

# *Lactobacillus* sp.—A Threat to Pathogenic Microorganisms and Tumor Cells

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**How to cite this paper:** Sadhu, A. and Ganguly, K.K. (2017) *Lactobacillus* sp.—A Threat to Pathogenic Microorganisms and Tumor Cells. *Journal of Cancer Therapy*, 8, 96-111.

<https://doi.org/10.4236/jct.2017.82009>

**Received:** December 9, 2016

**Accepted:** February 6, 2017

**Published:** February 9, 2017

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## Abstract

Beneficial bacteria, often used as probiotics, play efficient role in providing protection against pathogenic microorganisms in humans. Probiotic bacteria like many *Lactobacillus* sp. (*L. acidophilus*, *L. casei* etc.), *Bifidobacterium* sp. *Streptococcus thermophiles*, *Bacillus coagulans*, etc. are beneficial and nowadays are used as supportive therapeutics. Even *Lactobacillus* is highlighted for showing the anticancer effects on some human cancer cells (cervical, gastric, colon, breast cancer). Some specific antibiotics like peptide antibiotic, Acidolin; some specific bacteriocins and some metabolites like H<sub>2</sub>O<sub>2</sub>, acetic acid, lactic acid produced by *Lactobacillus* sp. kill or inhibit other microorganisms mainly gram positive and gram negative bacteria, including both enteropathogens and spore formers. Proteins like Enterolisin A, Labyrinthin A2, etc. show promising anti-cancer activities. *Lactobacillus* has effective role in clinical and industrial fields. Clinically it is used to manufacture medicines, some hormones and industrially used for broad fermentations, etc. Studies are going on to use *Lactobacillus* in more broad ways, by improving strains, increasing specificity, making more effective and to find out some other characteristics to prepare them as more natural therapeutic modality.

## Keywords

Probiotics, *Lactobacillus*, Anti-Microbial, Anti-Tumor, Antibiotics, Bacteriocin, Proteins, Metabolites

## 1. Introduction

Despite of several antibiotic therapies, surgery, chemo preventive even radio therapeutic approaches diseases, like some microbial diseases and obvious cancer, show poor prognostic outcome. The main downfall of modern science nowadays

is the lack of specificity. For example in the case of cancer, all the traditional cancer therapies, including various surgeries, hormonal therapies, immune therapies, etc. show a lack of efficacy in terms of long-term outcome because of their failure to target cancer cells and toxicity due to non-specific effects on normal cells [1]. Bacteria and fungus may exert deleterious effects on their host in several ways, like conversion of toxic metabolites from ingested material, secretion of toxic substances directly into host, and trigger the inflammatory pathways. Alternative approaches try to boost normal body immune system to fight against those conditions. But a comparatively new strategy has arisen from the development of the field of “Microbiome” in treating different human diseases.

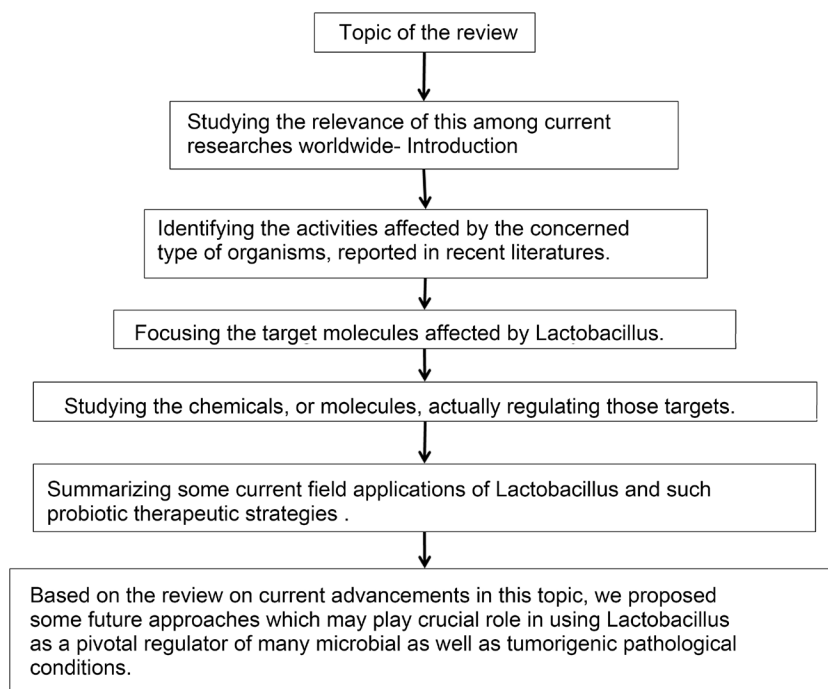
Beneficial bacteria mainly “probiotics” play efficient role in providing benefits to humans. During the past two decades, probiotic (health promoting) microorganisms mainly of genus *Lactobacillus* have been increasingly included in various types of food products, medicines etc., especially in fermented milk products [2]. Beneficial effects conferred by lactobacilli include inhibition of pathogenic organisms, such as *Salmonella*, *Shigella*, *Helicobacter* (causing gastric ulcer), *Staphylococcus* (causing Boils, impetigo, food poisoning, toxic shock syndrome, etc), *Enterococcus* and pathogenic *E. coli* (causing Urinary Tract Infection (UTIs), endocarditis, bacteremia, wound infections, intra-abdominal, pelvic infections, etc.), *Aspergillus niger* (causing Aspergillosis, allergic reaction, fungal growth) etc. *Lactobacillus* is more highlighted for showing the anticancer effects on some cancer cell lines of human (HeLa, cervical, colon, gastric, AGS; HT-29; breast, MCF-7), and on human normal cell line (human umbilical vein endothelial cells [HUVEC]). *Lactobacillus* is so important because it exhibits desirable properties and activities with no significant cytotoxic effects. Overall, *Lactobacillus* showed favorable potential as a bioactive therapeutic agent [3].

This article is focused to review some of the current findings highlighting anti-microbial and anti-tumor effect of some human beneficial bacteria. This will also indicate some important molecules which may show in future significant clinical and industrial applications. Here we have followed the given pattern of data collection strategy as shown in **Figure 1**.

