Available online at www.jibresearch.com; ISSN: 2348-6473 (online)

Review Article

Journal of Innovative Biology December 2014 Vol. 1, Issue 4, P. 189-194

Current scenario of antimicrobial compounds produced by food grade bacteria in relation to enhance food safety and quality

Ami Patel*, Nihir Shah

Division of Dairy and Food Microbiology, Mansinhbhai Institute of Dairy & Food Technology-MIDFT, Dudhsagar Dairy campus, Mehsana-384 002, Gujarat state, India

Abstract: The review enlightens on the current scenario of antimicrobial substances produced by food grade bacteria with special emphasis on bacteriocins. Development of new technologies allowed us to utilize specific features of the starter bacteria for specific applications. Apparently, most of the researches proposed combined effect of each antimicrobial compound produced by the specific starter organism during the fermentation that helps them to combat with spoilage or illness causing microbes in a food or beverage. Consumers demand for natural and safe functional foods in addition to the stringent regulations to prevent foodborne infectious diseases have motivated researchers into finding novel technologies for antimicrobials delivery which should result in improved safety and quality of the food products over the storage period.

Keywords: Antimicrobials, Bacteriocin, Bioactive food packaging, Nisin, Reuterocyclin

Received: 25 September 2014 / Accepted: 20 November 2014 / Published Online: 05 December 2014

Fermentation is one of the oldest methods known to mankind in order to enhance the shelf life of food. A well-known example is lactic acid fermentation, which is widely used for the preparation of several fermented dairy and food products, such as dahi (curd), yoghurt, sour cream, acidophilus milk, shrikhand, cheeses, vegetables and sourdough. In the modern dairy industry, starter cultures are pre-requisite for the production of safe products of uniform quality (Caplice and Fitzgerald, 1999; Farnworth, 2008). Starter cultures are carefully selected microorganisms, which are deliberately added to milk and related products to initiate and carry out desired fermentation under controlled conditions in the production of fermented food products. Lactic acid bacteria (LAB) are used for manufacturing of fermented milks and considered as heart of fermentation. LAB mainly involves *Lacto-coccus, Lactobacillus, Streptococcus* and *Leuconostocs* genus. In some cases, few nonlactic starters (Bacteria, yeast and mold) are also used along with LAB during manufacturing of specific fermented milk products, such as kefir, koumiss; mold ripened cheeses, villi, etc.

Quick Response CODE:
Patel et al., 2014

The article may be access online @ http://www.fa.jibresearch.com/?page_id=174

QR CODE

LAB were first isolated from milk and since then have been found in diverse fermented dairy products and food products such as vegetables (sauerkraut, kimchi, pickles), meat sausages, sea foods, beverages and bakery products. LAB exists in human and animal body too, as normal flora of the gastrointestinal tract, vagina, skin and mouth. LAB produces small organic compounds that give the aroma and flavor to the fermented product (Robinson, 2002). LAB plays an important role in processing animal feeds like silage (Holzer et al. 2003). Toxic or harmful substances derived from the raw material, such as cyanides, proteinase inhibitors, phytic acid, oxalic acid, glucosinolates and indigestible carbohydrates, are partly degraded during fermentation (Farnworth, 2008). LAB have been used as a flavoring and texturizing agent as well as a preservative in food for centuries. Many species of lactobacilli, *L. lactis*, and *Streptococcus thermophilus* inhibit food spoilage and pathogenic bacteria and preserve the nutritive qualities of raw food material for an extended shelf life (O'Sullivan et al. 2002, Patel et al. 2013). Recently, the use of metabolites of LAB as biological preservatives in active food packaging has been gained

Corresponding Author:
Patel A, (✉) Mansinhbhai Institute of Dairy & Food Technology-MIDFT, Dudhsagar Dairy campus, Mehsana-384 002, Gujarat, India
Email: amiamipatel@yahoo.co.in

much interest (Pirttijarvi et al. 2001; Sung et al. 2013). Moreover, clinical applications of antimicrobials like bacteriocins derived from LAB on several pathogens have gained much attention in recent years.

