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REVIEW

Bacteriocin encapsulation for food and pharmaceutical applications: advances in the past 20 years

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Abstract The encapsulation of bacteriocins from lactic acid bacteria has involved several methods to protect them from unfavourable environmental conditions and incompatibilities. This review encompasses different methods for the encapsulation of bacteriocins and their applications in both food and pharmaceutical fields. Based on the bibliometric analysis of publications from well-reputed journals including different available patents during the period from 1996 to 2017, 135 articles and 60 patents were collected. Continent-wise contributions to the bacteriocins encapsulation research were carried out by America (52%), Asia (29%) and Europe (19%); with the United States of America, Brazil, Thailand and Italy the countries with major contributions. Till date, different methods proposed for encapsulation have been (i) Film coatings (50%), (ii) Liposomes (23%), (iii) Nanofibers (22%) and (iv) Nanoparticles (4%). Bacteriocins encapsulation methods frequently carried out in food protection (70%); while in the pharmaceutical field, 30% of the research was conducted on multi drug resistant therapy.

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Introduction

Bacteriocins are antimicrobial activity (AMA) peptides produced by various bacteria including Lactic Acid Bacteria (LABs). Bacteriocins such as nisin, subtilosin, pediocins, and lactacins have demonstrated their potential applications in protection and preservation of food against pathogenic and spoilage bacteria (Cleveland et al. 2001). Currently, antibacterial peptides are one of the most promising substances to be used as antibiotics; specifically, peptides containing lanthionine (lantibiotics) due to their broad spectrum of inhibition against a variety of Gram-positive bacteria (Al-Mahrous and Upton 2011; Jamuna et al. 2005). In the past century, nisin, a FDA approved natural antimicrobial substance produced by *Lactococcus lactis* subsp. *lactis* was permitted for preservation of foods by food industries in more than 40 countries (Arevalos-Sánchez et al. 2012; de Arauz et al. 2009; Gharsallaoui et al. 2016; Khan and Oh 2016; Ross et al. 2002). On the other hand, its use as an antibiotic in health care, against multidrug resistant pathogens are still at the level of potential utilization (Breukink and de Kruijff 2006; Benmechernene et al. 2013). Even though the scientific community proposes the applications of bacteriocin in food protection, the

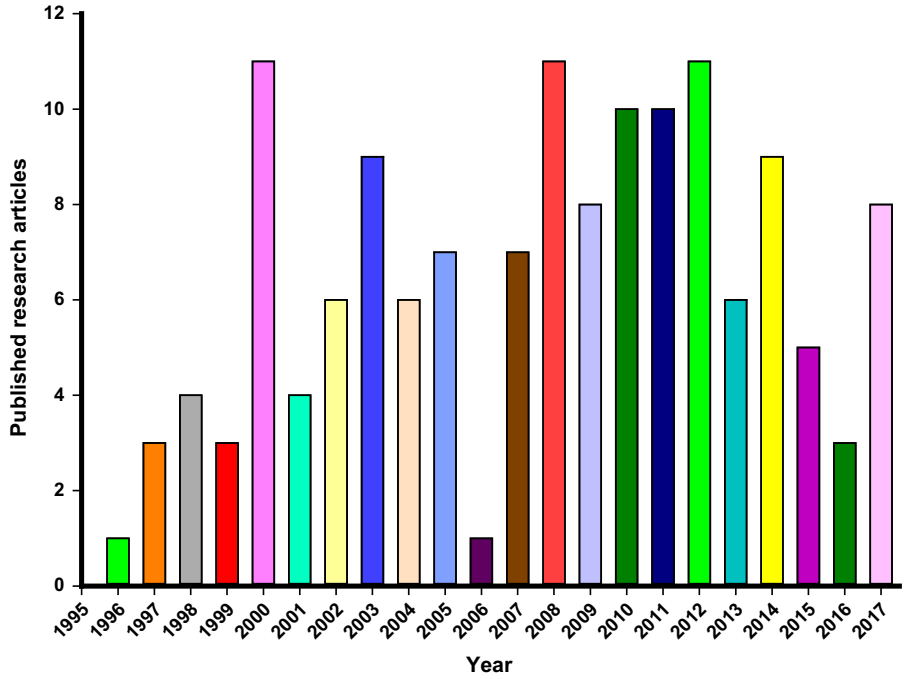

Fig. 1 Global contribution on encapsulation of bacteriocins between 1996 and 2017 using the following on-line editorial databases: Science Direct, Scopus, Springerlink, Ingenta, Wiley and Scielo

bacteriocin activity would be affected due to proteolytic degradation within food matrixes, among other factors. To overcome the above mentioned difficulties, relatively new methodologies such as nanoencapsulation systems (metal nanoparticles, chitosan, nanofibers, and liposomes) are being considered to protect them from degradation, thereby enhancing the preservative effects.

Nanotechnology is a new generation platform for the development of nano-structured materials with antimicrobial activities in the pharmaceutical industries (Mozafari 2007; Sanguansri and Augustin 2006; Shrivastava and Dash 2009). Bacteriocin encapsulation technology has led to the development of novel antimicrobial packaging without any changes to food components (Lopes and Brandelli 2017; Sidhu and Nehra 2017). However, the ability of nanocarriers to act as protective layers must be improved to be effective over extended storage times (Fahim et al. 2017).