## 2. Spectrum of Activities

### 2.1. Antimicrobial Activity of *Lactobacillus*

Studies show that *Lactobacillus* is capable of inhibiting growth of other microorganisms or killing them. *Lactobacillus* shows antibacterial activity against *Staphylococcus*, *Enterococcus* and *E. coli* by recording the zone of inhibitions for all cases. <sup>2</sup>NRRL B-227, an active strain of *Lactobacillus* sp. as well as Acidolin an antibiotic produced by *Lactobacillus* shows various activities against Gram positive and Gram-negative target strains, including both entero-pathogens and spore formers especially human intestinal bacterial pathogens [4] [5]. Though it was not effective against some of the lactic acid bacteria including the organism with which it was associated, *L. acidophilus* 2181 [5]. Studies also show that *Lactobacillus* bacteriocin inhibits the growth of bacteria like *Bacillus mycoides*,



**Figure 1.** Flow chart to illustrating the selection process of relative literatures.

*Staphylococcus aureus*, *Proteus vulgaris* and *Streptococcus faecalis*. Though *Bacillus cereus*, *Bacillus amyloliquifaciens*, *Pseudomonas aeruginosa* and *Salmonella typhi* shows resistant to the isolates producing antibacterial substances [6]. Another metabolite hydrogen peroxide ( $H_2O_2$ ) produced from *Lactobacillus sp.* inhibits the growth of *E. coli* and *Bacillus sp.* and the application of minimum concentration results in growth inhibition of many infectious bacteria like *Gardnerella*, *Salmonella sp.*, *Chlamydia*, *Trichomonas* and *Neisseria*, isolated from cervicovaginal infections [7]. *Lactobacillus* also shows the ability to inhibit the formation of *Staphylococcus sp.* biofilm and also acts as an antibiofilm agent [8]. All reports prove that *Lactobacillus* has an effective anti-microbial activity.

## 2.2. Antifungal Activity of *Lactobacillus*

Reports say that *Lactobacillus* also has an effective antifungal activity. Studies show that *Lactobacillus* shows antifungal activity against some pathogenic fungus like *R. solani* and *F. oxysporum*. The obtained results showed that the isolates were significantly active on both *R. solani* and *F. oxysporum* as compared to the control. It shows the growth inhibition (GI %) against both fungus ranges from 26.7% to 52.3%, and 17.1% to 51.2% respectively [2]. Strong antifungal activity of *Lactobacillus brevis* KR3, KR4, KR51 and KR53 against *A. awamori* and *P. claviforme* was detected in repeated (triplicate) tests. A full inhibition in most of the samples with *A. niger* and *F. graminearum* was also obtained. But exceptionally *L. brevis* KR53 shows no effects on *A. niger* and *F. graminearum* [9]. Another study shows that *Lactobacillus sp.* inhibits the growth of fungus like *A. fumigatus* and *A. niger* spores and mycelia [10].

### 2.3. Tumor Cell Migration Inhibition

Reports also show that *Lactobacillus* can inhibit tumor cell migration. Lactic acid bacteria (LAB) show effects on some specific types of cancers like colorectal cancer, liver cancer, bladder cancer, breast cancer, gastric cancer. Effect of *Lactobacillus* was also reported on some human cancer cell lines like [11] SNU-1 [12] SNU-C2A, a colon adenocarcinoma cell line [13]. DLD1, a colon adenocarcinoma cell line, a pseudo diploid human cell line with the chromosome number of 46, shows retarded migration in response to *Lactobacillus* [14] [15] [16]. K562, a leukemia cell line. In K-562 cell line the stemline chromosome number is triploid, also shows appreciable decrease in migration under same bacterial activity [17] [18] [19]. Reports have shown A549, a lung carcinoma cell line showing migration inhibition in presence of the same bacteria. The rate with higher ploidies was low. There were 6 markers present in single copies in all cells. Though most cells had two copies of both X and Y chromosomes, one or both Y chromosomes were seen to be lost in 40% of 50 cells that were analyzed. N2 and N6 chromosomes had single copies per cell and N12 and N17 had 4 copies [20] [21] [22]. A498 is a kidney carcinoma cell line. It is a cell line with Hypertetraploid chromosomes and its modal chromosome number is 96 [23] [24]. HT-1376 a urinary bladder carcinoma cell line with  $2n = 46$ , hypertetraploid chromosome. Its modal chromosome number varies from 104 to 121 [25]. HeLa is cervix carcinoma cell line. Its modal chromosome number is 82. There are four types of HeLa marker chromosomes have been identified. HeLa Marker chromosomes contain 1 copy of M1, 1 copy of M2, 4 - 5 copies of M3, and 2 copies of M4. M1 is a rearranged with the long arm of chromosome 3 and centromere of chromosome 1, M2 is a hybrid of long arm of chromosome 5 and short arm of chromosome 3, M3 is an iso-chromosome of the short arm of chromosome 5 and M4 consists of the long arm of chromosome 11 and a chromosome 19 arm [26] [27] [28] [29]. Reports with MCF7 showed some biosurfactants produced by *Lactobacillus paracasei* subsp. *paracasei* A20 having potential for breast cancer treatment [25] [30] [31] [32] [33]. HepG2 is a hepatocarcinoma cell line. Its modal chromosome number is 55 and has a rearranged chromosome 1 [34] [35]. PC3 is a prostate carcinoma cell line. The line is near-triploid with a number of 62 chromosomes. Nearly 20 marker chromosomes commonly found in each cell was reported. But normal N2, N3, N4, N5, N12, and N15 are not found. No normal Y chromosome was detected [36] [37]. Report shows that *Lactobacillus* bacteriocins have a cytotoxic effect on neoplastic cell lines of both human and animal. The effect on cells from animal origin is more than human origin [38]. Another study shows that concentrated filtrate of *Lactobacillus acidophilus* had a significant cytotoxic effect on growth of AMN cell line [39].

### 2.4. Tumor Cell Proliferation Inhibition

*Lactobacillus* is capable to modulate cell proliferation and apoptosis. Such activities are useful for future cancer prevention strategies. In vitro studies have reported the anti-proliferative and pro-apoptotic effects of *Lactobacillus* in various

cancer cell lines while in vivo studies have shown the inhibitory activity of probiotics on liver, bladder and colon tumors [40]. LAB has the probiotic characteristics including acid tolerance, L-lactate production and has the ability to attach with the epithelium cells. *Lactobacillus acidophilus* and *Lactobacillus casei* shows inhibitions of cell growth. In particular, the HK cells of *Lactobacillus acidophilus* appeared to be the most effective at inhibiting the growth of cancer cell lines like HeLa, SNU-1, HT-29 (an epithelial cell line) with modal chromosome number 71. In HT-29 the stem line chromosome is hyper-triploid with occurrence rate of 2.4%. There is a presence of seventeen marker chromosomes (single copy per chromosome) mostly found in metaphases [41] [42] [43] [44] and PANC-1 is a pancreatic epithelioid carcinoma. Chromosome studies show that about 22% of the cells were found with modal chromosome number 63 and about 32% of cells were found with the modal chromosome number 61. This is a hyper triploid human cell line [45]. The HK cells of *Lactobacillus acidophilus* were less effective, however on U-87 cells (modal chromosome number of 44). It is a brain glioblastoma; astrocytoma cell line. This is a hypodiploid human cell line with the occurrence of 48% of cells. The rate of higher ploidy was 5.9%. Reports shows that there are twelve markers were common to all cells in which only one copy of normal X was present [46] [47] [48]. The HK cells of *Lactobacillus casei* exerted anti-proliferative effects on all cell lines with the exception of the PANC-1 cells [49].