The antimicrobial effect of LAB is primarily due to organic acid production especially lactic acid causing the pH of the growth environment to decrease. Furthermore, LAB also produce acetaldehyde, hydrogen peroxide, diacetyl, carbon dioxide, polysaccharides and bacteriocins (Robinson, 2002; Caplice and Fitzgerald, 1999), some of which may exert antagonistic activity against other organisms (Figure 1). The different kind of antimicrobials synthesized by several food grade bacteria with their possible mode of action and antimicrobial spectrum is shown in Table 1. In brief, this article discusses role of various antimicrobial compounds produced by LAB and related genera in food preservation and bioactive packaging with future perspectives.

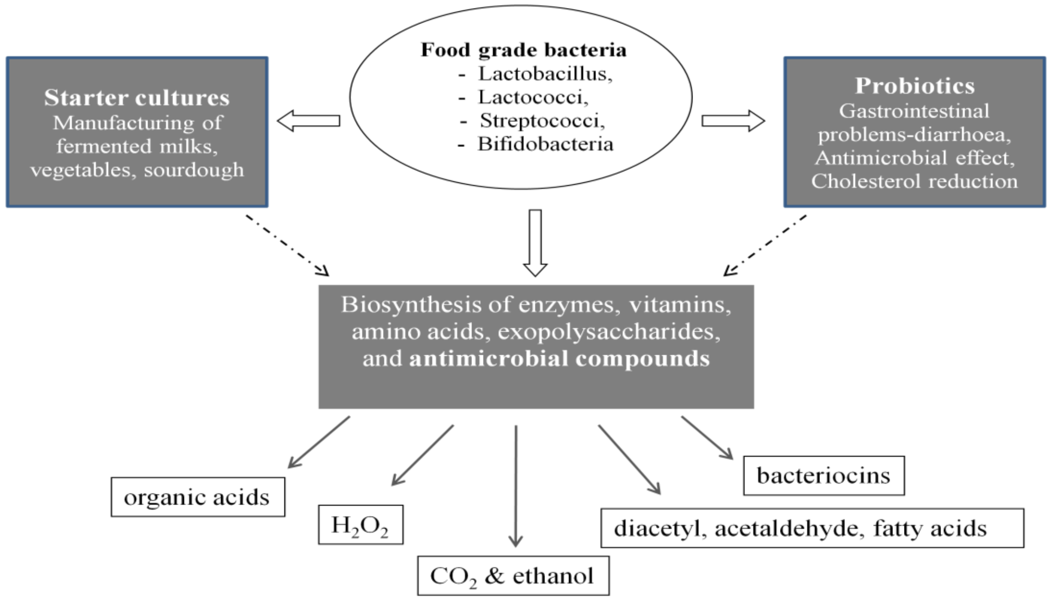

Figure 1 Role of food grade bacteria and antimicrobial compounds

Table 1 Antimicrobial compounds produced by food grade bacteria

Name of antimicrobial compound	Mode of Action	Activity Spectrum
Organic acids - Lactic acid - Acetic acid - Propionioc acid - Benzoic acid - Phenyllactic acid	disturb functions of cytoplasmic membrane causing solubilisation of membrane lipids and interferes with the maintenance of membrane potential	Broad spectrum of activity-Antibacterial activity, antifungal activity
Hydrogen peroxide (H_2O_2)	- peroxidation of membrane lipids - production of free radicals such as superoxide (O^{-2}) and hydroxyl (OH^{-})	Broad spectrum of antimicrobial activity
Diacetyle & acetaldehyde	interfere with the utilization of arginine or arginine binding proteins	More inhibitory to Gram-negative bacteria, yeasts and moulds than Gram positive
Fatty acids	reduction in pH lead to disturb function of cytoplasmic membrane in a cell	Inhibition of Gram-positive bacteria and fungi
Carbon dioxide and ethanol	-inhibits enzymatic decarboxylation, -affects membrane permeability	
Bacteriocins - Nisin, - Pediocin PA-1/AcH - Reuterin - Acidophilin	Majority affects membrane permeability	Majority of them have Narrow spectrum activity (nisin) while few have broad spectrum activity (acidophilin)
Antibiotics e.g. Reuterocyclin	disrupts membrane potential	gram-positive bacteria

