk, Ahmed M. M. (2023). Preparation of Functional Milk Beverages Fortified with Coconut Extract. *Egypt. J. Chem. Vol. 66*, No. 5 pp. 349 – 356.
- [31] Mohamed, H.N.; Man, Y.C.; Mustafa, S. and Manap, Y.A. (2012) Tentative identification of volatile flavor compounds in commercial budu, a Malaysian fish sauce, using GCMS.*Molecules*, 17(5): 5062–5080.
- [32] Kumar, P.; Chatli, M.K.; Verma, A.K.; Mehta, N.; Malav, O.P. and Kumar, D. (2017) Quality, functionality, and shelf life of fermented meat and meat products: A review.*Critical Reviews in Food Science and Nutrition*, 57(13): 2844–2856.
- [33] Legrand, T.P.; Wynne, J.W.;Weyrich, L.S. and Oxley, A.P. (2020)A microbial sea of possibilities: Current knowledge and prospects for an improved understanding of the fish microbiome. *Reviews in Aquaculture*, 12(2): 1101–1134.
- [34] Lv, X.; Li, Y.; Cui, T.; Sun, M.; Bai, F.; Li, X. and Yi, S. (2020)Bacterial community succession and volatile compound changes during fermentation of shrimp paste from Chinese Jinzhou region. *LWT-Food Science and Technology*, 122: 108998.
- [35] Farouk, A.; Abd El- Mageed, Magda and Shaaba, H. (2022). Influence of appropriate starter cultures on the sensory qualities and volatiles of fermented broccoli and onion pickle. *Egypt. J. Chem. Vol. 65*, No. 2 pp. 93 - 101.
- [36] Adebo, O.A. and Gabriela Medina-Meza, I. (2020) Impact of fermentation on the phenolic compounds and antioxidant activity of whole cereal grains: A mini review. *Molecules*, 25(4): 927.
- [37] Mahmoud, Engy; Ramadan, Manal; Ismail, M.; Fadel, M. and Abass, M. (2022). Production of Flavors from Agro waste of *Ocimumbasilicum* L. by Different Microorganisms Using Solid-State Fermentation. *Egypt. J. Chem. Vol. 65*, No. 7, pp. 259 – 273.
- [38] Mohamed, Eman H.; Ebeid, H. M.; Ashoush, I. S.; Mahmoudc, K. F.; Albehairyra, S. A. (2023). Nano-Capsulation of Ginger, Red Cabbage and Broccoli Ball Mill Extracts As Sources of Anti-Oxidant and Anti-Cancer and Application in Lentil Soup Powder. *Egypt. J. Chem. Vol. 66*, No. 7 pp. 361 – 379.
- [39] Patra, J.K.; Das, G.; Paramithiotis, S. and Shin, H.S. (2016)Kimchi and other widely consumed traditional fermented foods of Korea: A review. *Frontiers in Microbiology*, 7: 1493.
- [40] Palani, K.; Harbaum-Piayda, B.;Meske, D.; Keppler, J.K.; Bockelmann, W. and Heller, K.J. (2016) Influence of fermentation on glucosinolates and glucobrassicin degradation products in sauerkraut.*Food Chemistry*, 190: 755–762.
- [41] Ho, C.W.; Lazim, A.M.; Fazry, S.; Zaki, U.K.H.H. and Lim, S.J. (2017) Varieties, production, composition and health benefits of vinegars: A review. *Food Chemistry*, 221: 1621–1630.

- [42] Chakravorty, S.; Bhattacharya, S.; Chatzinotas, A.; Chakraborty, W.; Bhattacharya, D. and Gachhui, R. (2016) Kombucha tea fermentation: Microbial and biochemical dynamics. *International Journal of Food Microbiology*, 220: 63–72.
- [43] Antunes, A.E.; Vinderola, G.; Xavier-Santos, D. and Sivieri, K. (2020) Potential contribution of beneficial microbes to face the COVID-19 pandemic. *Food Research International*, 136: 109577.
- [44] Dai, J.; Tao, L.; Shi, C.; Yang, S.; Li, D.; Sheng, J. and Tian, Y. (2020). Fermentation Improves Calcium Bioavailability in *Moringa oleifera* leaves and Prevents Bone Loss in Calcium-deficient Rats. *Food Sci Nutr*. 2020;8:3692–3703. DOI: 10.1002/fsn3.1653.