Scientific publication of global research on bacteriocins encapsulation methods

A database which includes 135 published articles and 60 patents concerning the encapsulation of bacteriocins from 1996 to 2017 was made from Science Direct, Scopus, Springerlink, Ingenta, Wiley and Scielo, for research papers; and from Espacenet, PatentScope, Google patents, Lens and Upsto for patents. All references were organized in a Microsoft Excel™ spreadsheet. Data were initially classified on the basis of publication year and country of origin as well as affiliation of the corresponding author. The exploration on effective encapsulation of bacteriocin in well-reputed scientific journals, showed majorly contributions during the years 2000, 2008 and 2012 (Fig. 1). Globally, America, Asia and Europe contributed with 52, 29 and 19%, respectively, to the reported research on the encapsulation of bacteriocin in the last two decades; with the United States of America, Brazil, Thailand, and Italy being the countries that majorly contributed to the research on bacteriocin encapsulation for food and pharmaceutical applications (Fig. 2). Based on our data collection, ten reputed journals published maximum number of

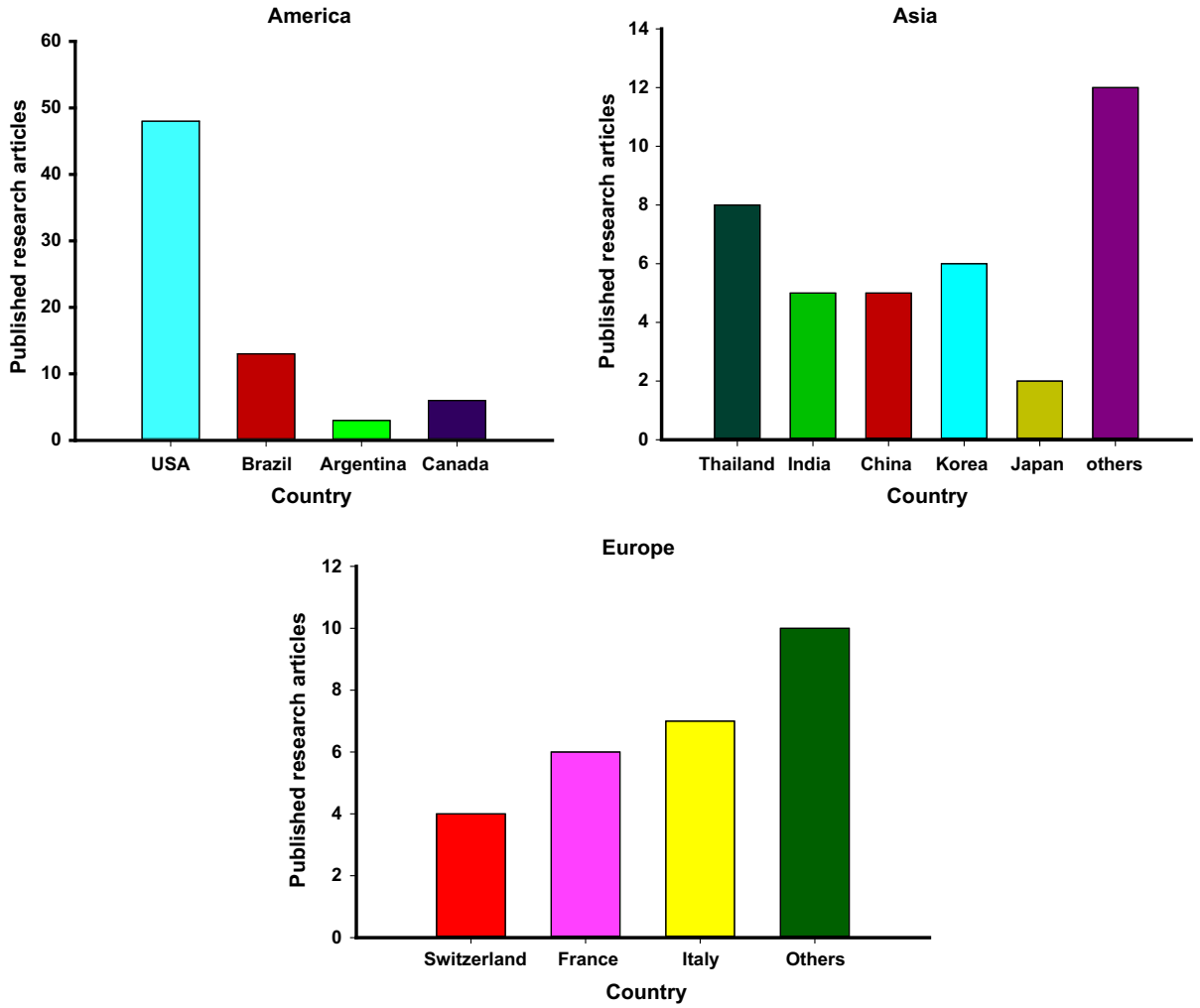

Fig. 2 Investigation on encapsulation of bacteriocin in the respective continent, using the following on-line editorial databases: Science Direct, Scopus, Springerlink, Ingenta, Wiley and Scielo, between 1996 and 2017

research articles, review articles, and short communications in the percentage-wise contribution of 22.72% (Journal of Food Protection), 13.63% (International Journal of Food Microbiology), 13.63% (Food Microbiology), 10.60% (Food Control), 10.60% (Probiotics and Antimicrobial Proteins), 7.57% (Food Research International), 6.06% (LWT—Food Science and Technology), 6.06% (Food Microbiology and Safety), 4.54% (Journal of Agricultural and Food Chemistry) and 4.54% (Letters in Applied Microbiology) (Fig. 3). Furthermore, bacteriocin encapsulation was majorly carried out using antimicrobial film coatings (50%), liposomes (23.40%), nanofibers (22.34%) and nanoparticle systems (4.25%) (Fig. 4a). Moreover, the collected articles were also classified by application field: food protection and pharmaceutical field (Fig. 4b). On the other hand, the 1996–2017 period's patent database showed two major contributions in 2000 and 2016 (Fig. 5). The granted patents on bacteriocin encapsulation processes, characterization, and constancy in situ or ex situ applications in foodstuffs or health matters, have been released mainly by the United States Patent Office (USPTO), World Intellectual Property Organization (WIPO/PCT), European Patent Office (EPO), and Australian Patent Office (AU) (Fig. 6a), involving applications in the food and pharmaceutical industries, mainly (Fig. 6b).