### 3. Nature of Components Secreted by Those Beneficial Bacteria

All micro-organisms have some special components like metabolites, proteins, toxins, bacteriocins, etc. that are secreted to inhibit other micro-organisms, or to kill cells, inside the host cells or in vitro.

#### 3.1. Antibiotic

Many bacteria produce some specific antibiotic to inhibit the growth of other microorganisms. *Lactobacillus* is one of them that produce antibiotics. *Lactobacillus* produces an antibiotic named peptide antibiotic. This peptide antibiotic leads to the antimicrobial activity. After purification and characterization of that antibiotic it is found that the peptide antibiotic is a bacteriocin antibiotic [4]. Another antibiotic Acidolin is a low molecular weight molecule about approximately 200 Da. It is acidic in nature. It is highly hygroscopic and thermo stable and reported to possess a yellow-brown color, produced by *Lactobacillus acidophilus* that kill or inhibits other microorganisms mainly of gram positive and gram negative strains including both enteropathogens and sporeformers. It was not effective against some of the lactic acid bacteria including the organism with which it was associated, *L. acidophilus* 2181 [5].

#### 3.2. Bacteriocins

*Lactobacillus* sp. is capable to produce its specific biofilm and bacteriocin as well.

Bacteriocin shows strong antimicrobial activity against many pathogenic bacteria like *Streptococcus faecalis*, *Bacillus mycooides*, *Staphylococcus aureus* and *Proteus vulgaris*. It is also reported that *Pseudomonas aeruginosa*, *Bacillus amyloliquifaciens*, *Salmonella typhi* and *Bacillus cereus* shows resistance to bacteriocin. The resistant activity is different from strain to strain. The degree of inhibition was grouped as very strong inhibition (15 - 18 mm), moderate inhibition (6 - 9 mm) and no inhibition. Bacteriocins isolated from strains like BFL1 and GAL2 strongly inhibit the growth of *Bacillus mycooides* BFL2, GAL2 and GAL3 inhibit *Staphylococcus aureus* moderately and BFL1, GAL1CWL1, CWL17, CWL25 and CWL29 inhibit *Staphylococcus aureus* very strongly. Bacteriocin inhibited *Proteus vulgaris* and *Streptococcus faecalis* at a higher range compared to other strains. *Klebsiella pneumonia* is strongly inhibited by BFL1 and GAL1 strains. Bacteriocin also shows ability to inhibit the growth of human cancer cell lines. Different concentrations of bacteriocin shows significance inhibitory on of RD and MDCK cell lines [40]. RD is a muscle rhabdo-myosarcoma cell line. It is reported that the RD cell line is unstable within a hyperdiploid bimodal stemline number of 49 and 50. It is seen that there are a total of twenty-two cells had chromosome associations i.e. 15 cells contains micro-chromosomes, 2 cells contains breaks, 2 cells with fragments, 2 cells had achromatic gaps and 1 cell with a secondary constriction [50] [51]. MDCK is a kidney cell line. Reports shows that it is a hyper diploid canine cell line with a modal chromosome number of 76 and has low polyploidy rate. Several unidentifiable marker chromosomes were present in most of the cells [41] [52]. Bacteriocins like Lsl\_003, Lsl\_0554, and Lsl\_0510 shows anticancer activity [53].

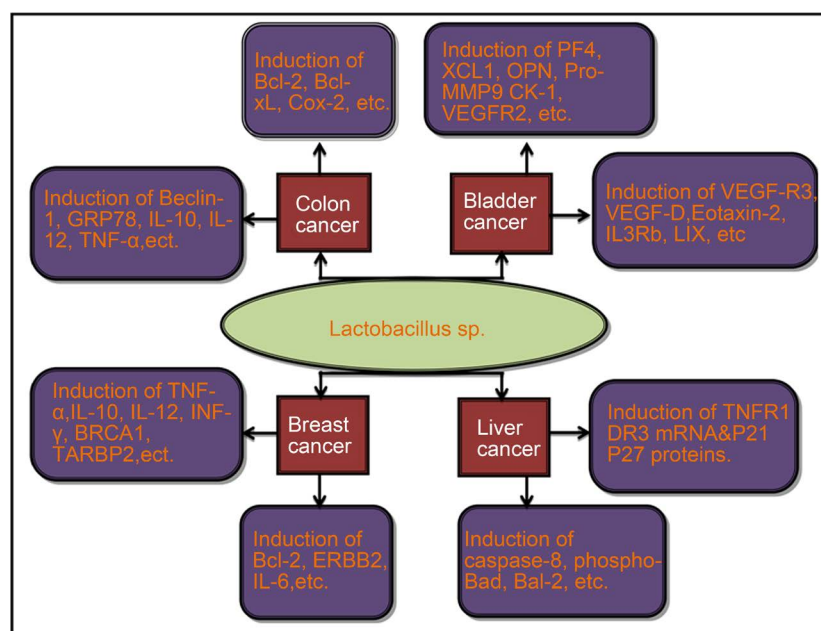
### 3.3. Proteins

Various proteins contained in bacteria, or secreted from the bacteria are responsible for antimicrobial activity as well as antitumor activities. Studies show that the antimicrobial activity of *Lactobacillus* was responsible for the expression of heterologous protein. GFP expression was confirmed by the presence of a 27-kDa protein [54]. Another report shows that bacteriocins produced by lactic acid bacteria exert similar characteristics to microcins. These gene-encoded bacteriocins are peptides with low molecular weight (less than 60 amino acids) [55]. The gram positive bacteriocins are generally divided into class I which are modified peptides called lantibiotics. Lantibiotics are peptide antibiotics that contain the polycyclic thioether amino acids like lanthionine or methyl anthionine, as well as two unsaturated amino acids 2-aminoisobutyric acid and dehydroalanine [56] [57] [58]. Class II are generally unmodified peptides called non-lanthionine. Lanthionine is reported a non-proteinogenic amino acid with the chemical formula (HOOC-CH(NH<sub>2</sub>)-CH<sub>2</sub>-S-CH<sub>2</sub>-CH(NH<sub>2</sub>)-COOH). It is them on osulfide analog of cystine, lanthionine is composed of two alanine residues that are crosslinked on their  $\beta$ -carbon atoms by a thioether linkage [59]. Class III is large proteins and is heat unstable. Class I bacteriocins are again subdivided into antibiotics (e.g. Line arpeptidenisin and globular peptide mersacidin), labyrinth

