CHAPTER 2

REVIEW OF LITERATURE

Review of Literature

2.1. Fermented food – An overview

Fermentation is one of the oldest and cost-effective methods for producing and preserving foods. In addition to preservation, fermented foods can also have the added value of ameliorated texture, aroma, increased digestibility, enhanced shelf life of food, improved nutritional as well as pharmacological values. Fermentation involves the action of promising microorganisms, or their enzymes, on food substrates leading to biochemical changes, which results in significant changes to the food. Fermentation may also contribute to the detoxification and destruction of detrimental factors present in the raw foods such as phytates, tannins and polyphenols[1]. The fermented food preparation and processing under household conditions varies throughout the world to a greater extent, such as type of inherent microbial culture present or added, the nature of substrate used, water to solids ratio, and the kind of finished product expected. Fermented foods are produced world-wide using a variety of traditional methods incorporating different natural resources and starter culture. Traditional methods or customary practice of ethnic fermented foods and their mode of consumption may be helpful to understand the unexplored knowledge of food production. These are produced in villages, towns, homes and small-scale industries. Many ethnic groups residing in rural areas have diverse food habit and different methods of preparation of fermented food products as part of their usual diet. There is never-ending strive between man and microbes to witness which will be the first to consume the available food supplies[2]. Traditional fermented foods prepared from raw materials such as milk, cereals, fruits, vegetables, wood sap and meat products are well known in many parts of the world. Some are utilized as pickle, spices, preservative, beverages or light meal foods, while a few of them are used as main foods in the diet. Fermented foods have probiotic effects since their consumption leads to the ingestion of large numbers of live bacteria which may exert health benefits. Probiotic have been extensively employed in the food industry and their application is rapidly increasing over the years. Lactic Acid Bacteria are the most commonly used microorganisms in fermented foods which are associated mainly with their physiological features such as substrate utilization, metabolic capabilities and probiotic properties. Their common occurrence in foods contributes to their acceptance as Generally Recognized as Safe (GRAS) for human consumption[3].

Probiotic foods are beneficial for health and capable of boosting immunity. Though antibiotics are prescribed for treating illnesses, their frequent intake can also destroy the good bacteria present in the gut and intestinal tract, which in turn can affect digestion and absorption of nutrients in the body. Therefore probiotic play an important role in supplementing the presence of the good bacteria in the body.

2.2. Soy based traditional fermented foods

Soybean (Glycine max) plays an important role as protein rich source of food and oil extracted from its seed is consumed worldwide. The highest production of soybean throughout the world is contributed by Brazil, USA, Argentina, China, and India[4]. Soybeans, most likely introduced to South Asia after the year 1000 AD. The soybeans grown in the foothills area of northern half of the subcontinent probably originated from central China and distributed across the Tibetan Plateau then down into northeast region of India including Assam, Manipur and the Naga Hills. Fermented soybean products have drawn profound interest from many researchers and are considered nutritionally augmented healthy food. A variety of traditional fermented soybean foodstuff is well recognized world-wide such as tempeh, chungkookjang, natto, kinema, and thua nao. Ethnic communities of Northeast India, particularly Sikkim, Manipur, Meghalaya, Nagaland, Mizoram and Arunachal Pradesh have developed the fermentation processes for converting raw soybean to palatable and nutrient rich traditional fermented food which include kinema, hawaijar, tungrymbai, aakhone, bekang and peruyyan[5]. Fermented soybean food products are reported for their significant nutritional and medicinal attributes such as maintaining blood pressure, fibrinolytic activity, and prevention of osteoporosis, etc. The types of fermented soybean food product produced throughout the world and their biological significance is listed below.