- [45] Amin, H. F.; Ahmed, O. M. and Attia, M. T. (2020). Chemical, Microbial and Organoleptic Properties of Egyptian Fesikh Produced by Traditional and Artificial Fermentation Techniques. *Aqu. Sci. & Fish Res.* 1 (2020) 17-22. DOI:10.21608/asfr.2020.48180.1009
- [46] El-Gendy, S. M. (1983) Fermented Foods of Egypt and the Middle East. *Journal of Food Protection*. Vol. 46, No.4 Pages 358-367 (April 1983) Copyright, International Association of Milk, Food and Environmental Sanitarians.
- [47] Obafemi, Y. D.; Oranusi, S. U.; Ajanaku, K. O.; Akinduti, P. A.; Leech, J. and Cotter, P. D. (2022) African fermented foods: overview, emerging benefits, and novel approaches to microbiome profiling. *npj Science of Food* (2022) 6:15 ; <https://doi.org/10.1038/s41538-022-00130-w>.
- [48] Mapelli-Brahm, P.; Barba, F.J.; Remize, F.; Garcia, C.; Fessard, A.; Mousavi-Khaneghah, A. and Mel'endez-Martínez, A.J. (2020) The impact of fermentation processes on the production, retention and bioavailability of carotenoids: An overview. *Trends in Food Science and Technology*, 99:389–401.
- [49] Hayes, M. and García-Vaquero, M. (2016) Bioactive compounds from fermented food products (pp. 293–310). *Novel Food Fermentation Technologies*.
- [50] Izquierdo-González, J.J.; Amil-Ruiz, F.; Zazzu, S.; Sánchez-Lucas, R.; Fuentes-Almagro, C.A.; and Rodríguez-Ortega, M.J. (2019) Proteomic analysis of goat milk kefir: Profiling the fermentation-time dependent protein digestion and identification of potential peptides with biological activity. *Food Chemistry*, 295: 456–465.
- [51] Wang, J.; Li, C.; Xue, J.; Yang, J.; Zhang, Q. and Zhang, H. (2015) Fermentation characteristics and angiotensin I-converting enzyme-inhibitory activity of *Lactobacillus helveticus* isolate H9 in cow milk, soy milk, and mare milk. *Journal of Dairy Science*, 98(6): 3655–3664.
- [52] Mora, L.; Escudero, E.; Aristoy, M.C. and Toldrà, F. (2015) A peptidomic approach to study the contribution of added casein proteins to the peptide profile in Spanish dryfermented sausages. *International Journal of Food Microbiology*, 212: 41–48.
- [53] Chen, Y.; Li, C.; Xue, J.; Kwok, L.Y.; Yang, J. and Zhang, H. (2015) Characterization of angiotensin-converting enzyme inhibitory activity of fermented milk produced by *Lactobacillus helveticus*. *Journal of Dairy Science*, 98(8): 5113–5124.
- [54] Pérez-Díaz, I.M. (2019) Fermented vegetables as vectors for relocation of microbial diversity from the environment to the human gut. In *How fermented foods feed a healthy gut microbiota* (pp. 91–123). Cham: Springer.
- [55] Bartkiene, E.; Bartkevics, V.; Mozurienė, E.; Lele, V.; Zadeike, D. and Juodeikiene, G. (2019) The safety, technological, nutritional, and sensory challenges associated with lactofermentation of meat and meat products by using pure lactic acid bacteria strains and plant-lactic acid bacteria bioproducts. *Frontiers in Microbiology*, 10: 1036.
- [56] Laranjo, M.; Potes, M.E. and Elias, M. (2019) Role of starter cultures on the safety of fermented meat products. *Frontiers in Microbiology*, 10: 853.
- [57] Ryan, E.P. (2011). Bioactive food components and health properties of rice bran. *Journal of the American Veterinary Medical Association*, 238(5): 593–600
- [58] Kang, D.; Su, M.; Duan, Y. and Huang, Y. (2019) *Eurotium cristatum*, a potential probiotic fungus from Fuzhuan brick tea, alleviated obesity in mice by modulating gut microbiota. *Food and Function*, 10(8): 5032–5045.