peptins (eg. globular peptide labyrinthopeptin A2) and sactibiotics (e.g. globular peptide subtilisin A). Class II bacteriocins are generally less than 10 kDa consists of 30 - 60 amino acids, which exhibits properties like heat tolerance, positive charge and unmodified non-lanthionine. Class III bacteriocins are generally greater than 30 kDa *i.e.* large molecular weight proteins. They are heat unstable. They can be again sub-divided into two groups. Group A bacteriocins are the bacteriolytic enzymes which kills bacteria by lysis of the cell wall, (e.g. Enterolysin A). Group B bacteriocins are non-lytic proteins (eg. Caseicin 80 and Helveticin) [55]. There are three hypothetical bacteriocins, namely Lsl\_003, Lsl\_0554, and Lsl\_0510 which are functionally similar to Azurin (mainly found in *Pseudomonas* sp.) shows anticancer activity by inhibiting cancer cell proliferation [53]. Azurin reported to inhibit growth of cancer cells by inhibition of cell signaling, inhibition of angiogenesis and stabilization of p53. Azurin is a periplasmic blue copper protein found in some bacteria, that undergoes oxidation-reduction reactions between Copper atoms (Cu (I) and Cu (II)), and transfers electrons between enzymes. Reports show that in spite of Azurin, Laz (lipidatedazurin) produced by the members of Gonococci/Meningococci, including *Neisseria meningitidis* shows anticancer effects. Laz contains an H.8 epitope which is an additional 39 amino acid moiety present in the N-terminal part of the azurin which triggers Laz to cross the entry barrier to brain tumors such as glioblastomas [60]. The architecture of azurins seems like plastocyanins, with the presence of a “back flap” The additional back flip formed by two  $\alpha$ -helices which are located between the fifth and sixth  $\beta$ -strands. Azurins and pseudoazurins undergoes oxidative deamination of primary amines and denitrification processes by shuttling electrons from aromatic amine dehydrogenase to cytochrome oxidase and from some *c*-type cytochromes to nitrite reductases [61]. Azurin has the ability to penetrate cancer cells without membrane disruption and an efficient anticancer activity suggests that Azurin may be effective against different types of tumors with less side effects than current anticancer therapeutics [59].

### 3.4. Other Organic Secretions

Other organic compounds like some acids, polysaccharides, some metabolites, etc. *Lactobacillus* is well known for its ability to produce lactic acid, acetic acid. The acids make the medium extremely acidic hence inhibit the growth of other microorganisms. Some strains of *Lactobacillus* produces high amount of hydrogen peroxide ( $H_2O_2$ ) as their metabolite. This  $H_2O_2$  is responsible for the antimicrobial activity.  $H_2O_2$  inhibits the growth of *Streptococcus* sp., *E. coli*, *Bacillus* sp. etc. [7] [62]. *Lactobacillus* is known to inhibit cancer cells. A polysaccharide fraction of *L. acidophilus* causing a death of HT-29 cancer cell lines by inducing apoptosis, also polysaccharide isolated from *Lb. acidophilus* were significantly regulated the expression of BCL-2 interacting protein and cell division cycle protein [39]. The chemicals and proteins we have just discussed, is summarized in **Figure 2**.



**Figure 2.** Some proteins of different cancer cells are either inhibited or induced by *Lactobacillus sp.* to prevent tumor formation: the figure has summarized some of the target molecules, by regulation of which *Lactobacillus sp.* is reported restrict formation and/or progression of the carcinoma of breast, liver, colon or bladder.

#### 4. Molecular Mechanisms That Leads to the Activities

It is believed that the anti-microbial or anti-cancer activities by a microorganism exerted some basal intracellular mechanisms or some mode of actions. This section will highlight the mechanisms of some of the important metabolites, bacteriocins or proteins are discussed as follows. Peptide antibiotics are known for its anti-microbial and anti-cancerous activities. Examples are bacitracin, actinomycin, colistin, and polymyxin B. The mechanism of action of peptide antibiotic suggested by the model of Gregory *et al. i.e.* “polypeptides antibiotics induce the transient existence of a chaotic pore state by creating structural destruction and tensions when they situate in a lipid bilayer” [63] [64]. The detailed mechanisms of action of other polypeptide antibiotics are largely unknown but assuming it is directed to bacterial membranes [65]. Acidolin inhibits pathogenic microorganisms by preventing them from attaching or penetrating to the host cells. It is done by making the barrier effect of the intestinal mucosa stronger and releasing of metabolites that protects the gut. The metabolites may be arginine, glutamine, short-chain fatty acids, conjugated linoleic acids, etc. [66]. Bacteriocins produced by *Lactobacillus sp.* not only can be divided on the basis of their structures, but also on the basis of their mode of action. Some of the members of class I *i.e.* lantibiotic bacteriocins, such as nisin, reported to have a dual mode of action. The mode of action involves the binding of bacteriocin proteins to lipid II, and prevents the transport of peptidoglycan subunits to the cell wall, and therefore leads to the synthesis of incorrect cell wall, results in cell death. They can also use lipid II as a docking molecule that can initiate a process of pore formation and membrane insertion that leads to cell death. A two-peptide lantibiotic, e.g.



lactacin 3147 that can have these dual activities with the distribution across two peptides, whereas mersacidin has only the lipid-II-binding activity, but it does not form pores. Generally class II peptides have a helical structure that is amphiphilic in nature, which helps them to insert into target cell membrane and leads cell death. Large bacteriolytic proteins like lysostaphin, can function directly on the Gram-positive cell wall, leading to death and lysis of the target cell [67]. Azurin is a copper containing redox anticancer protein. Azurin enters into the cytosol of cells and travels to the nucleus and increases the intracellular levels of p53 and Bax, which in turn triggers the release of cytochrome-c from mitochondria to the cytosol that activates the caspase cascade, and results in apoptosis [68]. Oxidative biocides like H<sub>2</sub>O<sub>2</sub> are reported to have multiple targets within a cell and the biomolecules present in the cells. The action includes disruption of membrane layers, enzyme inhibition, impaired energy production, oxidation of nucleosides, disruption of protein synthesis and finally cell death [69]. Other metabolites like lactic acid, acetic acid also exerts some basal mechanisms. They make the surrounding environments acidic that inhibits the growth of other microorganisms. So, naturally these molecules do not show any specificity in choosing their target cells, which may confer some physiological tissue damage. But at the same time we should consider that the dose of these chemicals, produced by *Lactobacillus* is not of that level which can cause organ or systemic damage. This again indicates the usefulness of some therapeutic strategy which is already a component of normal microbial flora or our innate immune system.