Table 2.1: Types of traditional fermented soybean products consumed in various Asian countries, including China, Indonesia, Japan, Korea, and Vietnam

Fermented soybean products	Douchi	Kanjang	Doenjang	Cheonggukjang
Origin	China	Korea	Korea	Korea
Dominant microorganisms	*Aspergillus*-type (i.e. Liuyang douchi and Yangjiang douchi etc.), *Mucor*-type (i.e. Yongchuan douchi), *Rhizopus*-type (i.e Indian tempe) and Bacterial type (i.e. Qianxi douchi, Babao douchi & Japanese natto)	*A. oryzae,* *B. subtilis*	LAB (*Leuconostoc mesenteroides*, *Tetragenococcus halophilus*, and *Enterococcus faecium*); *Bacillus* species, (*B. subtilis* and *B. licheniformis*); Fungi (*Mucor plumbeus*, *Aspergillus oryzae*, and *Debaryomyces hansenii*)	*B. subtilis*
Raw materials used	Black soybeans	Cooked soybean (Meju)	Soybeans (meju) with brine	Steamed soybeans without salts
Potential health benefits	Fibrinolytic activity, antihypertensive and antioxidant activities	Antioxidants from fermentation process are known to prevent cancer	Antioxidative activity, Fibrinolytic activity, anti-mutagenicity, and anticancer effects.	Poly-γ-glutamate (γ-PGA) produced from *Bacillus subtilis* showed antitumor effects.
References	6, 7, 8, 9,10	11,12	13,14, 15, 16,17	18

Table 2.1: Types of traditional fermented soybean products consumed in various Asian countries, including China, Indonesia, Japan, Korea, and

Fermented soybean products	Tuong	Tempeh	Natto
Origin	Vietnam	Indonesia	Japan
Dominant microorganisms	*A. oryzae;* *B. subtiilis*; *Bacillus sp.*; *Enterobacter mori*	*Rhizopus oligosporus* or *Rhizopus oryzae*	*Bacillus subtilis*
Raw materials used	Soybean, cooked sticky rice, salt	Yellow soybeans	Natto soybeans
Potential health benefits	Fibrinolytic activity	Potent antioxidants	Anti-hypertensive, Fibrinolytic activity
References	19	20	21 , 22

Table 2.2: Traditional fermented soybean products consumed in India

Fermented soybean products	Kinema	Hawaijar	Bekang	Aakhone
Origin	Sikkim, Darjeeling hills, Assam	Manipur	Mizoram	Nagaland
Dominant microorganisms	*B. subtilis, B. licheniformis, B. cereus, B. circulans, B. thuringiensis, B. sphaericus, E. faecium, C. parapsilosis, Geotrichum candidum*	*B. subtilis, B. licheniformis, B. amyloliquefaciens, B. cereus, S. aureus, S. sciuri, Alkaligenes sp., Providencia rettgers, Proteus mirabilis*	*B. subtilis, B. brevis, B. circulans, B. coagulans, B. licheniformis, B. pumilus, B. sphaericus, Lysinibacillus fusiformis*	*B. subtilis, Proteus mirabilis*
Raw materials used	Small-sized yellow cultivar soybean dry seeds	Small-sized boiled soybean seeds kept in bamboo basket lined with leaves of *Ficus hispida*	Small sized, yellow variety of soybean	Soybeans are wrapped in leaves of banana or *Phrynium pubinerve Blume*
Potential health benefits	Antioxidant, digested protein, essential amino acids, vitamin B complex, low-cholesterol content, etc.	Protein diet source	Protein diet source	Protein diet source
References	23, 24,25,26	27, 28, 26	29	28, 25

Table 2.2: Traditional fermented soybean products consumed in India

Fermented soybean products	Tungrymbai	Libi Churpi	Peruyaan
Location	Meghalaya	Arunachal Pradesh	Arunachal Pradesh
Dominant microorganisms	*B. subtilis, B. licheniformis, B. pumilus*	*B. amyloliquefaciens, B. subtilis, B. pumilis, B. altitudinis*	*B. subtilis, B. amyloliquefaciens, Vagococcus lutrae, P. acidilactici, E. faecalis*
Raw materials used	Cooked local soybeans packed with leaves of *Clinogyne dichotoma* or *Phrynium pubinerve*	Local soybean (Libi)	Cooked soybeans lined with fresh ginger leaves, locally called "taki yannii". The
Health benefits	Protein source	Probiotics and cellylolytic properties; Animal feed	Protein diet source
References	29	Present study	28, 26