- [59] Keller, A.C.; Weir, T.L.; Broeckling, C.D. and Ryan, E.P. (2013) Antibacterial activity and phytochemical profile of fermented *Camellia sinensis* (fuzhuan tea). *Food Research International*, 53(2): 945–949.
- [60] Oh, M.R.; Park, S.H.; Kim, S.Y.; Back, H.I.; Kim, M.G.; Jeon, J.Y. and Park, T.S. (2014) Postprandial glucose-lowering effects of fermented red ginseng in subjects with impaired fasting glucose or type 2 diabetes: A randomized, double-blind, placebo-controlled clinical trial. *BMC Complementary and Alternative Medicine*, 14(1): 237.
- [61] Hwang, J.E.; Kim, K.T. and Paik, H.D. (2019) Improved antioxidant, anti-inflammatory, and anti-adipogenic properties of hydroponic ginseng fermented by *Leuconostoc mesenteroides* KCCM 12010P. *Molecules*, 24(18): 3359.
- [62] Dimidi, E.; Cox, S. R.; Rossi, M. and Whelan, K. (2019). Fermented Foods: Definitions and Characteristics, Impact on the Gut Microbiota and Effects on Gastrointestinal Health and Disease. *Nutrients* 2019, 11, 1806; doi:10.3390/nu11081806.
- [63] Vald'es, I.; Lazo, L.; Hermida, L.; Guillen, G.E. and Gil González, L. (2019) Can complementary prime-boost immunization strategy be an alternative and promising vaccine approach against dengue virus? *Frontiers in Immunology*, 10: 1956.
- [64] Murray, P.J. and Wynn, T.A. (2011) Protective and pathogenic functions of macrophage

- subsets. *Nature Reviews Immunology*, 11(11): 723–737.
- [65] Nishihira, J.; Nishimura, M.; Moriya, T.; Sakai, F.; Kabuki, T. and Kawasaki, Y. (2018) *Lactobacillus gasser* potentiates immune response against influenza virus infection. In *Immunity and inflammation in health and disease* (pp. 249–255). Academic Press.
- [66] Li, Q. and Ganzle, M.G. (2020) Host-adapted lactobacilli in food fermentations: Impact of metabolic traits of host adapted lactobacilli on food quality and human health. *Current Opinion in Food Science*, 31: 71–80.
- [67] Nacher-Vazquez, M.; Ballesteros, N.; Canales, A.; Saint-Jean, S.R.; Pérez-Prieto, S.I.; Prieto, A. and López, P. (2015) Dextrans produced by lactic acid bacteria exhibit antiviral and immunomodulatory activity against salmonid viruses. *Carbohydrate Polymers*, 124: 292–301.
- [68] Fanning, S.; Hall, L.J.; Cronin, M.; Zomer, A.; MacSharry, J.; Goulding, D. and van-Sinderen, D. (2012) Bifidobacterial surface-exopolysaccharide facilitates commensal-host interaction through immune modulation and pathogen protection. *Proceedings of the National Academy of Sciences*, 109(6): 2108–2113.
- [69] Vivier, E. and Ugolini, S. (2011) Natural killer cells: From basic research to treatments. *Frontiers in Immunology*, 2: 18.
- [70] Pasoli, E.; De-Filippis, F.; Mauriello, I.E.; Cumbo, F.; Walsh, A.M.; Leech, J. and Ercolini, D. (2020) Large-scale genome-wide analysis links lactic acid bacteria from food with the gut microbiome. *Nature Communications*, 11(1): 1–12.
- [71] Ashaolu, T.J. (2020) Immune boosting functional foods and their mechanisms: A critical evaluation of probiotics and prebiotics. *Biomedicine and Pharmacotherapy*, 130: 110625.
- [72] Oliphant, K. and Allen-Vercoe, E. (2019) Macronutrient metabolism by the human gut microbiome: Major fermentation by-products and their impact on host health. *Microbiome*, 7(1): 1–15.
- [73] Calder, Philip C. and Kew, Samantha (2002) The immune system: A target for functional food? *The British J. of Nutrition*, 88 (Suppl. 2): S165–177.