## 5. Clinical and Industrial Implication

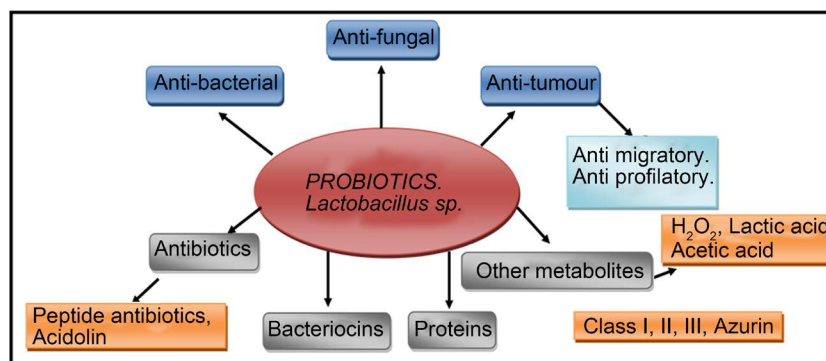
*Lactobacillus* is well known for its probiotic nature. *Lactobacilli* live in the urinary, digestive and genital tracts of humans. *Lactobacillus* prevents diarrhea in children, or bacterial vaginal infections, prevents infection from *Helicobacter pylori*, inflammatory diseases, Bowel syndromes, allergy and also improves mucosal immunity. However, it cannot prevent infections in urinary tract, ineffective against lactose intolerance, and yeast infections [70] [71]. Many *Lactobacillus* sp. having promising therapeutic properties like anti-inflammatory, antimicrobial, anti-cancerous and some other activities like prevents dental caries. *Lactobacillus* produces metabolites lactic acid, acetic acid; hydrogen peroxide that inhibits growth other micro-organisms, hence prevents infection. *Lactobacilli* can also be used to restore particular physiological balance such as in the vaginal eco-system [72]. The antibacterial and antifungal activity of *Lactobacillus* is based on the production of bacteriocins and compounds with low-molecular weight that inhibits these microorganisms. *Lactobacillus* is also known for some antibiotics, peptides, insulin, etc. On the other hand *Lactobacillus* has many industrial applications. *Lactobacillus* fermentation is popular in industries to produce milk products, probiotics like yogurt. Other products like cheese, pickles, beer, wine, kimchi, cocoa, etc. *Lactobacillus* is also applied for food preservation as it has a effective antimicrobial activities.

## 6. Future Perspectives

In present world use of probiotics has received much importance as an inexpensive great remedy to curing disease as well as maintaining health. Probiotics are more highlighted due to its promising anti-microbial effects and due to presence of high nutrient contents. With the use of probiotics the use of antibiotics may be neglected as they lead to side effects. As discussed earlier that any treatments may be diseases or cancer needs high specificity. The lactobacillus may be used for specific reasons like its high specificity in future. Future research must investigate the mechanisms of infections by different microorganisms and how they can be prevented by probiotics. With this knowledge, optimal strains can be developed. One of the main parameter of probiotics is the viability for developing various food products. New technologies can be developed to enable high cell yield, metabolites at large scale and to keep the probiotic effects in foods for a long period of time. Various food matrices, dairy and non-dairy, have been used with probiotics and were briefly discussed earlier. In future the probiotics may be used as medicines for specific diseases. Probiotics can be used to produce hormones like insulin in large scale and has a capability of fermentation and in future researches may increase the fermentation rate. With different current technologies like microencapsulation, cell immobilization and continuous fermentation many important metabolites like enzymes, antibiotics, hormones etc can be produced. In future the application of probiotics can be spread outside the pharmaceutical and supplement industries [73]. The conceptual summary of the bacteria- cancer cells interactions are given in Figure 3.

## 7. Conclusion

*Lactobacillus* is effectively beneficial to human welfare. The uses of probiotics cover a wide range of diseases and industrial applications. The use of probiotics in medical practice is rapidly increasing, as are studies that demonstrate the efficacy of probiotics. *Lactobacillus* has positive effects on anti-microbial, anti-cancer, anti-inflammatory, anti-diabetic activities. It prevents harmful infections by inhibiting some pathogenic bacteria. The probiotics like yogurt are useful



**Figure 3.** *Lactobacillus* sp. shows the discussed activities with some important secretory products: The above diagram is showing a glance of different types of secretory chemicals which actually confer the anti-microbial as well as anti-tumor activities.

for humans. Current researches are going on *Lactobacillus* to improve strains, making more effective and to find out some other effective characteristics. Collectively, the spectrum of the activities of probiotic organisms is increasing as an alternative and/or combinatorial therapeutics as well as a suitable vector to introduce target molecules within human body.

### Acknowledgements

We would like to express our special gratitude to the Dr. G.M. Helaluddin, Principal, Michael Madhusudan Memorial College and Dr. Abhijit Sengupta, Principal, Guru Nanak Institute of Pharmaceutical Science and Technology; for giving us this opportunity and academic support for completing this review project.

We would also like to express our thanks of gratitude to Dr. Swati Chakraborty, Mrs. Tamalika Chakraborty, Dr. Bhaskar Chowdhury (assistant professor of GNIPST) who co-operated in all the time.