2.3. Traditional fermented dairy products

The milk is regarded as nature's complete food. It provides an ideal medium for the growth of beneficial microorganisms and thereby fermented dairy product are rich source of novel probiotics. Traditionally milk and milk derived products are consumed in different forms around the world. Fermented milk products are of great importance for humans due to its cultural significance, alleviating lactose intolerance, nutritional and their therapeutic value. The physico-chemical properties of milk obtained from cow, buffalo, sheep, yak, goat and mare milks differ considerably. It is a rich source of fundamental nutrients such as proteins, lactose, fat, vitamins, enzymes and minerals. This offers an exclusive opportunity for production of dairy based functional food to meet nutritional demands. For instance, our country, India, is the highest producer of buffalo milk in the world. Buffalo milk is specially suited for producing certain dairy products, viz. Domiati cheese, Paneer, Khoa and Ghee, etc. Different types of fermented milk product produced throughout the world and their source milk are listed below.

Table 2.3: Some traditional fermented milk products consumed worldwide

Dairy Fermented products	Jameed	Russian sour cream	Gariss	Kurkut	Kumis or Koumiss	Fermented mare milk	Dadih
Location	Jordan, Palestine, Syria and Iraq	Kalmykiya, Buryats, and Tuva regions of Russia	Sudan	Qinghai (China)	Turkic and Mongol origin, Central Asian steppes, Kyrgyzstan, Kazakhstan	Indonesia	Indonesia
Dominant microorganisms	Lactic acid bacteria and yeast	*L. helveticus* and *L. plantarum*	*S. bovis*, *K. marxianus*	*L. delbrueckii* subsp. *bulgaricus* and *S. thermophilus*	*Lactobacilli and yeast*	*L. rhamnosus, L. fermentum*; *L. acidophilus, L. brevis*	*L. paramesenteroides* and other LAB
Raw materials used	Sheep or goat milk	Cow milk	Sudanese fermented camel's milk product	fermented Yak milk	Mare milk	Mare milk	Buffalo milk
Potential health benefits	ACE inhibitory and antioxidant activities	Nutritional food supplements	Supplemen-tary diet source	Angiotensin-converting enzyme inhibitory activity and antihypertensive effect	Cholesterol-lowering effects	Source of potential probiotics and alleviation of lactose intolerance	Hypocholest-erolemic effect
References	30	31	32	33	34	35, 35, 37	38, 39

Table 2.4: Some traditional fermented milk products consumed in India

Dairy Fermented products	Churpi cheese	Buttermilk (chaach)	Lassi	Chilika curd	Dahi (Indian yoghurt)
Origin	Arunachal Pradesh	Various parts of India especially in Gujarat and Rajasthan	Various parts of India	Odisha	All parts of India
Dominant microorganisms	*Lactobacillus paracasei* and *Lactobacillus plantarum.*	Mixed LAB cultures	*L. acidophilus*, and *S. thermophiles*	*Lactobacilli sp., Leuconostoc sp., Lactococcus sp., Streptococcus sp. and* yeast	Mixed lactic cultures
Raw materials used	Yak milk	Regular milk or *dahi*	dahi (Indian yoghurt)	buffalo milk	Cow or buffalo milk
Potential health benefits	Nutritional diet source	Rich source of calcium and protein, Digestive drink	Nutritional diet source	Nutritional diet source, antifungal properties	Source of B-complex vitamins, folic acid, and riboflavin
References	40	41	42	43	44