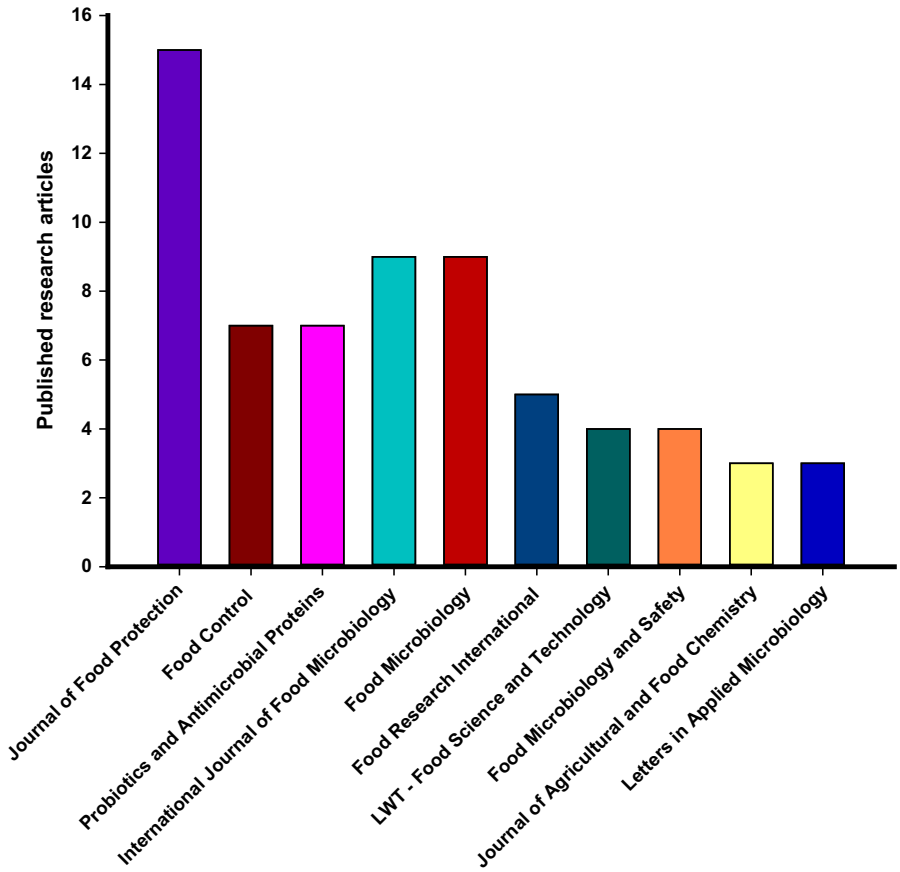

Fig. 3 Main journals that published research concerning the encapsulation of bacteriocins. Source databases: Science Direct, Scopus, Springerlink, Ingenta, Wiley and Scielo, between 1996 and 2017 (total number of articles, 135)

Different types of nanoencapsulation systems

According to the National Nanotechnology Initiative (NNI) nanotechnology had a scientific archetype focused on the science of 1–100 nm elements that was manipulated to perform encapsulation. The basic advantage of nanoencapsulation of bacteriocins using nanomaterials lies in the necessity to increase its pharmacokinetics by altering physical characteristics, such as solubility, half-life and bioavailability (Reis et al. 2006; Soppimath et al. 2001; Yadav et al. 2011; Zhang et al. 2010).

Metal NPs systems

Encapsulation as NPs may offer a potential solution to protect bacteriocins, improving its efficacy and stability in practical applications. Metal NPs primarily gold (Thakor et al. 2011), palladium (Coppage et al. 2013) and silver (Thio et al. 2012) were among the most commonly used in established drug delivery systems. Owing to their small size and positive charge, metal ions act as free radicals diffusing into and disrupting the cellular membranes (Lewinski et al. 2008). Magnetic nickel NPs uniformly coated with a nanolayer biofilm of polyacrylic acid was used to immobilize the AMP LL-37, against *Escherichia coli* (Chen et al. 2009). In addition, metal NPs moulded into different shapes and sizes were used to enhance the overall therapeutic effect. Table 1 shows some representative published articles regarding bacteriocins along with NPs for food and pharmaceutical applications.

Solid lipid nanoparticles (SLN)

The lipid-based formulation systems are generally composed of a triglyceride core and a phospholipid