- [74] Gill, H.S. (1998) Stimulation of the immune system by lactic cultures. *International Dairy Journal*, 8(5–6): 535–544.
- [75] Helenius, A. (2018) Virus entry: Looking back and moving forward. *Journal of Molecular Biology*, 430(13): 1853–1862.
- [76] Doms, R.W. (2016) Basic concepts: A step-by-step guide to viral infection. In *Viral Pathogenesis* (pp. 29–40). Academic Press.
- [77] Miranda, R.C. and Schaffner, D.W. (2019) Virus risk in the food supply chain. *Current Opinion in Food Science*, 30: 43–48.
- [78] Heylen, E.; Neyts, J. and Jochmans, D. (2017) Drug candidates and model systems in respiratory syncytial virus antiviral drug discovery. *Biochemical Pharmacology*, 127: 1–12.
- [79] McKimm-Breschkin, J.L.; Jiang, S.; Hui, D.S.; Beigel, J.H.; Govorkova, E.A. and Lee, N. (2018) Prevention and treatment of respiratory viral infections: Presentations on antivirals, traditional therapies and host-directed interventions at the 5th ISIRV Antiviral Group conference. *Antiviral Research*, 149: 118–142.
- [80] Villena, J.; Vizoso-Pinto, M.G. and Kitazawa, H. (2016) Intestinal innate antiviral immunity and immunobiotics: Beneficial effects against rotavirus infection. *Frontiers in Immunology*, 7: 563.
- [81] Harikrishnan, R.; Balasundaram, C. and Heo, M.S. (2010) Effect of probiotics enriched diet on *Paralichthys olivaceus* infected with lymphocystis disease virus (LCDV). *Fish and Shellfish Immunology*, 29(5): 868–874.
- [82] Aslam, H.; Green, J.; Jacka, F.N.; Collier, F.; Berk, M. and Pasco, J. (2020) Fermented foods, the gut and mental health: A mechanistic overview with implications for depression and anxiety. *Nutritional Neuroscience*, 23(9): 659–671.
- [83] Rozga, M.; Cheng, F.W. and Handu, D. (2020) Effects of probiotics in conditions or infections similar to covid-19 on health outcomes: An evidence analysis center scoping review. *Journal of the Academy of Nutrition and Dietetics*, 121(3): 1841–1854.
- [84] Taubenberger, J.K. and Morens, D.M. (2008) The pathology of influenza virus infections. *Annual Review of Pathology: Mechanisms of Disease*, 3: 499–522.
- [85] Jung, Y.J.; Lee, Y.T.; Le Ngo, V.; Cho, Y.H.; Ko, E.J.; Hong, S.M. and Kim, C.H. (2017) Heat-killed *Lactobacillus casei* confers broad protection against influenza A virus primary infection and develops heterosubtypic immunity against future secondary infection. *Scientific Reports*, 7(1): 1–12.
- [86] Kawashima, T.; Hayashi, K.; Kosaka, A.; Kawashima, M.; Igarashi, T.; Tsutsui, H. and Obata, A. (2011) *Lactobacillus plantarum* strain YU from fermented foods activates Th1 and protective immune responses. *International Immunopharmacology*, 11(12): 2017–2024.
- [87] Park, M.K.; Vu, N.G.O.; Kwon, Y.M.; Lee, Y.T.; Yoo, S.; Cho, Y.H.; Moon, D.W. (2013) *Lactobacillus plantarum* DK119 as a probiotic confers protection against influenza virus by modulating innate immunity. *PLoS One*, 8(10): e75368.
- [88] Zuo, T.; Zhang, F.; Lui, G.C.; Yeoh, Y.K.; Li, A.Y.; Zhan, H. and Ng, S.C. (2020) Alterations in gut microbiota of patients with COVID-19 during time of hospitalization. *Gastroenterology*, 159(3): 944–955.
- [89] Shook, N.J.; Sevi, B.; Lee, J.; Oosterhoff, B. and Fitzgerald, H.N. (2020) Disease avoidance in the time of COVID-19: The behavioral immune system is associated with concern and preventative health behaviors. *PLoS One*, 15(8): Article e0238015.