2.4. Lactic Acid Bacteria as probiotic

Most commercially marketed probiotics belong to the genera *Bifidobacterium* and *Lactobacillus*. Since birth every human being in the world are exposed to these species through the foods, lifestyle and environment. LAB species are so diverse that they occupy various niches, including gastrointestinal (GI) tract of vertebrates, milk, plants, grains and the meats, yet because of their similarities they produce the common metabolic end product, lactic acid. LABs are Gram-positive, nonsporulating bacteria. This group contains several species from the order *Lactobacillales*. LAB genomes have low GC contents and range in size from 1.8 Mb for *Oenococcus oeni* to 3.3 Mb for *Lactobacillus plantarum*. They plays important role in the production and preservation of a various fermented food products and also reported to imparts health benefits.

2.5. *Bacillus* as probiotics

Bacillus species are gram positive sporulating bacteria and have been marketed as probiotics for more than 50 years with the Italian product known as Enterogermina® registered 1958 in Italy as an OTC (over-the-counter) medicinal supplement. However, extensive research on *Bacillus* probiotics needs to be explored. The Bacillus species that have been most extensively evaluated are *Bacillus subtilis, Bacillus cereus, Bacillus clausii, Bacillus licheniformis and Bacillus coagulans*[45]. Of this species, *Bacillus coagulans* is first Bacillus probiotic to be considered as "Generally Recognized as Safe" (GRAS). Endospores containing members of the genus *Bacillus* (in single doses of up to 10^9 spores/g or 10^9 spores/ml) are utilized commercially in probiotic products, and has an advantage over other non-spore formers common *Lactobacillus* products of surviving indefinitely in a desiccated form[46].

2.6. Probiotic benefits and their mode of action

2.6.1. Hypocholesterolemic effects of probiotics

Bile salt hydrolase (BSH) active LAB or products containing them have been reported to lower cholesterol levels through interaction with host bile salt metabolism[47]. Sanders et al[48] proposed the mechanism that certain probiotic

Lactobacilli and *Bifidobacteria* deconjugate bile acids via BSH enzyme, releasing bile acid through excretion system. Cholesterol, being a precursor of bile acids, the synthesis of new bile salts from cholesterol can curtail the serum cholesterol levels in the body to maintain the bile acids that are secreted by body in deconjugation process.

2.6.2. Immune modulation

The immunomodulatory effects of probiotic strains have been widely documented using different in vitro co-culture assays[49] that involves various types of immune cells and based on cytokine production profiles[50]. The signaling cascade is triggered by interaction between probiotics with host epithelial cells. In past few years, many researchers have conducted *in-vivo* studies to validate the immune-stimulatory attributes of probiotics. The probiotic isolates showed various effects on immune profile such as *Lactobacillus rhamnosus* CICC 6141 and *Lactobacillus gasseri* PA16/8 prevented *Candida albicans* infection in poultry and mouse through immunomodulation of IL-8, TLR2/4 and human β-defensin 2 and 3[51, 52]; *Lactobacillus rhamnosus* GG, *Lactobacillus rhamnosus* CRL1505, *Bifidobacterium longum* SP07/3 and *Bifidobacterium bifidum* MP20/5 inhibited Th2-cytokines (IL-4 and IL-5) from allergens and triggered the production of IFN-γ[53]. TLRs contributes in innate immune response through recognition of pathogen motif. It was observed that *Bacillus subtilis* B10 and *Saccharomyces boulardii* ameliorate immunological functions of chicken bone marrow dendrite cells (chi-BMDCs) by targeting TLRs (TLR1, TLR2, TLR4, TLR15), up-regulating gene expression of MHC-II, CD40, CD80 and CD86 and modulating the level of other linked factors (NFκ- B, IL-4, IL-8, IL-10, IL-17, INF-γ, IL-1β and transforming growth factor β (TGF-β)[54]. *Bacillus coagulans* exhibited bactericidal activity against the pathogens such as *Streptococcus agalactiae*, *Staphylococcus aureus*, *Klebsiella oxytoca*, *Escherichia coli*, *Vibrio vulnificus* and *Pseudomonas aeruginosa*[55]. These pathogens deteriorate host immunity by releasing pro-inflammatory cytokines and inducing cytotoxicity. *Lactobacillus plantarum* 06CC2 strain isolated from Mongolian dairy products was efficient in elevating the the levels of IL-12 and IFN-γ in co-culture with mouse spleen cells[51] and level of IL-12p40 (a component of IL-12 and IL-23), acting as a chemo-attractant and associated in pathogenic immune responses in co-culture with mouse macrophage J774.1 cell line[56]..