Organic acids
Fermentation by LAB is characterized by the accumulation of organic acids such as lactic acid, acetic acid, propionic acid and butyric acid with simultaneous reduction in pH. The levels and types of organic acids produced during the fermentation process depend on the species of organisms, culture composition and growth conditions. The antimicrobial activity is believed to result from the action of organic acids on bacterial cytoplasmic membrane. It causes solubilisation of lipids from the cell membrane which diffuses into the cytoplasm, interfere with the maintenance of membrane potential and inhibits active transport and may be mediated by both dissociated and un-dissociated acid (Gottschalk, 1988).
The antimicrobial activity of each of the acids at given molar concentration is not equal. Besides this acetic acid and propionic acids claimed to be stronger antimicrobials than lactic acid and can inhibit yeasts, moulds and bacteria. Microgard is a Food and Drug Administration (FDA)-approved commercial food additive that is a growth extract of *Propionibacterium freudenreichii* subsp. *shermanii* which contains propionic acid and is used in yogurts, cottage cheese, sour cream, dairy desserts and filled chocolate confections in US. BioProfit is other product containing viable cells of *P. freudenreichii* subsp. *shermanii* strain JS and is effective or inhibiting bacteria and yeasts growth in dairy products, sourdough and also used to preserve grain and produce good quality silages (Suomalainen et al. 1999).

Bifidobacteria synthesize more amount of acetic acid than lactic acid (3:2 ratio) while several bacteria unusually found to produce phenyllactate and benzoic acid during their growth. Phenyllactic acid (PLA) has been recognized as the major factor responsible for antifungal activity and prolonged shelf-life of food products (Lavermicocca et al. 2000). The inhibitory properties of PLA have been demonstrated against several fungal species isolated from bakery products, flour and cereals, including some mycotoxigenic species such as *Aspergillus ochraceus, Penicillium verrucosum and Penicillium citrinum,* and against some bacterial contaminants, namely *Listeria* spp., *Staphylococcus aureus* and *Enterococcus faecalis* (Dieuleveux and Gueguen, 1998; Lavermicocca et al. 2003).

Hydrogen peroxide (H_2O_2)
Some obligatory homofermentative LAB are found to produce hydrogen peroxide. The antimicrobial effect of H_2O_2 may result from the oxidation of sulfhydryl groups causing denaturation of a number of enzymes, and from the peroxidation of membrane lipids thus increases membrane permeability. H_2O_2 may serve as a precursor for the production of bactericidal free radicals such as superoxide (O^{2-}) and hydroxyl (OH^-) radicals which can damage DNA (Yadav et al. 1993).

Flavour compounds
Diacetyl and acetaldehyde: LAB found to produce certain flavour compounds like diacetyl and acetaldehyde that could exert antimicrobial activity. Diacetyl (2, 3-butanediol) is form during citrate metabolism and is responsible for aroma and flavour of butter and some other fermented milk products. Many LAB including strains of *Leuconostocs, Lactococcus, Pediococcus*, and *Lactobacillus* may produce diacetyl. Gram-negative bacteria, yeasts and moulds are more sensitive to diacetyl than Gram-positive bacteria and its mode of action is due to interference with the utilization of arginine or arginine binding proteins (Yadav et al. 1993; Rattanachaikunsopon and Phumkhachorn, 2010). On the other hand, acetaldehyde could get converted into H_2O_2 by xanthine oxidase enzyme. Nevertheless, the amount of flavour compounds is much lower than the level that is considered necessary to achieve inhibition of microorganisms.

Fatty acids
Some lactobacilli and lactococci possess lipolytic activity and may lead to produce significant amounts of fatty acids in fermented milks. The antimicrobial activity of fatty acids has been recognized for many years. The unsaturated fatty acids are active against Gram-positive bacteria, and the antifungal activity of fatty acids is dependent on chain length, concentration, and pH of the medium (Yadav et al. 1993). The antimicrobial action of fatty acids has been thought to be due to the undissociated molecule, not the anion, since pH had profound effects on their activity, with a more rapid killing effect at lower pH.

Carbon dioxide and ethanol
Carbon dioxide is mainly produced by heterofermentative LAB and precise mechanism of its antimicrobial action is still unknown. However, CO_2 may play a role in creating an anaerobic environment which inhibits enzymatic decarboxylation reaction and the accumulation of CO_2 in the membrane lipid bilayer may cause a dysfunction in permeability. CO_2 can effectively inhibit the growth of many food spoilage microorganisms, especially Gram-negative psychrotrophic bacteria and had a strong antifungal activity (Yadav et al. 1993).

Although ethanol may be produced by certain strains of heterofermentative LAB, again the levels produced in food systems are so low that the contribution to antibiosis is negligible.