### References

- [1] Hu, Y. and Fu, L. (2012) Targeting Cancer Stem Cells: A New Therapy to Cure Cancer Patients. *American Journal of Cancer Research*, **2**, 340-356.
- [2] Ali, F.S., Saad, O.A.O. and Salwa, A.H. (2013) Antimicrobial Activity of Probiotic Bacteria. *Egyptian Academic Journal of Biological Sciences*, **5**, 21-34.
- [3] Nami, Y., Abdullah, N., Haghshenas, B., Radiah, D., Rosli, R. and Khosroushahi, A.Y. (2014) Assessment of Probiotic Potential and Anticancer Activity of Newly Isolated Vaginal Bacterium *Lactobacillus plantarum* 5BL. *Microbiology and Immunology*, **58**, 492-502. <https://doi.org/10.1111/1348-0421.12175>
- [4] Atta, H.M., Refaat, B.M. and El-Waseif, A.A. (2009) Application of Biotechnology for Production, Purification and Characterization of Peptide Antibiotic Produced by Probiotic *Lactobacillus plantarum*, NRRL B-227. *Global Journal of Biotechnology & Biochemistry*, **4**, 115-125.
- [5] Hamdan, I.Y. and Mikolajcik, E.M. (1974) Acidolin: An Antibiotic Produced by *Lactobacillus acidophilus*. *The Journal of Antibiotics*, **27**, 631-636. <https://doi.org/10.7164/antibiotics.27.631>
- [6] Mohankumar, A. and Murugalatha, N. (2011) Characterization and Antibacterial Activity of Bacteriocin Producing *Lactobacillus* Isolated from Raw Cattle Milk Sample. *International Journal of Biology*, **3**, 128-143. <https://doi.org/10.5539/ijb.v3n3p128>
- [7] Dasari, S., Devanaboyaina, R.N., Wudayagiri, R. and Valluru, L. (2014) Antimicrobial Activity of *Lactobacillus* against Microbial Flora of Cervicovaginal Infections. *Asian Pacific Journal of Tropical Disease*, **4**, 18-24. [https://doi.org/10.1016/S2222-1808\(14\)60307-8](https://doi.org/10.1016/S2222-1808(14)60307-8)
- [8] Abd-Alkareem, A.Y. (2014) *Lactobacillus Acidophilus* as Antibiofilm Formed by *Staphylococcus aureus* in *Vitro*. *Diyala Journal of Medicine*, **7**, 24-34.
- [9] Tropcheva, R., Nikolova, D., Evstatieva, Y. and Danova, S. (2014) Antifungal Activity and Identification of *Lactobacilli*, Isolated from Traditional Dairy Product "Katak". *Anaerobe*, **28**, 78-84. <https://doi.org/10.1016/j.anaerobe.2014.05.010>
- [10] Guo, J., Brosnan, B., Furey, A., Arendt, E., Murphy, P. and Coffey, A. (2012) Antifungal Activity of *Lactobacillus* against *Microsporum canis*, *Microsporum gypseum* and *Epidermophyton floccosum*. *Bioengineered Bugs*, **3**, 102-111.

- [11] Kim, J.E., Kim, J.Y., Lee, K.W. and Lee, H.J. (2007) Cancer Chemopreventive Effects of Lactic Acid Bacteria. *Journal of Microbiology and Biotechnology*, **17**, 1227-1235.
- [12] Park, J.G., Frucht, H., LaRocca, R.V., Bliss, D.P.J., Kurita, Y., Chen, T.R., Henslee, J.G., Trepel, J.B., Jensen, R.T., Johnson, B.E., *et al.* (1990) Characteristics of Cell Lines Established from Human Gastric Carcinoma. *Cancer Research*, **50**, 2773-2780.
- [13] Park, J.G., Oie, H.K., Sugarbaker, P.H., Henslee, J.G., Chen, T.R., Johnson, B.E. and Gazdar, A. (1987) Characteristics of Cell Lines Established from Human Colorectal Carcinoma. *Cancer Research*, **47**, 6710-6718.
- [14] Chen, T.R., Hay, R.J. and Macy, M.L. (1983) Intercellular Karyotypic Similarity in Near-Diploid Cell Lines of Human Tumor Origins. *Cancer Genetics and Cytogenetics*, **10**, 351-362. [https://doi.org/10.1016/0165-4608\(83\)90092-4](https://doi.org/10.1016/0165-4608(83)90092-4)
- [15] Chen, T.R., Dorotinsky, C.S., McGuire, L.J., Macy, M.L. and Hay, R.J. (1995) DLD-1 and HCT-15 Cell Lines Derived Separately from Colorectal Carcinomas Have Totally Different Chromosome Changes but the Same Genetic Origin. *Cancer Genetics and Cytogenetics*, **81**, 103-108. [https://doi.org/10.1016/0165-4608\(94\)00225-Z](https://doi.org/10.1016/0165-4608(94)00225-Z)
- [16] Trainer, D.L., Kline, T., McCabe, F.L., Faucette, L.F., Field, J., Chaikin, M., Anzano, M., Rieman, D., Hoffstein, S., Li, D.J., *et al.* (1988) Biological Characterization and Oncogene Expression in Human Colorectal Carcinoma Cell Lines. *International Journal of Cancer*, **41**, 287-296. <https://doi.org/10.1002/ijc.2910410221>
- [17] Koeffler, H.P. and Golde, D.W. (1980) Human Myeloid Leukemia Cell Lines: A Review. *Blood*, **56**, 344-350.
- [18] Ortaldo, J.R., Oldham, R.K., Cannon, G.C. and Herberman, R.B. (1977) Specificity of Natural Cytotoxic Reactivity of Normal Human Lymphocytes against a Myeloid Leukemia Cell Line. *Journal of the National Cancer Institute*, **59**, 77-82.
- [19] Lozzio, C.B. and Lozzio, B.B. (1975) Human Chronic Myelogenous Leukemia Cell-Line with Positive Philadelphia Chromosome. *Blood*, **45**, 321-334.
- [20] Giard, D.J., Aaronson, S.A., Todaro, G.J., Arnstein, P., Kersey, J.H., Dosik, H. and Parks, W.P. (1973) *In Vitro* Cultivation of Human Tumors: Establishment of Cell Lines Derived from a Series of Solid Tumors. *Journal of the National Cancer Institute*, **51**, 1417-1423.
- [21] Goodrum, F.D. and Ornelles, D.A. (1997) The Early Region 1B 55-Kilodalton Oncoprotein of Adenovirus Relieves Growth Restrictions Imposed on Viral Replication by the Cell Cycle. *Journal of Virology*, **71**, 548-561.
- [22] St Geme, J.W., Cutter, D. and Barenkamp, S.J. (1996) Characterization of the Genetic Locus Encoding *Haemophilus influenzae* Type b Surface Fibrils. *Journal of Bacteriology*, **178**, 6281-6287. <https://doi.org/10.1128/jb.178.21.6281-6287.1996>
- [23] Fogh, J., Wright, W.C. and Loveless, J.D. (1977) Absence of HeLa Cell Contamination in 169 Cell Lines Derived from Human Tumors. *Journal of the National Cancer Institute*, **58**, 209-214.
- [24] Faust, J.B. and Meeker, T.C. (1992) Amplification and Expression of the bcl-1 Gene in Human Solid Tumor Cell Lines. *Cancer Research*, **52**, 2460-2463.
- [25] Duarte, C., Gudiña, E.J., Lima, C.F. and Rodrigues, L.R. (2014) Effects of Biosurfactants on the Viability and Proliferation of Human Breast Cancer Cells. *AMB Express*, **4**, 40. <https://doi.org/10.1186/s13568-014-0040-0>
- [26] Vanderzant, C. and Splittstoesser, D.F. (1992) Compendium of Methods for the Microbiological Examination of Foods. 3rd Edition, American Public Health Association, Washington DC, 423-431.
- [27] Baldi, A., Boccia, V., Claudio, P.P., De Luca, A. and Giordano, A. (1996) Genomic