Different mechanisms proposed for Treg induction by probiotics[57] are:
(i) Probiotics induce the production of immunosuppressive cytokines such as IL-10 and TGF-β through TLR cascade reaction. Additionally, transcription factor FoxP3 along with TGF-β lead to Treg stimulation and production resulting into suppression of activated CD8+ and Th17 cells.
(ii) Probiotic cells adhere to the lectin dendritic cell [DC-specific intercellular adhesion molecule 3-grabbing nonintegrin (DC-SIGN)] and promote Tregs capable of producing higher levels of IL-10.
(iii) Probiotics produces short chain fatty acids like propionate, acetate, and butyrate after metabolizing the dietary fibers such as inulin, starch, β-GOS, FOS etc. These SCFAs lead to activation of G protein-coupled receptors (GPCRs)- GPR43 and GPR109A on Treg cells. GPR43 is activated by all three SCFAs, on the other hand, GPR109A is activated by butyrate only. This communication between SCFAs and GPCRs results into stimulation and development of Treg cells proficient in inhibition of activated $CD8^+$ and Th17 cells population by producing elevated levels of IL-10 and TGF-β. Furthermore, SCFAs mediated induction of immune cells also involves supression of histone deacetylases (HDACs) which is responsible for increased secretion and suppressive action of $FoxP3^+$ Tregs by inducing the acetylation of FoxP3 protein. Moreover, SCFAs alleviate the production of prostaglandin E2 (PGE2) which is involved in increased production of suppressive cytokine IL-10 and directly inhibit the secretion of other proinflammatory cytokines. PGE2 also enhances the activation, maturation, and migration of dendritic cells (DCs), results into improved interaction between DCs and Tregs leading to better immune response.
(iv) *L. paracasei* NCC2461 probiotic strain is involved in breakdown of β-lactoglobulin (BLG) into peptides, resulting into higher production of IL-10.

2.6.3. Antimicrobial property

The probiotics have been utilized as biopreservatives due to their antimicrobial and organoleptic properties. The LAB as a probiotic in food biopreservation probably is one of the best natural method of food preservation practiced by humans. The majority of the LAB are well established GRAS and their biopreservative attributes are mainly exhibited by the production of organic acids, carbon dioxide or hydrogen peroxide and also the action of bacteriocins, defined as ribosomally synthesized small peptides inhibiting closely related bacteria. The advantageous attributes of a bacteriocin producing probiotic strain is the ability to produce natural peptide such as bacteriocins that offer competition against pathogens and better colonization of the gastrointestinal tract.

2.6.3.1. Classification of bacteriocins[58]

Class I or lantibiotics: This class is lantionine or peptides containing b-lantionine which are subcategorized into Type A (linear molecules such as Nisin, subtilin, epidermine) and Type B (globular molecule such as Mersacidin).

Class II: These are heterogeneous class of small thermostable peptides, subdivided into Subclass IIa including antilisterial-pediocine bacteriocins type such as Pediocin, enterocin, sakacin; Subclass IIb containing two peptides such as Plantaricin and lactacin F; Subclass IIc (Lactococcin).

Class III: These are large thermolabile peptides such as Helveticin J and millericin B.

2.7. References

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