# Fermented Foods in Respiratory Health

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Fermented foods state that "foods that have been transformed due to fermentation process via microbes such as bacteria, yeast, fungi and their enzymes". The word fermentation is derived from the Latin word "*fervere*" meaning "to boil" or "fermentare" meaning "to leaven". By simple means, fermented foods (FFs) are microbiologically processed raw materials (vegetables, meats, etc.).

fermented foods | probiotics | Lactobacillus | respiratory infection

## 1. Introduction

Fermented foods state that "foods that have been transformed due to fermentation process via microbes such as bacteria, yeast, fungi and their enzymes". The word fermentation is derived from the Latin word "*fervere*" meaning "to boil" [1] or "fermentare" meaning "to leaven" [2]. By simple means, fermented foods (FFs) are microbiologically processed raw materials (vegetables, meats, etc.). The International Scientific Association for Probiotics and Prebiotics defined FFs as "foods made through desired microbial growth and enzymatic conversions of food components" [3]. FFs are mainly available in the form of pickles, fermented juices, dairy, and meat products. The use of FFs varies depending on the availability of raw materials, region, and ethnicity [4]. FFs and beverages are enzymatically altered by the microorganisms in such a way that they taste and smell appealing to humans for consumption [5]. In addition, this improves the palatability of foods and insists on preservation [6]. The traditional preparation of FFs involves the natural fermentation process. The microorganisms responsible for the fermentation process define the products' quality and type. Lactic acid bacteria (LAB), *Bacillus* spp., yeast, and molds are the commonly found critical microbes in fermented food products [7]. The FFs have been used to improve health status. Even though FFs have a long history, recently, due to increased attention from biologists, technologists, and consumers, many studies have been engaged in demonstrating that FFs can enhance gastrointestinal and systemic health [8][9][10][11]. The beneficial effects of the continuous consumption of FFs on inflammatory bowel disease [12], immunity boost [13], oxidative stress [14], cardiovascular diseases [15] cognitive enhancement [16], anxiety [17], and metabolic disorders [18] have been previously described. Nutritional intervention with fermented foods enhances immune function and alleviates upper respiratory tract infections (URTIs) [19], as well as improving intestinal and extra-intestinal health [20]. Zhang et al. [21] reported that daily consumption of Qingrun yogurt (fermented milk) for 12 weeks reduces the common cold in adults living in Northern China [21]. Ingestion of LAB-fermented food modulates the gut microbiome through their health promoting properties and production of metabolites such as biopeptides, vitamins, organic acids, bacteriocins, and anti-microbial compounds during fermentation [22].

Respiratory tract infections, such as URTIs and lower respiratory tract infections (LRTI), are a universal health threat among developed and developing countries [23]. LRTI, such as pneumonia, can be fatal in young and elderly individuals [24]. Viruses are responsible for causing more than 90% of URTIs [25]. The only way to prevent RTIs is to improve the immune function [19]. URTIs are infection in the mucosal surfaces of upper airways, such as the nose, sinuses, pharynx, or larynx, resulting in non-allergic rhinitis, acute sinusitis, acute pharyngitis/laryngitis, acute epiglottis, and acute otitis media [26][27][28]. Some of the viruses responsible for common respiratory infections are the influenza virus, respiratory syncytial virus, parainfluenza virus, rhinovirus, enterovirus, adenovirus, coronavirus, and others [28][29][30]. The influenza virus causes serious health threats, which may lead to morbidity [31]. The recent pandemic SARS-COV-2 virus and its associated respiratory infections create an alarming call about strengthening immune responses against a wide range of organisms that cause RTIs [32]. Acute respiratory infections in children is a serious health threat across the world, which also results in increased morbidity and mortality [33]. In this COVID-19 pandemic situation, respiratory and gastrointestinal tract infections are the most severe health issues affecting human beings of all age groups, especially children. Several treatments are available to treat respiratory infection [34]. However, a well-balanced diet, preferably comprised of probiotics or fermented functional foods, is also crucial for maintaining body homeostasis and fighting against respiratory and alimentary tract viruses. The probiotics in FFs enhance antiviral activity by producing bioactive compounds. These bioactive compounds improve immune function and lessen viral infections [35]. Naturally, the human body encompasses mechanical defense systems against the respiratory tract viruses, such as mucus, ciliated cells, and macrophages, which ward off the virus particles entering the system [36][37]. The LAB in FFs exhibit antiviral activity against the respiratory tract virus [38]. Certain FFs have proven to have anti-influenza functions. For example, kimchi, which contains Lactobacillus casei DK128, possesses antiviral activity against the influenza H3N2 virus [39]. The intervention of Lactobacillus rhamnosus GG in fermented milk product for 3 months demonstrated the prevention of respiratory discomforts in children attending daycare centers [40]. Probiotic delivery through fermentation is a combined approach; thus, probiotics in fermented foods produces added benefits and is advantageous over non-fermented products [41][42].