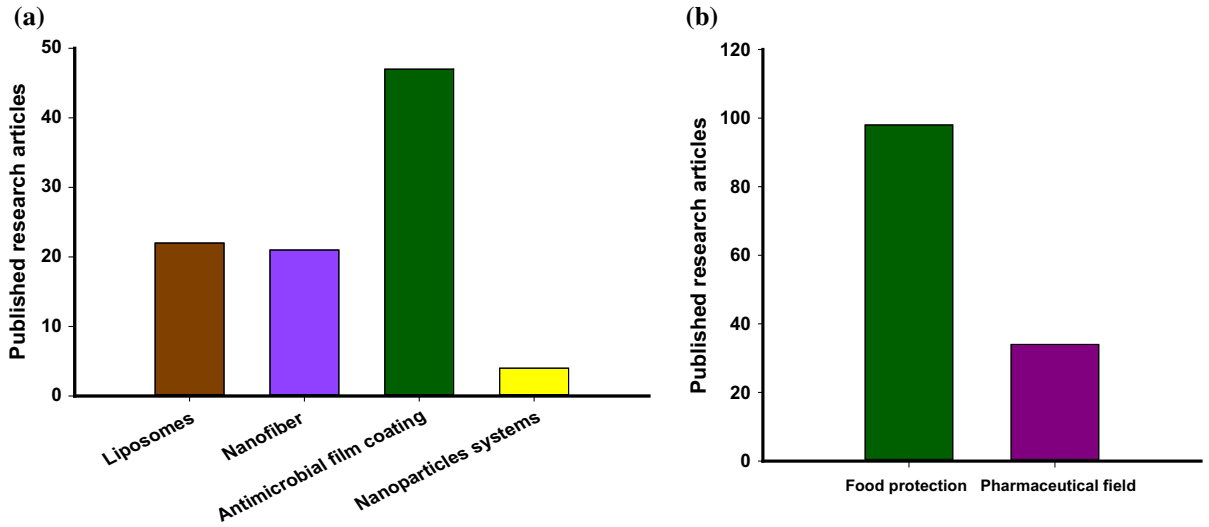

Fig. 4 **a** Main types of encapsulation methods involved in bacteriocin encapsulation, and **b** fields of application of encapsulated bacteriocin (on the basis of the on-line editorial databases: Science Direct, Scopus, Springerlink, Ingenta, Wiley and Scielo, from 1996 to 2017)

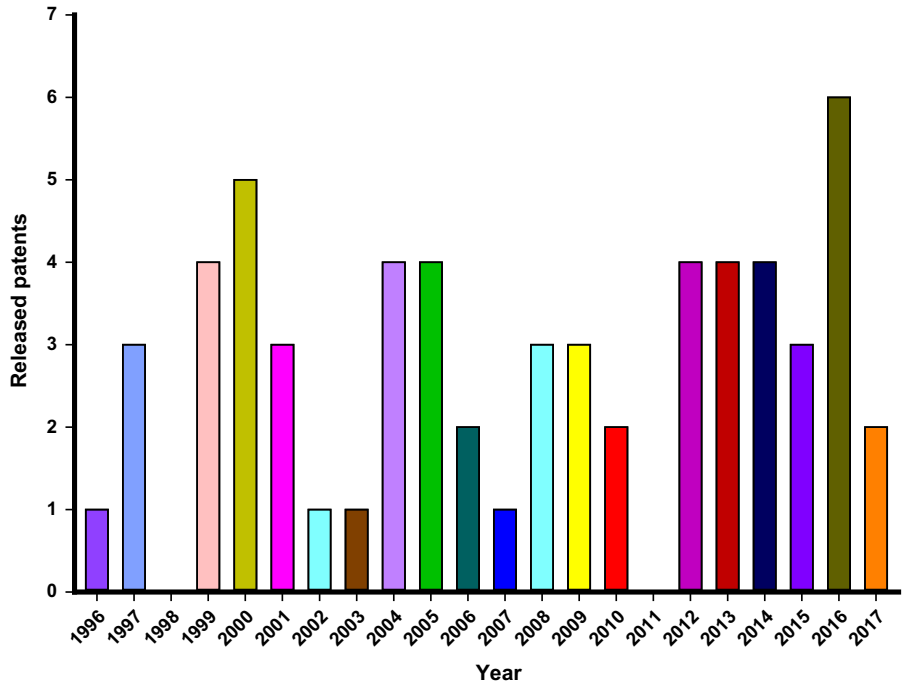

Fig. 5 Patent contribution on bacteriocin encapsulation between 1996 and 2017 on the basis of the following on-line databases: Espacenet, Patent Scope, Lens, Upsto and Google patents

coat with high-melting point, which is actually responsible for a solid state character, both at room and human body temperatures (Puri et al. 2009). Nisin has been incorporated into SLN carriers, exhibiting a continuous release for about 25 days, based on the pH

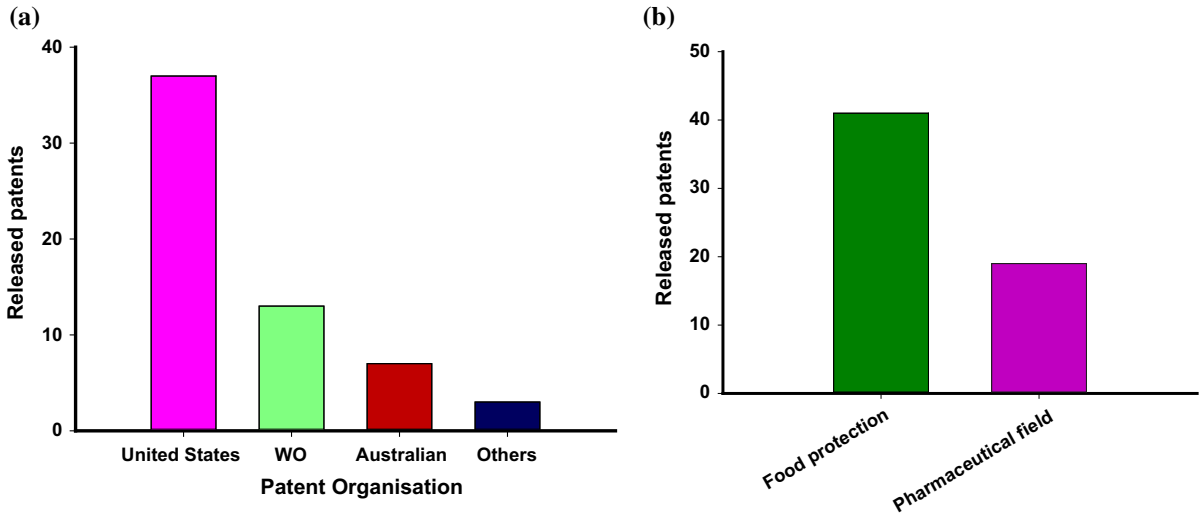

Fig. 6 Granted patents concerning the encapsulation of bacteriocins from 1996 to 2017: **a** Major organizations that issued patents. **b** Patents concerning both food and pharmaceutical applications (on the basis of the on-line databases Espacenet, PatentScope, Lens, Upsto and Google patents)

and the salt concentration of the buffer solution (Prombutara et al. 2012).

