Table 1
Alternative methods of bovine mastitis prevention and/or treatment

Product category	Product used for treatment	*In vitro / in vivo* tests; administration route	Results	Source
Probiotics	*Lactococcus lactis* LMG 7930	*in vitro* (reference strains causing bovine mastitis in cattle and sheep)	Inhibition of *Staphylococcus aureus*, *Staphylococcus chromogenes*, *Staphylococcus epidermidis*, *Staphylococcus intermedius, Streptococcus agalactiae*	[8]
	Lactobacillus paracasei subsp. *paracasei*, *Lactobacillus plantarum*	*ex vivo* (epithelial cells of the nipple canal in cows) / *in vitro*	Inhibition *of Staphylococcus xylosus*, *S. aureus*, *S. epidermidis*, *Streptococcus uberis*, *S. agalactiae*, *E. coli*	[9]
	Lactobacillus casei BL23	*ex vivo* (epithelial cells of the nipple canal in cows)	Anti-inflammatory effect. Immunomodulatory potential in the mammary gland. Inhibition of *S. aureus* internalization	[10]
	Lactobacillus perolens CRL 1724, L. lactis subsp. *lactis* CRL 1655	*in vivo* Holstein cows; i/mam	Activation of the innate immune response. Reduction of the number of somatic cells. Inhibition of 15 *S. aureus* strains by coaggregation	[11]
	Lactobacillus rhamnosus ATCC 7469, *L. plantarum* 2/37	*in vitro*	Destruction of *S. aureus*, *S. xylosus*, *S. epidermidis* biofilms and replacing them with their own	[12]
	L. lactis DPC 3147	*in vivo* Holstein-Frisian breed cows; i/mam	Interleukin-8 increase. Reduction of the somatic cell number.	[13]
	L. rhamnosus GG	*in vivo* Indian buffaloes; i/mam	White blood cells increase. Inhibition of *Pseudomonas* spp. Reduction of the somatic cell number	[14]
	L. rhamnosus GR-1	*ex vivo* (epithelial cells of the nipple canal in cows)	Inhibition of cell apoptosis induced by *E. coli*	[15]
	Bifidobacterium breve	*in vivo* Holstein cows; i/mam	Inhibition of pathogens. Activation of the innate immune response. Reduction of the somatic cell number	[16]
	Enterococcus mundtii H81	*in vivo* Balb/c mice; i/mam	Inhibition of *S. aureus.* Anti-inflammatory effect. Protection of mammary epithelial barrier integrity	[17]
	Bacillus subtilis C-3102	*in vivo* Holstein breed cows; orally	Reduction of the inflammatory process. Increase in CD4+ T-cells levels in blood. Increased levels of CD11c+ CD172a^{high} dendritic cells in the blood	[18]
	L. lactis subsp. *lactis* CRL 1655, *Schleiferilactobacillus perolens* CRL 1724	*ex vivo* (epithelial cells of the nipple canal in cows)	Inhibition of adhesion *S. aureus*, *S. chromogenes*, *S. uberis* and *E. coli*	[19]