## 2. Traditional and Modern Aspects of the Production of FFs

Fermented food products, such as wine, beer, dairy products, and baked foods, are emerging globally and date back to 13,000 BC [43]. Fermentation can be categorized into indigenous fermentation (FFs produced traditionally by spontaneous fermentation) used for small scale production and technological fermentations (FFs produced using modern technological facilities) used for industrial scale production [2][43]. Extended shelf life, food safety, and improved organoleptic properties, such as aroma, taste, and texture, are important factors for fermentation practices [44]. The FFs play a prominent role in the socio-economic status of developing countries. The fermentation involves various biochemical processes by microorganisms and enzymes, resulting in significant food modification. The evolution of fermentation has been initiated ever since the beginning of human civilization. The traditional fermentation method is uncontrolled, as it depends on microorganisms from the environment [45]. The traditional fermentation process is of great economic value and reasonable food preservation method. Traditionally, the fermentation of foods occurs through two methods. Natural fermentation of foods and beverages are known as ‘wild ferments’ [46], where fermentation occurs by naturally available autochthonous or indigenous microbiota present in the food raw materials, which was subjected to changes depending on the surrounding environmental conditions, resulting in the characteristic FFs. The FFs are specific according to their geographic locations [43][47]. The second method is called ‘culture-dependent ferments’ [46][47][48][49][50][51]. Every new batch of fermentation was started with back-slopping, where a small amount of successful previous fermented batch product was used as an inoculum or natural starter culture [48].

The nutritional health benefits, increased food safety, and organoleptic features lead to the growing demand for FFs. Meanwhile, this leads to the increased awareness of food safety measures, standardization measures, industrial control of food production, starter cultures, and fermentation process control etiquettes at the industrial level [43]. The demand for FFs and increasing customers leads to an industrial standardization of fermentation. The first and prudent step is the selection of starter cultures, which is very important in determining the total fermentation process, their safety, organoleptic properties, and necessary changes in the food substrates [49]. From identifying various fermentation microbes and starter cultures, the progression of the development of fermentation techniques becomes pertinent. The current development in molecular biology techniques, next-generation sequencing (NGS), multi-omics and bioinformatics tools, and highly advanced statistical tools leads to further advancements, such as studying the genome sequence of industrially important microbes, their diversity, functions, and metabolic pathways. These outcomes result in great progress in the fermentation industry [50].

The term starter culture usually represents the prepared inoculum containing viable microorganisms that belongs to one or two or more than the two selected microbial species or strains. Thus, the desirable changes in the final product is obtained by using these selected commercial starter cultures while processing the raw materials to initiate the fermentation process. The purpose of starter cultures in fermentation is to fasten the process and to produce characteristic fermented foods. These starter cultures are specifically identified and isolated with the help of advanced microbiological techniques and are currently used in the industrial fermentation process to produce beverages such as beer, alcohol, and vinegar, and foods such as bread and other meat, as well as dairy products [52]. Such inoculation with selected microbes minimizes the risk of foodborne diseases [53][54]. The starter cultures had also been selected from the screened isolates, which yielded end products with high organoleptic features in previous fermentation processes [55]. Molecular approaches, such as high-throughput screening (HTS) of target genes, genetic engineering of specific and well-adapted starter cultures, are synthesized and incorporated to create better-improved fermentation [52].