Bacteriocins
Bacteriocins are generally proteins or related compounds formed by food grade bacteria that are inhibitory to themselves and closely related species (Robinson, 2002). However, some of the bacteriocins of LAB have wide spectrum activities. Bacteriocin is found to be produced by different LAB belonging to genus *Lactobacillus, Leuconostocs, Pediococcus, Lactococcus* and *Weissella* (Servin, 2004; Patel et al. 2013). The exact mechanisms for synthesis and other characteristics of many bacteriocins are still not clear but their synthesis is regulated by ribosome in cell.

Bacteriocins produced by LAB are classified into three main groups, lantibiotics being the most documented and industrially exploited. As shown in figure 2, there are four groups of bacteriocins, viz., lantibiotics (Class I), nonlantibiotics, small heat-stable peptides (Class II), large heat-labile protein (Class III) and complex bacteriocins containing glycol and/or lipid moieties (Class IV) (Servin, 2004; O'Sullivan, et al. 2002). Among different bacteriocins, nisin is the only one which is fully characterized and it is legally permitted to use in food preparations as biopreservative. In Table 2, several bacteriocins produced by food grade bacteria and their activity spectrum are revealed.

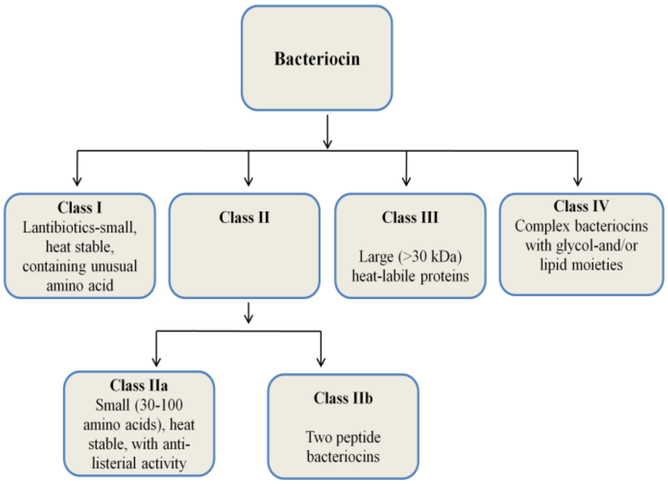

Figure 2 Classes of bacteriocins produced by lactic acid bacteria

Nisin is the well known bacteriocin produced by *Lactococcus lactis* subsp. *lactis*. It is having a narrow spectrum activity and is effective against spore formers, clostridia, mastitis causing bacteria- *S. aureus*. It is synthesize as pronisin inside the cell and then releases in outerlayer as peptide containing 34 amino acids. Nisin is commercially available as food additive E234. The nisin variants A and Z, differing by one amino acid, are approved for use in foodstuffs by food additive legislating bodies in more than 50 countries including US and Europe. In, addition, a new nisin variant, nisin Q, has been isolated from a *L. lactis* strain found in river water in Japan. Nisin Q differs in four amino acids as a mature peptide and in two amino acids of the leader sequence (Zendo et al. 2003).

Nisin is incorporated in cheese, canned products, salad dressings, bakery products and cooked meat sausages. However, application of nisin is somewhat limited by comparatively narrow spectrum of activity since it is not effective against Gram-negative bacteria or yeast and molds. Further, it is most effective at low pH. Thomas et al. (2000) stated that the effectiveness of nisin against Gram-negative bacteria can be improved if chelating agents, such as EDTA, are present. It works by increasing the permeability of the bacterial cell wall to nisin. It is relatively stable in foodstuffs since 15 – 20% of nisin is lost in heat treatment. Nisin used to improve food quality and sensory properties such as increasing the rate of proteolysis or in the prevention of gas blowing defect in cheese (Perez et al., 2014). The mode of action of nisin differs slightly for sensitive bacteria. As mentioned by Nissen-Meyer et al. (1992) and McAuliffe et al.(2001), nisin