Phytoglycogen NPs

Phytoglycogen is a high-density carbohydrate NPs used for formulating novel efficient nanoconstructs (Chen et al. 2015). According to Bi et al.(2011b) Nisin had been effectively carried by phytoglycogen particles, proved against *L. monocytogenes*, but the deepest activity had associated with the octenyl succinate and β-amylolysis substitutions. In a related study, phytoglycogen octenyl succinate has been successfully used to form an oil-in-water emulsion for delivering nisin against *L. monocytogenes* (Bi et al. 2011a).

Gold nanoparticles (Au-NPs)

Metal NPs induce oxidative stress by generating reactive oxygen species, with toxicity due to the accumulated free-metal ions (Seil and Webster 2012). Thirumurugan et al. (2013) tested NPs obtained from the combination of Au-NPs with nisin, obtaining higer AMA against three pathogens, compared with the components alone. In other investigation, Mossallam et al. (2014) used *Lactobacillus acidophilus* CH1 bacteriocins combined with Au-NPs aganist spores of the fungus *Enterocytozoon bieneusi*, wchich causes intestinal microsporidiosis. They obtained a reduction of both spore extrusion and the infectivity of *E. bieneusi*, after exposure to bacteriocins/Au-NPs complex (Mossallam et al. 2014).

Silver nanoparticles (Ag-NPs)

Ag-NPs were used in numerous applications, extending from coating medical devices, wound dressings, coating textile fabrics, water treatment and filtration. Ag-NPs were majorly recognized in view of the broad-spectrum AMA against certain organism of clinical importance, including drug-resistant pathogens (Lara et al. 2009; Zinjarde 2012). Specifically, enterocin-capped Ag-NPs exhibited excellent efficiency against three food pathogenic organisms, namely *E. coli*, *L. monocytogenes* and *S. aureus* (Sharma et al. 2012).

Chitosan system

Chitosan is a linear polysaccharide produced by the deacetylation of chitin and it has been used for fabrication of NPs (Nitta and Numata 2013). The combination of chitosan (CS) and alginate (ALG), gives a composite with better delivery behaviour than the polymers alone. Such specific combination had been effectively used to nanoencapsulate nisin, with 95% entrapment efficiency (Zohri et al. 2010). In other hand, the nisin-loaded CS-ALG NPs showed a tremendous level of AMA against *L. monocytogenes*

Table 1 Published articles regarding bacteriocins along with NPs in food and pharmaceutical applications

Fabrication method	NPs	Bacteriocins	Particles size	Entrapment efficiency	Target pathogenic organisms	Effect of nanoformulation	References
High pressure homogenization	Solid lipid nanoparticles (SLNs)	Nisin	159–175 nm based on nisin concentration	69.2–73.6%	*L. monocytogenes* and *L. plantarum*	Extended the AMA for a longer period	Prombutara et al. (2012)
Adsorption of nisin to emulsion of NPs	Carbohydrate NPs	Nisin	336 and 50.2 nm based on phytoglycogen	NR	*L. monocytogenes*	Retained the efficacy for a longer period	Bi et al. (2011b)
NR	Ag NPs	Enterocin	325 nm	NR	A group of Gram-positive and Gram-negative bacteria	Broad-spectrum inhibition against food pathogens without any toxicity to red blood cells	Sharma et al. (2012)
NR	Chitosan/ alginate NPs	Nisin	50–205 nm	90–95%	*S. aureus*	Maximized and prolonged the AMA with minimum concentration of nisin	Zohri et al. (2010)
Semi continuous compressed CO_2 anti-solvent precipitation	Poly-L-lactide NPs	Nisin	200–400 nm based on nisin concentration	About 95%	Sustained AMA	Extended the AMA for a longer period	Salmaso et al. (2004)
NR	Chitosan/ alginate NPs	Nisin	50–205 nm	90–95%	*L. monocytogenes* ATTC25923 and *S. aureus* ATTC19117	Enhanced the AMA with less damaging effect on the tested food	Zohri et al. (2013)
Dielectric barrier discharge glow plasma fluidized bed	Magnetic NPs	Antimicrobial peptide	240 nm	NR	*E. coli*	NPs immobilizing antimicrobial peptides could effectively increase the antimicrobial rate	Chen et al. (2009)

NR not reported, *NPs* nanoparticles

and *S. aureus* (Zohri et al. 2013). Studying Ni-CS-ALG NPs (Bernela et al. 2014) and Ni-CS-Carageenan (Chopra et al. 2014), researchers obtained important AMA against *M. luteus* MTCC1809, *P. aeruginosa* MTCC424, *S. enterica* MTCC1253 and *E. aerogenes* MTCC2823 during 20 days; furthermore, when added this NPs in tomato juice, they observed no changes in the food quality during 6 months.

Nanofibers

Nanofibers are designed by spinning a polymer solution using high potential electric field. Nanofibers have attracted a lot of attention due to their large surface area, small pore size, huge physical stability, strong encapsulation ability, target specific delivery and sustained release of a variety of drugs (Luong-Van et al. 2006; Maretschek et al. 2008). In healthcare environments, exposed chronic wounds are extremely susceptible to nosocomial infections; in response to this problem, among the alternatives it has been recently reported the wound dressing production by bacteriocins-loaded nanofiber technology to promote wound healing with interesting results against *S. aureus* in a mice model (Heunis et al. 2013).