The starter cultures are improved through another novel technology, CRISPR/Cas9 (Clustered Regularly Interspaced Short Palindromic Repeats/CRISPR-associated protein 9), where the genome of the specific target microbe is precisely edited [56]. Thus, the microbiome manipulation using CRISPR-based technologies improves specific genes in starter cultures [57]. Advanced genetic engineering can rule out undesirable microbial populations and enhance the desirable microbiota, leading to optimized FFs [58]. Recent scientific advances could aid in developing the whole food microbial ecosystem, their interactions, and pathways owing to desirable fermentation processes [59]. Despite the desired quality of starter cultures produced through recombinant DNA technology, those strains, and their genetically modified food ingredients are restricted from usage due to stern food regulations and a lack of acceptance from consumers [60]. Various other technologies include dominant selection, random mutagenesis, natural competence, and conjugation [61].

In the traditional method, the microbial composition of the fermented products depends on the microbial culture used. Outdated plate cultivation method is unable to provide accurate microbial profile information; henceforth, recent NGS technology encompassing collective studies of metagenomics, meta-transcriptomics, meta-proteomics, and metabolomics enables the identification of accurate microbiome from different microbial communities, which pave the way to the detailed study of microbe–microbe interactions in fermentation ecosystems [62]. FFs contain different types of microbial ecosystems such as bacteria, fungi, and yeast; altogether, they are responsible for the quality and safety of FFs [63]. Integrated multi-omics technologies, next-generation nucleic acid, and protein studies enhance the microbes used for the fermentation process, and provide improved fermented products with prolonged shelf life and desirable characteristics. The stability and safety of fermentation and FFs have been improved. The genome editing and molecular approaches rapidly improved the microbial functions, resulting in better quality products with increased safety and an extended shelf life. The next-generation nucleic acid and protein-based approaches provide adequate details about the microbial community for better fermentation and desired products with more shelf life [64].

## 3. Functional Properties of Fermented Food and Beneficial Effects against Respiratory Tract Infection

By definition, FFs can be either plant or animal-based and are produced through back-slopping or by spontaneous fermentation via enzymatic actions of microorganisms so that raw materials are converted into FFs. FFs are rich in nutrients with better taste and provide health benefits [65][66]. Every so often, FFs and beverages are supplemented with probiotics to improve nutritional and health properties [67]. FFs are familiar because of their health benefits and safety standards. Not all FFs have live organisms; in some products, they have been heat-treated, inactivating the microbes. Moreover, FFs are a rich source of bioactive microbes [14]. FFs are functional foods that generally boost the immune functions and metabolism of the consumer [51]. Probiotics are used to ferment the foods traditionally, hence, probiotics and fermented foods are closely related [68]. During fermentation, various bioactive peptides, oligosaccharides, lipids, and other components are synthesized. These components improve the functionality of the product, such as antioxidants, antihypertensive, and other bioactivities [69][70][71]. The health benefits of FFs include preventing metabolic diseases, cardiovascular diseases, enhancing immune function, and improving cognition [12][14][15][17][72]. In 1907, Metchnikoff explained the health benefits of fermented milk products [73]. The traditional fermented milk products are highly rich in bioactive compounds such as peptides, amino acids, vitamins, and minerals [74]. Bioactive compounds are found in unprocessed counterparts such as organic acids, fatty acids, bacteriocins, amino acids, and exopolysaccharides [75][76]. Naturally, bioactive compounds are being released into the system in two different ways. One is that it is released from raw materials because of high acidity. Another way is due to the hydrolyzing enzymes of the probiotic microflora [77]. The FFs are involved in the improvement of intestinal permeability and barrier function [78] and demonstrate positive effects on atherosclerosis, inflammatory bowel diseases, colon cancer [79], anger, depression, and anxiety [80]. FFs aid in maintaining the gut microflora with the presence of bioactive chemicals, neuropeptides, antioxidants, and anti-inflammatory activity [81].

Probiotic bacteria bind directly to the virus and disrupt the adhesion of virus cells onto the mucosal cells [82]. Muhialdin et al. reviewed the connection between FFs, their probiotics with the anti-viral mechanisms and the immune system, and proficient antiviral activity against respiratory and alimentary tract ailments [35]. The antiviral mechanisms involve various systemic changes such as enhancing natural killer cells (NK cells), pro-inflammatory cytokines, and cytotoxic T lymphocytes ($CD3^+$, $CD16^+$, and $CD56^+$) [83]. Bioactive yogurt compounds resist upper respiratory tract infections [84][85][86][87][88] and remain potentially beneficial by preventing the common cold and influenza [89][90].

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