Table 2 Bacteriocins of food grade bacteria and their inhibitory spectrum

Producer	Bacteriocin	Inhibitory spectrum
L. lactis subsp. *lactis*	Nisin	Active against Lactococci, *Clostridia*, *S. aureus,* Micrococci
L. lactis subsp. *cremoris*	Diplococcin	*L. lactis* subsp. *lactis,* *L. lactis* subsp. *cremoris*
L. acidophilus	Lactacin B Lactacidin Acidophilin Acidolin	*Lactobacilli* Broad spectrum active against. Gram +ve and Gram –ve bacteria Lactic acid bacteria, spore formers, *salmonella* spp., *E. coli, S. aureus, pseudomonas* Broad spectrum, spore formers, enteric pathogens
L. reuteri	Reuterin	Broad spectrum-*Salmonella*, *Shigella*, Listeria, Clostridia, yeasts-candida
L. plantarum	Plantaricin C	Active against different *Lactobacillus* spp., *Pediococcus*, Clostridia, *L. monocytogenes.*
L. sake	Sakacin A	Active against different species of *Pediococcus*, *Lactobacillus*, *L. monocytogenes*
Pediococcus strains	Pediocin PA-1/AcH	Active against Carnobacterium, Enterococcus, Lactobacillus, Lactococcus, Leuconostoc, Pediococcus, Streptococcus, L.monocytogenes, B. cereus, Staphylococcus *spp.* and *Clostridium spp.*
Enterococcus faecalis	Enterocin AS-48	Active against different species of, *Enterococcus*, *Lactobacillus*, *Pediococcus*, and *L. monocytogenes.*
Bifidobacterium spp	Bifidocin B	Gram-positive bacteria- *Lactobacillus*, *L. monocytogenes*

accumulates on the cell membrane, inserts into it, and then aggregates within the membrane to form a water-filled pore . Another model proposed that nisin binds by electrostatic interactions to the anionic membrane surface, leading to a high local concentration that disturbs the lipid dynamics and causes localized strains, forcing the nisin into the membrane (Driessen et al. 1995). Nisin is also known to inhibit peptidoglycan biosynthesis by interacting with cell wall precursors, lipid I and lipid II (Wiedemann et al. 2004). Further, it is documented that nisin inactivate endospores by preventing post-germination swelling and subsequent spore outgrowth (Thomas et al. 2000).

Nisin is chiefly marketed under the trade name Nisaplin(r) by Danisco. Other players in the global market include Rhodia, S.A. (France) along with numerous producers and providers of various antimicrobial products based in China. Some of these Chinese sources are in joint ventures or alliances with European-based corporate entities. Recently, Kawada-Matsuo et al. (2013) showed that nisin-based injectable drug can control almost 99.9% of bacteria causing mastitis (udder infection in milch animals) such as Streptococcus agalactiae and Staphylococcus aureus after drug administration. In Japan, a group of scientist succeeded in developing a nisin A-containing hand wash and oral hygiene gel namely NeonisinTM and Oralpeace™. It was shown to be effective in controlling tooth cavities (caused by S. mutans) and bacterial gingivitis (caused by *Porphyromonas gingivalis*) (Yamakami et al. 2013) Also, Yamakami et al. (2013) developed a liposome-encapsulated nisin that showed significantly prolonged activity than uncovered nisin in inhibiting the synthesis of S. mutans glucan-biofilm.

Next to nisin, pediocin PA-1/AcH from some *Pediococcus* strains and enterocin AS-48 (class IIc) from *Enterococcus faecalis* have been most likely candidates to be used for bio-preservatives. Pediocin PA-1/AcH is a stable protein produced by strains of Pediococcus acidilactici, which has generally recognized as safe (GRAS) status and is active against many Gram-positive bacteria over a wide pH range (Jones et al. 2005, Perez et al., 2014). *Pediococci* are commonly employed as starter cultures for fermented sausage products, where their presence helps to inhibit both spoilage bacteria and pathogens because of production of pediocin. The pediocin PA-1/AcH producing *Pediococcus pentosaceus* BCC 3772 when used as starter culture for Nham, a traditional Thai fermented pork sausage, effectively controlled the growth of L. monocytogenes without compromising the quality of Nham (Kingcha et al. 2012). Other bacteriocins including acidophilin, bulgaricin, lactacin and plantaricin produced by different species of lactobacilli which have not been exploited yet commercially, are attracting interest. It is observed that majority of bacteriocin produced by the strains of L. acidophilus have broad spectrum of activity against foodborne pathogens and spoilage bacteria.

In contrast to other bacteriocins, reuterin, chemically identified as 3-hydroxy propionaldehyde is a non-protein bacteriocin produced by certain strains of *Lactobacillus* reuteri. It has a wide spectrum of activity and is effective against both Gram-positive and Gram-negative bacteria, yeasts and moulds. Further, reuterin is water-soluble; quite stable over a wide pH range which makes it a prospective food preservative (Rattanachaikunsopon and Phumkhachorn, 2010).