- Structure of the Human Retinoblastoma-Related Rb2/p130 Gene. *Proceedings of the National Academy of Sciences of the United States of America*, **93**, 4629-4632. <https://doi.org/10.1073/pnas.93.10.4629>
- [28] McKnight, K.L. and Lemon, S.M. (1996) Capsid Coding Sequence Is Required for Efficient Replication of Human Rhinovirus 14 RNA. *Journal of Virology*, **70**, 1941-1952.
- [29] Macville, M., Schrock, E., Padilla-Nash, H., Keck, C., Ghadimi, B.M., Zimonjic, D., Popescu, N. and Ried, T. (1999) Comprehensive and Definitive Molecular Cytogenetic Characterization of HeLa Cells by Spectral Karyotyping. *Cancer Research*, **59**, 141-150.
- [30] Sugarman, B.J., Aggarwal, B.B., Hass, P.E., Figari, I.S., Palladino, M.A.J. and Shepard, H.M. (1985) Recombinant Human Tumor Necrosis Factor-Alpha: Effects on Proliferation of Normal and Transformed Cells *in Vitro*. *Science*, **230**, 943-945. <https://doi.org/10.1126/science.3933111>
- [31] Takahashi, K. and Suzuki, K. (1993) Association of Insulin-Like Growth-Factor-I-Induced DNA Synthesis with Phosphorylation and Nuclear Exclusion of p53 in Human Breast Cancer MCF-7 Cells. *International Journal of Cancer*, **55**, 453-458. <https://doi.org/10.1002/ijc.2910550322>
- [32] Soule, H.D., Vazquez, J., Long, A., Albert, S. and Brennan, M. (1973) A Human Cell Line from a Pleural Effusion Derived from a Breast Carcinoma. *Journal of the National Cancer Institute*, **51**, 1409-1416.
- [33] Geiger, T., Müller, M., Dean, N.M. and Fabbro, D. (1998) Antitumor Activity of a PKC-Alpha Antisense Oligonucleotide in Combination with Standard Chemotherapeutic Agents against Various Human Tumors Transplanted into Nude Mice. *Anti-Cancer Drug Design*, **13**, 35-45.
- [34] Knowles, B.B., Howe, C.C. and Aden, D.P. (1980) Human Hepatocellular Carcinoma Cell Lines Secrete the Major Plasma Proteins and Hepatitis B Surface Antigen. *Science*, **209**, 497-499. <https://doi.org/10.1126/science.6248960>
- [35] Cuthbert, C., Wang, Z., Zhang, X. and Tam, S.P. (1997) Regulation of Human Apolipoprotein A-I Gene Expression by Gramoxone. *The Journal of Biological Chemistry*, **272**, 14954-14960. <https://doi.org/10.1074/jbc.272.23.14954>
- [36] Carter, R.E., Feldman, A.R. and Coyle, J.T. (1996) Prostate-Specific Membrane Antigen Is a Hydrolase with Substrate and Pharmacologic Characteristics of a Neuropeptidase. *Proceedings of the National Academy of Sciences of the United States of America*, **93**, 749-753. <https://doi.org/10.1073/pnas.93.2.749>
- [37] Nupponen, N.N., Hyytinen, E.R., Kallioniemi, A.H. and Visakorpi, T. (1998) Genetic Alterations in Prostate Cancer Cell Lines Detected by Comparative Genomic Hybridization. *Cancer Genetics and Cytogenetics*, **101**, 53-57. [https://doi.org/10.1016/S0165-4608\(97\)00060-5](https://doi.org/10.1016/S0165-4608(97)00060-5)
- [38] AL-Tememy, W.K.M., Al-Ani, A., Al-Ani, M.Q. and Ismail, S. (2011) Isolation of *Lactobacillus salivarius* from Children and Purification of Bacteriocin to Inhibition Cancer Cell *in Vitro*. Islamic World Science Citation Center, Shiraz, 104-108.
- [39] Salih, R.H. (2012) Evaluation the Cytotoxic Effect of *Lactobacillus acidophilus* Concentrated Filtrate on Growth of Tumor Cell Lines. *Journal of Al-Nahrain University*, **15**, 168-172.
- [40] Di Luccia, B., Manzo, N., Baccigalupi, L., Calabro, V., Crescenzi, E., Ricca, E. and Pollice, A. (2013) *Lactobacillus gasseri* SF1183 Affects Intestinal Epithelial Cell Survival and Growth. *PLoS ONE*, **8**, e69102. <https://doi.org/10.1371/journal.pone.0069102>
- [41] Didier, E.S., Rogers, L.B., Orenstein, J.M., Baker, M.D., Vossbrinck, C.R., Van Gool,