Electrospinning method

Bacteriocins have been loaded onto nanofibers in a process called electrospinning (Williams et al. 2012; Heunis and Dicks 2010). Nanofibers were investigated for bacteriocin potential uses in biomedical applications, and most studies pointed the promising relevance for the development of tissue engineering scaffolds (Pham et al. 2006). In electrospinning, a mixture of polymers and bacteriocin is dissolved in a solvent and loaded into a syringe. A high voltage is applied to electrodes in the polymer-bacteriocins solution; as a result, bacteriocins loaded polymer nanofibers are formed and collected by a metal screen collector. The resulting nanofibers have nano- to micrometer diameters and are uniformly loaded with bacteriocins. Interestingly, specifically Nisin-PEO (poly(ethylene oxide)) and PDLLA (poly(D,L-lactide)) (50:50) blend nanofibers exhibited an in vitro AMA against methicillin-resistant *S. aureus* (MRSA) for at least 4 days (Heunis et al. 2013). Furthermore, nisin-PEO-PDLLA nanofibers enriched with 2,3-dihydroxybenzoic acid (DHBA), decreased by 88% the MRSA biofilm formation after 24 h of exposure (Ahire and Dicks 2015). In another study, PEO-PDLLA nanofibers enriched with nisin and Ag-NPs exhibited broad AMA against both Gram-positive and Gram-negative bacteria (Ahire et al. 2015). Plantaricin 423 encapsulated in PEO nanofibers produced by electrospinning, exhibited AMA against *E. faecium* and *L. sakei* (Heunis et al. 2010). Table 2 presents some selected published articles on bacteriocins-loaded nanofiber applied for AMA in food and pharmaceutical applications.

Liposomes

Thin film hydration method

Liposomes are composed of one or more lipid bilayers forming vesicles. Phosphatidylcholine (PC) consists of a mixture of natural phospholipids made of a polar end formed by a choline and a phosphate group linked to the hydrophobic portion linked by ester bonds with the glycerol. Liposomes could entrap and protect different substances from undesired interactions that can affect their functionality (Sant'Anna et al. 2011). The encapsulation of bacteriocins into liposomes would be achieved by the thin film hydration method; by this technique, a preformed lipid film is hydrated with an aqueous buffer containing the bacteriocin, at a phase transition temperature of lipids. The bacteriocins entrapped into lipids composition and perhaps attributed to electrostatic and hydrophobic electrostatic and hydrophobic interactions between bacteriocin and phospholipids (Were et al. 2003). Most bacteriocins are cationic amphiphilic molecules; therefore, they possibly are encapsulated in the inner aqueous phase of liposome and also immobilized into liposome membranes. Bacteriocins have been entrapped into PC nanovesicles performing the direct applications of food protection such as proteolytic degradation or interaction with food components) (da Silva Malheiros et al. 2010c). On the other hand, nisin-loaded PC nanovesicles caused no significant inhibition of target pathogens in comparison to free nisin, whereas PC:Phosphatidylglycerol (PG) (8:2 and 6:4) liposomes produced a significant inhibition, suggesting PG-containing nanovesicles to release their contents more efficient (Taylor et al. 2008). Liposomes prepared from different proliposomes (Pro-lipos® H, S, C and DUO) with lower contents of negatively

Table 2 Some published articles on bacteriocin loaded nanofiber used for AMA in food and pharmaceutical applications

Bacteriocin	Particles size	Target pathogenic organisms	Effect of nanoformulation	References
Nisin	330 ± 79 nm	*S. aureus*	Constant AMA against skin infection and acceleration of the wound healing process	Heunis et al. (2013)
Nisin	200–250 nm	*S. aureus* (Methicillin-resistant *S. aureus*)	Increased the AMA in presence of 2,3-dihydroxybenzoic acid	Ahire and Dicks (2015)
Nisin with AgNPs	288 ± 63 nm	*S. aureus, P. aeruginosa* *K. pneumonia, E. coli, S. typhimurium*	Broad-spectrum AMA was established by the incorporation of nanofibers containing a combination of AgNPs and nisin	Ahire et al. (2015)
Bacteriocin ST4SA	200 to 450 nm	*E. faecium* HKLHS	Highly inhibited growth of organisms	Heunis et al. (2011)
Plantaricin 423	288 nm	*L. sakei* DSM 20017, *E. faecium* HKLHS	Highly inhibited growth of organisms	Heunis et al. (2010)
Nisin	246 ± 57 nm	*S. aureus*, *L. monocytogenes*	Producing ultrafine gelatin-nisin fiber mats that exhibit AMA	Dheraprasart et al. (2009)
Subtilosin	278 nm	Herpes simplex virus type (HSV-1)	Strongly proven that the bacteriocin loaded fibers retain AMA against HSV-1	Torres et al. (2013)

charged phospholipids were less susceptible to the nisin-membrane destabilizing action in comparison with other liposomes (Laridi et al. 2003).

Reversed-phase method

Alternatively, in the reversed-phase method an aqueous solution of the bacteriocin is dropped into the lipid solution to form a water in oil emulsion, which is then, sonicated yielding a homogeneous opalescent dispersion of reverse micelles. The organic solvent was evaporated, resulting in a highly viscous organogel, which is reverted to nanovesicles after addition of ultrapure water (Teixeira et al. 2008).

These two methodologies were compared to encapsulate the nisin in PC nanovesicles, also testing both probe-type and bath-type ultrasound. Film hydration using bath-type ultrasound resulted in liposomes of smaller size and with adequate maintenance of AMA (da Silva Malheiros et al. 2010a). This nanovesicle was applied in milk as a food model, inhibiting the *L. monocytogenes* growth (da Silva Malheiros et al. 2010b). Nisin and BLIS (bacteriocin-like inhibitory substance) P34 were encapsulated in PC liposomes and incorporated into *Minas frescal* cheese (da Silva et al. 2012a). Liposome encapsulation prolonged the nisin and BLIS-P34 antilisterial activities due to gradually releasing as compared with both free nisin and BLIS-P34 (da Silva Malheiros et al. 2012b). Current study (Imran et al. 2016) released rates of fluorescently labelled nisin from liposomal nanocarriers. Interestingly, acidic pH and convenient ethanol concentrations in food-simulating liquid (FSL) improved the stability and retention capacity of loaded drug. The partition coefficient (i.e., nisin concentration in FSL/nisin concentration in nanoliposomes, at equilibrium) values were from 0.23 to 8.78, strong dependencies on nisin affinity toward encapsulating systems as well as on the surrounding FSL (i.e., phosphate-buffered saline, pH 6.8; acetic acid 0.3%, pH 2.8, or ethanol 10%, pH 7). Table 3 includes some articles about bacteriocin liposomes methods applied for antilisterial activity.