There are numerous ways in which bacteriocin can be incorporated into a food to improve its safety: (a) by using a purified or semi-purified bacteriocin preparation as food ingredient; (b) by introducing an ingredient that has earlier been fermented with a bacteriocin producing strain; (c) by using a bacteriocin-producing culture in fermented products to produce the bacteriocin in situ; or (d) incorporating bacteriocin in form of a thin coating onto a layer of packaging material i.e. bioactive packaging, a process that can protect the food from external microbial contaminants (Woraprayote et al., 2013).

Reuterocyclin

It is the first antibiotic detected from LAB and the spectrum of inhibition of the antibiotic is restricted to gram-positive bacteria including *Lactobacillus* spp., *Bacillus subtilis, B. cereus, E. faecalis, S. aureus* and *Listeria innocua* (Rattanachaikunsopon and Phumkhachorn, 2010). Unlike nisin, reuterocyclin does not form pores but selectively dissipates the transmembrane proton potential that led to disturb cell membrane.

There are several benefits associated with relevance to application of antimicrobial compounds as food preservatives such as: (i) prolonged shelf-life of dairy & food products as natural preservatives without addition of chemical preservatives, (ii) decrease of the intensity of heat treatments resulting in better preservation of food nutrients and sensory properties of the food, (iii) amelioration of the risk of transmission of foodborne pathogenic bacteria, (iv) reduction in economic losses due to food spoilage, and (v) marketing of "novel" or "functional" foods, the bacteriocin producing LAB strains isolated from foods and human origins are expected to be effective probiotic candidates.

Conclusion

New fields of application have arisen on the basis of extensive scientific studies that allowed utilizing specific features of the culture organisms for specific applications. Several strains of LAB and other food grade bacteria, including probiotics are very promising sources for novel products and applications, especially those that can satisfy the increasing consumer's demands for natural products and functional foods. It is apparent to note that any food grade bacterium may produce a number of antimicrobial substances; its antagonistic potential is defined by the collective action of its metabolic products on undesirable bacteria. Natural antimicrobial substances have high potential for commercial food packaging applications and would be preferred by the consumers to produce safer food. Despite recent advances, the study of LAB and their functional ingredients is still an emerging

J Innov Biol December 2014 Vol. 1, Issue 4, P. 189-194

field of research that has yet to realize its full potential especially in the field of therapeutic applications.

References

Caplice E, Fitzgerald GF (1999) Food Fermentation: role of Microorganisms in food production & preservation. J Food Microbiol 50: 131-149

Dieuleveux V, Gueguen M (1998) Antimicrobial effects of d-3-phenyllactic acid on *Listeria monocytogenes* in TSB-YE medium, milk, and cheese. J Food Prote 61:1281–1285

Driessen, AJM, Van Den Hooven HW, Kuiper W, Van De Kamp M, Sahl HG, Konings RNH, Konings WN (1995) Mechanistic studies of lantibiotic-induced permeabilization of phospholipid vesicles. Biochem 34: 1606-1614

Farnworth ER (2008) Handbook of Fermented Functional Foods. In: The Health Benefits of Fermented Milk Products That Contain Lactic Acid Bacteria, CRC Press, Taylor & Francis Group, pp: 130-155

Gottschalk G (1988) Bacterial metabolism, 2nd ed. Springer-Verlag, New York

Holzer M, Mayrhuber E, Dannerr H, Braun R (2003) The role of *Lactobacillus buchneri* in forage preservation. Trends Biotechnol 21, 282-287

Jones E, Salin V, Williams GW (2005) Nisin and the market for commercial bacteriocins. TAMRC Consumer and Product Research Report No. CP-01-05

Kawada-Matsuo M, Oogai Y, Zendo T, Nagao J, Shibata Y, Yamashita Y, Ogura Y, Hayashi T, Sonomoto K, Komatsuzawa H (2013) Involvement of the novel two-component NsrRS and LcrRS systems in distinct resistance pathways against nisin A and nukacin ISK-1 in *Streptococcus mutans*. Appl Environ Microbiol 79:4751-4755.