Bacteriocins	Bovicin HC5 (bacteriocin *Streptococcus equinus* HC5)	*in vitro* (bacterial strains isolated from milk of cows with signs of mastitis)	Inhibition of the growth of cultures *S. aureus* and *S. agalactiae*	[20]
	Pm11 peptide	*in vitro* (bacterial strains isolated from milk of cows with signs of mastitis)	Inhibition of the growth of *E. coli*, *S. aureus*, *S. agalactiae* and *S. uberis* cultures	[21]
	Bactofencin A	*in vitro* (cultivated bacterial strains and isolates recovered from milk of cows with signs of mastitis)	Inhibition of *S. aureus* and *Listeria monocytogenes* growth	[22]
	Bactofencin A nisin, reuterin	*in vivo* Holstein breed cows; udder nipple treatment before and after milking	Inhibition of *Staphylococcus* spp., *Streptoccocus* spp. growth	[23]
	Nisin A	*in vitro* (cultivated bacterial strains and isolates recovered from milk of cows with signs of mastitis)	Inhibition of *Streptococcus dysgalactiae*, *S. agalactiae*, *S. aureus*, *S. intermedius*, *Enterococcus faecalis* and *E. coli* growth	[24]
	Garvicin, nisin	*in vitro* (cultivated bacterial strains and isolates recovered from milk of cows with signs of mastitis)	Inhibition of *Acinetobacter baumannii* and *S. aureus* growth	[25]
	Aureocin 4181	*in vitro* (pure culture strains and bacterial isolates recovered from milk of cows with signs of mastitis)	*S. aureus* lysis due to the cell wall destruction	[26]
Bacteriophages	24 (A2), 89A, 46A4a, 89B, P2g 4a, 46A3b, P2g4b, 89C, 24A1a	*in vitro* (bacterial strains isolated from milk of cows with signs of mastitis)	Lysis of antibiotic-resistant *S. aureus*, the combination of a phage with enzymes such as lysozyme or peptidoglycan hydrolase, can increase activity in the latent phase	[27]
	4086-1, 4086-2, 4086-3, 4086-4, and 4086-6 are phages of the *Podoviridae* family	*in vivo* Balb/c mice; i/mam	Lysis of antibiotic-resistant *S. aureus* CVCC 546, reduction of inflammatory infiltration in mammary glands of mice	[28]
	vB_sauM_JS25, family *Myoviridae*	*ex vivo* (epithelial cells of the nipple canal of cows)	*S. aureus* lysis	[29]
	vB_SauS_IMEP5, family *Siphoviridae*	*in vitro* (bacterial strains isolated from milk of cows with signs of mastitis)	Lysis of several *S. aureus* strains	[30]
	vB_EcoM-UFV13, family *T4 virus*	*in vivo* Balb/c mice; i/mam	Reduction of the total bacterial load of *E. coli* by 90%, stimulation of proinflammatory cytokines such as IL-6 and TNF-α	[31]
	S. aureus – specific phages of the families *Myoviridae* (STA1) and *Podoviridae* (EB1) and *L. plantarum*	*in vitro* (bacterial strains isolated from milk of cows with signs of mastitis)	The mixture of bacteriophages, as well as its combination with lactic acid bacteria, demonstrated high antimicrobial activity against *S. aureus*	[32]
	Phages acting against *E. coli* – SYGD1, SYGE1 and SYGMH1	*in vivo* Holstein cows; i/mam	Reduction of the total bacterial load of *E. coli*, the number of somatic cells and inflammatory factors	[33]

	S. aureus – specific phages M8 and B4, family *Podoviridae*	*in vitro* (lytic activity was tested in milk from cows with signs of mastitis)	Lysis of multidrug-resistant, methicillin-resistant and biofilm-forming strains of *S. aureus*, reduction of the total bacterial load in milk	[34]
Endolysins	Group A streptococcal C1 phage endolysin PlyC	Study of the effect of dose on cytotoxicity and oxidative response in bovine polymorphonuclear leukocytes	*S. uberis* lysis	[35]
	Streptococcal phage endolysins λSA2 and B30	*in vitro* determination of lytic activity in milk; C57BL6/SJL mice; i/mam	λSA2 lysine showed high lysis activity in cow's milk against *S. dysgalactiae*, *S. agalactiae* and *S. uberis.* Using a mouse model, the lysis of *S. agalactiae* and *S. uberis* by two endolysins and *S. dysgalactiae* by λSA2 lysine only	[36]
	LysKΔamidase	*in vitro* (bacterial strains isolated from milk of cows with signs of mastitis)	Inhibition of methicillin-resistant and methicillin-sensitive staphylococcal strains	[37]
	Endolysin Trx-SA1 of the staphylococcal phage IME-SA1	*in vivo* cows; i/mam	Reduction of the total bacterial load of *S. aureus* and the number of somatic cells	[38]
Nanoparticles	Copper nanoparticles	*in vivo* Wistar rats; i/musc	Inhibition of *S. aureus*, reducing the overall bacterial load	[39]
Plant extracts and essential oils	*Allium sativum*, *Bunium persicum*, *Oryza sativa*, *Triticum aestivum*	*in vitro* (bacterial cultivated strains)	*A. sativum* showed more extensive inhibition zones against *S. aureus*, *E. coli* and *Klebsiella pneumoniae* than *B. persicum*, *T. aestivum* and *O. sativa*. Methanol extracts and alkaloids had the highest antibacterial activity	[40]
	Minthostachys verticillata essential oil and limonene	*in vitro* (bacterial strains isolated from milk of cows with signs of mastitis)	The essential oil had an inhibitory effect on the growth of all strains, whereas limonene had an inhibitory effect only on *Bacillus pumilus*. Both substances inhibited the formation of biofilms	[41]
	Essential oils of *Thymus vulgaris* L., *Thymus serpyllum* L., *Origanum vulgare* L. and *Satureja montana* L.	*in vivo* Holstein-Frisian breed cows; i/mam	Inhibition of *Staphylococcus* spp.; *Streptococcus* spp.; *Klebsiella* spp.; *Proteus mirabilis*; *E. coli*; *S. uberis*; *S. marcenses* strains, reduction of total bacterial load	[42]

i/mam – intramammarly, i/musc – intramuscularly.