Food applications

Encapsulation technology has been exploited as an alternative to protect antimicrobials, potentially enhancing their efficacy and stability in foods (Mozafari et al. 2008). Current research focused on

Table 3 Published articles about bacteriocin loaded liposomes tested for antilisterial activity

Bacteriocin	Particles size	Entrapment efficiency	Effect of nanoformulation	References
Nisin and BLIS P34	218 nm for nisin; 158 nm for BLIS P34	88.9% for nisin; 100% for BLIS P34	Displayed higher AMA	da Silva Malheiros et al. (2012a)
Nisin	190, 181 &148 nm, depending on the method	94.12% with film hydration method	The free nisin was more potent and exhibited more sustained release compared to the encapsulated one	da Silva Malheiros et al. (2010c)
Nisin A	140 nm	94%	Both the free and the encapsulated bacteriocins exhibited the same AMA at low temperature	da Silva Malheiros et al. (2010b)
Pediocin	190 nm	80%	Encapsulated pediocin maintained the AMA for a longer time	de Mello et al. (2013)
Antimicrobial peptide P34	150 nm	100%	Both the free and the encapsulated P34 showed similar AMA	Sant'Anna et al. (2011)
BLIS P40	570 nm	NR	Maintained the AMA for a longer period	Teixeira et al. (2008)
BLIS P34	160 nm	100%	Both the free and the encapsulated bacteriocins the exhibited similar AMA	da Silva Malheiros et al. (2012b)
Nisin	495 nm	46 ± 2%	The particles hindered the growth of spoilage and pathogenic organisms in various meat systems	Boualem et al. (2013)

NR not reported

bacteriocin food biotechnologies delivered the antimicrobials via continuous or sustained release (Chi-Zhang et al. 2004). Controlled delivery improves the efficacy of bacteriocins by ensuring the peptides successfully overcome physiological barriers and preserve structure and functionality (Duncan 2011). Three leading approaches was involved bacteriocin in food: through the addition of purified bacteriocin to food products, the inoculation of a food with a LAB, which produces the bacteriocin itself, or the incorporation of an ingredient that was previously fermented with the bacteriocin-producer bacterium (Jones et al. 2005). Nisin encapsulated in alginate-cellulose nanocrystal beads containing 16, 31 and 63 µg/mL nisin, significantly reduced the *L. monocytogenes* counts by 2.65, 1.50 and 3.04 log CFU/g after 28 days of storage compared with free nisin (Huq et al. 2014). Recently, inventors claimed for a prolonged efficacy of a bacteriocin combined with carbohydrate nanoparticles against *L. monocytogenes* (Bhunia and Yao 2014). Other group assertion for spray dried bacteriocin lactocin 3147 that showed effective antimicrobial activity in foodstuff using conjunction with hydrostatic pressure (Ross and Hill 2004).

Antimicrobial film coatings

Nisin embedded in packaging materials or nisin adsorbed solid on surfaces such as polyvinylic or polysaccharide films allowed the for prolongation of the AMA (Cha et al. 2003; Coma et al. 2001; Hoffman et al. 2001; Natrajan and Sheldon 2000a, b). The AMA of edible hydroxyl propyl methyl cellulose (HPMC) film was obtained by the incorporation of nisin into the fatty acid (stearic acid) film-forming solution. The effect of stearic acid was reducing the inhibitory activity of HPMC film against *L. innocua* and *S. aureus* (Coma et al. 2001). Nilsson et al. (2000) examined the synergistic model of carbon dioxide (CO_2) and nisin evaluated against *L. monocytogenes* Scott A wild-type and nisin-resistant (Nisr) cells grown in broth at 4 °C. This synergism was examined mechanistically by CO_2 enhanced nisin-induced CF

Table 4 Some published articles concerning bacteriocin loaded films in food applications

Food packaging film	Bacteriocins	Target pathogenic organisms	Effect of formulation	References
Pectin-Gellan	BLIS from *S.infantarius* + EDTA	*L.monocytogenes, E.coli* and *S.aureus*	BLIS loaded film exhibited AMA against the tested bacteria in a culture medium containing "Barbocoa", a traditional meat product	Trejo-González et al. (2018)
Pectin-Gellan	BLIS from *S.infantarius* + EDTA	*L.monocytogenes, E.coli* and *S.aureus*	BLIS loaded film exhibited AMA against the three pathogens in a culture medium fresh cheese	Jiménez-Villeda et al. (2018)
Sodium Caseinate	Nisin	*L.innocua*	Nisin film caused a1.1 log CFE/g reduction in listeria counts in surface-inoculated cheese samples after 1 week of storage at 4 °C as compared to control	Cao-Hoang et al. (2010)
Cellulose	Nisin	*L. monocytogenes*	Significantly reduction of listerial growth on frankfurters at the lowest nisin concentration	Nguyen et al. (2008)
Ethylcellulose/ hydroxypropylmethylcellulose/ ethylcellulose	Nisin	*M. luteus*	Three-layer films were incorporated for efficient control and slowly release of nisin	Guiga et al. (2010)
Sodium Caseinate	Nisin	*L. monocytogenes*	Nisin loaded films effectively reduced the growth of pathogens	Kristo et al. (2008)
Soy protein	Nisin	*L. monocytogenes, S. gaminara,* and *E. coli* O157:H7	Malic acid (2.6%)-incorporated soy protein film exhibited the highest activity against the pathogens	Eswaranandam et al. (2004)
Chitosan	Nisin	*E. coli, S. aureus, S. typhimurium, L. monocytogenes* and *B. cereus*	*L. monocytogenes* was the most sensitive and susceptible to nisin loaded chitosan film	Pranoto et al. (2005)
Low-density polyethylene (LDPE)	Nisin	Three nisin-resistant strains of *L. monocytogenes*	Film incorporating 2000 IU/ cm^2 of nisin significantly inhibited the growth of *L. monocytogenes* when compared to control samples	Neetoo et al. (2008)