Kingcha Y, Tosukhowong A, Zendo T, Roytrakul S, Luxananil P, Chareonpornsook K, Valyaseyi R, Sonomoto K, Visessanguan W (2012) Anti-listeria activity of *Pediococcus pentosaceus* BCC 3772 and application as starter culture for Nham, a traditional fermented pork sausage. Food Contr 25:190-196

Lavermicocca P, Valerio F, Evidente A, Lazzaroni S., Corsetti A., Gobbetti M (2000) Purification and characterization of novel antifungal compounds from the sourdough *Lactobacillus plantarum* strain 21B. Appl Envi Microbiol, 66: 4084–4090

Lavermicocca P, Valerio F, Visconti A (2003) Antifungal activity of phenyllactic acid against molds isolated from bakery products. Appl Envi Microbiol 69: 634–640

Mcauliffe O., RP Ross, C Hill (2001) Lantibiotics: structure, biosynthesis and mode of action. FEMS Microbiol Rev 25: 285-308

Nissen-Meyer JH, Holo LS, Håvarstein K, Sletten IF (1992) A novel lactococcal bacteriocin whose activity de pends on the complementary action of two peptides. J Bacteriol 174: 5686-5692

O' Sullivan L, Ross RP, Hill C (2002) Potential of bacteriocin-producing lactic acid bacteria for improvements in food safety and quality. Biochemie 84, 593-604

Patel A, Shah N, Ambalam P, Prajapati JB, Holst O, Ljungh A (2013) Antimicrobial profile of lactic acid bacteria isolated from vegetables and indigenous fermented foods of India against clinical pathogens using microdilution method. Biomed Envi Sci 26:759-764

Perez RH, Zendo T, Sonomoto K (2014) Novel bacteriocins from lactic acid bacteria (LAB): various structures and applications. Microbial Cell Factories 13(Suppl 1):S3

Pirttijärvi TSM, Wahlström G, Rainey FA, Saris PEJ, Salkinoja-Salonen MS (2001) Inhibition of bacilli in industrial starches by nisin. J Ind Microbiol Biotechnol 26: 107-114

Rattanachaikunsopon P, Phumkhachorn P (2010) Lactic acid bacteria: their antimicrobial compounds and their uses in food production. Annals Bio Res 14: 218-228

Robinson RK (2002) Dairy Microbiology Handbook. In: Microbiology of Fermented Milks. John Wiley & Sons, Inc., Publication, New York, pp.367-421

Servin, AL (2004) Antagonistic activities of lactobacilli and bifidobacteria against microbial pathogens. FEMS Microbiol Rev 28: 405-440

Sung SY, Sin LT, Tee TT, Bee SO, Rahmat AR, Rahman WA, Vikhraman M (2013) Antimicrobial agents for food pack-aging applications. Trends Food Sci Technol 33: 110-123

Suomalainen TH, Mäyrä-Makinen AM (1999) Propionic acid bacteria as protective cultures in fermented milks and breads. Lait 79: 165-174

Thomas, LV, Clarkson MR, Delves-Broughton J (2000) Nisin. In: Natural Food Antimicrobial Systems, ed. A. S. Naidu.CRC Press, Boca Raton, FL, pp. 463-524

Wiedemann, I, Benz R, Sahl HG (2004) Lipid II-mediated pore formation by the peptide antibiotic nisin: a black lipid membrane study. J Bacteriol 286: 3259-3261

Woraprayote W, Kingcha Y, Amonphanpokin P, Kruenate J, Zendo T, Sonomoto K, Visessanguan W (2013) Anti-listeria activity of poly(lactic acid)/sawdust particle biocomposite film impregnated with pediocin PA-1/AcH and its use in raw sliced pork. Int J Food Microbiol 167:229-235

Yadav JS, Grover S, Batish VK (1993) A Comprehensive *Dairy Microbiology*, Metropolitan Publisher, New Delhi, India. pp. 463-524

Yamakami K, Tsumori H, Sakurai Y, Shimizu Y, Nagatoshi K, Sonomoto K (2013) Sustainable inhibition efficacy of liposome-encapsulated nisin on insoluble glucan-biofilm synthesis by *Streptococcus mutans*. Pharm Biol 51:267-270

Zendo T, Fukao M, Ueda K, Higuchi T, Nakayama J, Sonomoto K (2003) Identification of the lantibiotic nisin Q, a new natural nisin variant produced by *Lactococcus lactis* 61-14 isolated from a river in Japan. Biosci Biotechnol Biochem 67: 1616-1619