(carboxyfluorescein) leakage occurs at the cytoplasmic membrane.

Bacteriocin-activated plastic films were involved in storage of milk, hamburgers (Mauriello et al. 2005) frankfurters (Ercolini et al. 2010), cold smoked salmon (Neetoo et al. 2008), etc. Among the known bacteriocins, nisin is currently allowed in food as a pure substance (Deegan et al. 2006; Galvez et al. 2007; Settanni and Corsetti 2008). Some inventors (Nauth and Lynum 2000) patented a stabilized mayonnaise spread with nisin-containing whey inhibiting the growth of a contaminating microorganism. Enterocin 416K1, a bacteriocin produced by *Enterococcus casseliflavus* IM 416K1, is a promising effect for

nisin-alternative food packaging films (Iseppi et al. 2008). Partially purified active bacteriocin isolated from *L. curvatus*, lactocin 705 and lactocin AL705, were loaded onto multiple layers of packaging films exhibiting an AMA against *L. innocua* and *L. plantarum* for up to 45 days (Blanco Massani et al. 2012). Table 4 presents some published articles concerning bacteriocin coated films in food applications.

Pharmaceutical application

The efficacy of LAB-produced bacteriocins was evaluated for use in regulating oral biofilms (Zoumpopoulou et al. 2013). It is important to note that bacteriocin and bacteriocinogenic strains require generally recognized as safe (GRAS) status in order to be sold on the US market. In other hand, Tong and co-workers also studied exclusively for therapeutics treatment against oral biofilms, lantibiotic nisin, in combination with free amino acids against *Steptococcus mutans* biofilms. This result indicated mixtures of either the L or D-enantiomers of Glu, Asp or Cys in combination with nisin had been providing the impact of the lantibiotic against biofilms of *S. mutans* (Tong et al. 2014a). Another interesting study (Lobos et al. 2009) treated against oral pathogens, the combination of the bacteriocin PsVP-10, a non-lantibiotic (class II bacteriocins), with the antimicrobials substances (triclosan and chlorhexidine). In their results showed better synergistics effect against *S. mutans* and *S. sobrinus*. A recent research exhibited that nisin interacts synergistically with chloramphenicol were effectively against *Staphylococcus pseudintermedius* DSM21284 biofilms, though combinations of nisin I4V with penicillin were mainly potent against DSM21284 planktonic cells (Field et al. 2016a). In an additional emerged study, nisin synergy with ciprofloxacin or daptomycin was effectively used against methicillin-resistant *S. aureus* (MRSA) biofilms (Dosler and Mataraci 2013). Tong et al. (2014a) also reported the efficacy of nisin in synergy with chloramphenicol, ciprofloxacin or penicillin at controlling biofilms of the nosocomial pathogen, *E. faecalis* (Tong et al. 2014b).

Novel therapeutic studies suggested the combination of nisin with polymyxins or colistin against multidrug resistant bacteria (Field et al. 2016b). Field and co-workers demonstrated that 1/4 MIC (i.e., Minimum inhibitory concentration) Nisin plus 1/2 MIC polymyxins or 1/5 MIC colistin were affective against P. aeruginosa PA-01 biofilm formation. A study confirmed that synergistic activity of class II bacteriocin, durancin 61A and the broad-spectrum antimicrobial reuterin produced FIC (fractional inhibitory concentration) indices of 0.2 against Clostridium difficile (Schaefer et al. 2010). Interestingly, durancin 61A blends with vancomycin were also displayed synergistic effect against MRSA (*S. aureus* ATCC 700699) with FIC values of 0.3 attained (Hanchi et al. 2017). Notably nisin were encapsulated into polyethylene terephthalate (PET) fibers that had antibacterial properties against strains of *S. aureus* (Behary et al. 2013). In other study, subtilosin was loaded onto a poly(vinyl alcohol) nanofiber that showed virucidal activity against herpes simplex virus type 1 (oral herpes) (Torres et al. 2013). Inventors had patented a pharmaceutical compositions of nisin combined with glycerol monolaurate active for treatment of *H. pylori* infection particularly peptic ulcer and gastric (Blackburn et al. 1998). Bacteriocin-loaded, specifically nisin and ST4STA in brushite cement bone implants (van Staden et al. 2011, 2012) displayed remarkable activity against biofilm methicillin-resistant *S. aureus*. Then brushite cement impregnated with bacteriocin would be an alternative for bone replacement.

Conclusion

To date, bacteriocins have exhibited a promising prospective as antimicrobial alternatives for both the food and pharmaceutical industries. Moreover, during the last two decades, the bacteriocin encapsulation has been a meaningful improvement in the applications of these natural antimicrobials in Food Science and Pharmacy, according to original research reports as well as patents. Nonetheless, the challenges are still enormous and should consider the geographical integration of research groups (i.e. intensify international collaborations) to yield a fast and potent improvement of the bacteriocin encapsulation biotechnologies, especially the nanoencapsulation, which would provide convenient alternatives for the wellness of human being.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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