- T., Hartskeerl, R., Soave, R. and Beaudet, L.M. (1996) Characterization of *Encephalitozoon (Septata) intestinalis* Isolates Cultured from Nasal Mucosa and Bronchoalveolar Lavage Fluids of Two AIDS Patients. *Journal of Eukaryotic Microbiology*, **43**, 34-43. <https://doi.org/10.1111/j.1550-7408.1996.tb02470.x>
- [42] Santoro, I.M. and Groden, J. (1997) Alternative Splicing of the APC Gene and ITS Association with Terminal Differentiation. *Cancer Research*, **57**, 488-494.
- [43] Bermudez, L.E., Petrofsky, M. and Goodman, J. (1997) Exposure to Low Oxygen Tension and Increased Osmolarity Enhance the Ability of *Mycobacterium avium* to Enter Intestinal Epithelial (HT-29) Cells. *Infection and Immunity*, **65**, 3768-3773.
- [44] Tsao, H., Benoit, E., Sober, A.J., Thiele, C. and Haluska, F.G. (1998) Novel Mutations in the p16/CDKN2A Binding Region of the Cyclin-Dependent Kinase-4 Gene. *Cancer Research*, **58**, 109-113.
- [45] Wu, M.C., Arimura, G.K. and Yunis, A.A. (1978) Mechanism of Sensitivity of Cultured Pancreatic Carcinoma to Asparaginase. *International Journal of Cancer*, **22**, 728-733. <https://doi.org/10.1002/ijc.2910220615>
- [46] Lan, M.S., Hollingsworth, M.A. and Metzgar, R.S. (1990) Polypeptide Core of a Human Pancreatic Tumor Mucin Antigen. *Cancer Research*, **50**, 2997-3001.
- [47] Olopade, O.I., Jenkins, R.B., Ransom, D.T., Malik, K., Pomykala, H., Nobori, T., Cowan, J.M., Rowley, J.D. and Diaz, M.O. (1992) Molecular Analysis of Deletions of the Short Arm of Chromosome 9 in Human Gliomas. *Cancer Research*, **52**, 2523-2529.
- [48] Li, Y.M., Mitsuhashi, T., Wojciechowicz, D., Shimizu, N., Li, J., Stitt, A., He, C., Banerjee, D. and Vlassara, H. (1996) Molecular Identity and Cellular Distribution of Advanced Glycation End Product Receptors: Relationship of p60 to OST-48 and p90 to 80K-H Membrane Proteins. *Proceedings of the National Academy of Sciences of the United States of America*, **93**, 11047-11052. <https://doi.org/10.1073/pnas.93.20.11047>
- [49] Choi, S.S., Kim, Y., Han, K.S., You, S., Oh, S. and Kim, S.H. (2006) Effects of Lactobacillus Strains on Cancer Cell Proliferation and Oxidative Stress in Vitro. *Letters in Applied Microbiology*, **42**, 452-458. <https://doi.org/10.1111/j.1472-765X.2006.01913.x>
- [50] Jeffers, M., Taylor, G.A., Weidner, K.M., Omura, S. and VandeWoude, G.F. (1997) Degradation of the Met Tyrosine Kinase Receptor by the Ubiquitin-Proteasome Pathway. *Molecular and Cellular Biology*, **17**, 799-808. <https://doi.org/10.1128/MCB.17.2.799>
- [51] Massuda, E.S., Dunphy, E.J., Redman, R.A., Schreiber, J.J., Nauta, L.E., Barr, F.G., Maxwell, I.H. and Cripe, T.P. (1997) Regulated Expression of the Diphtheria Toxin a Chain by a Tumor-Specific Chimeric Transcription Factor Results in Selective Toxicity for Alveolar Rhabdomyosarcoma Cells. *Proceedings of the National Academy of Sciences of the United States of America*, **94**, 14701-14706. <https://doi.org/10.1073/pnas.94.26.14701>
- [52] Haass, C., Koo, E.H., Capell, A., Teplow, D.B. and Selkoe, D.J. (1995) Polarized Sorting of Beta-Amyloid Precursor Protein and Its Proteolytic Products in MDCK Cells Is Regulated by Two Independent Signals. *The Journal of Cell Biology*, **128**, 537-547. <https://doi.org/10.1083/jcb.128.4.537>
- [53] Shaikh, F., Abhinand, P. and Ragnath, P. (2012) Identification & Characterization of *Lactobacillus salivarius* Bacteriocins and Its Relevance in Cancer Therapeutics. *Bioinformation*, **8**, 589-594. <https://doi.org/10.6026/97320630008589>
- [54] Jalilsood, T., Baradaran, A., Song, A.A., Foo, H.L., Mustafa, S., Saad, W.Z., Yusoff, K. and Rahim, R.A. (2015) Inhibition of Pathogenic and Spoilage Bacteria by a

- Novel Biofilm-Forming *Lactobacillus* Isolate: A Potential Host for the Expression of Heterologous Proteins. *Microbial Cell Factories*, **14**, 96.  
<https://doi.org/10.1186/s12934-015-0283-8>
- [55] Yang, S., Lin, C., Sung, C.T. and Fang, J. (2014) Anti-Bacterial Activities of Bacteriocins: Application in Foods and Pharmaceuticals. *Frontiers in Microbiology*, **5**, 1-10.
- [56] Chatterjee, C., Paul, M., Xie, L. and van der Donk, W.A. (2005) Biosynthesis and Mode of Action of Lantibiotics. *Chemical Reviews*, **105**, 633-684.  
<https://doi.org/10.1021/cr030105v>
- [57] Goto, Y., Li, B., Claesen, J., Shi, Y., Bibb, M.J. and van der Dong, W.A. (2010) Discovery of Unique Lanthionine Synthetases Reveals New Mechanistic and Evolutionary Insights. *PLOS Biology*, **8**, e1000339.  
<https://doi.org/10.1371/journal.pbio.1000339>
- [58] Zhang, Q., Yu, Y., Velasquez, J.E. and van der Donk, W.A. (2012) Evolution of Lanthionine Synthetases. *Proceedings of the National Academy of Sciences of the United States of America*, **109**, 18361-18366.  
<https://doi.org/10.1073/pnas.1210393109>
- [59] Harpp, D.N. and Gleason, J.G. (1971) Preparation and Mass Spectral Properties of Cystine and Lanthionine Derivatives. A Novel Synthesis of L-Lanthionine by Selective Desulfurization. *The Journal of Organic Chemistry*, **36**, 73-80.  
<https://doi.org/10.1021/jo00800a017>
- [60] Hashimoto, W., Ochiai, A., Hong, C.S., Murata, K. and Chakrabarty, A.M. (2015) Structural Studies on Laz, a Promiscuous Anticancer Neisserial Protein. *Bioengineered*, **6**, 141-148. <https://doi.org/10.1080/21655979.2015.1022303>
- [61] De Rienzo, F., Gabdoulline, R.R., Menziani, M.C. and Wade, R.C. (2000) Blue Copper Proteins: A Comparative Analysis of Their Molecular Interaction Properties. *Protein Science*, **9**, 1439-1454. <https://doi.org/10.1110/ps.9.8.1439>
- [62] Dahiya, R.S. and Speck, M.L. (1968) Hydrogen Peroxide Formation by *Lactobacilli* and Its Effect on *Staphylococcus aureus*. *Journal of Dairy Science*, **51**, 1568-1572.  
[https://doi.org/10.3168/jds.S0022-0302\(68\)87232-7](https://doi.org/10.3168/jds.S0022-0302(68)87232-7)
- [63] Matsuzaki, K., Murase, O., Tokuda, H., Funakoshi, S., Fujii, N. and Miyajima, K. (1994) Orientational and Aggregational States of Magainin 2 in Phospholipid Bilayers. *Biochemistry*, **33**, 3342-3349. <https://doi.org/10.1021/bi00177a027>
- [64] Zhang, L., Rozek, A. and Hancock, R.E. (2001) Interaction of Cationic Antimicrobial Peptides with Model Membranes. *The Journal of Biological Chemistry*, **276**, 35714-35722. <https://doi.org/10.1074/jbc.M104925200>
- [65] Axelsen, P.H. (2008) A Chaotic Pore Model of Polypeptide Antibiotic Action. *Biophysical Journal*, **94**, 1549-1550. <https://doi.org/10.1529/biophysj.107.124792>
- [66] Hemaiswarya, S., Raja, R., Ravikumar, R. and Carvalho, I.S. (2013) Mechanism of Action of Probiotics. *Brazilian Archives of Biology and Technology*, **56**, 113-119.  
<https://doi.org/10.1590/S1516-89132013000100015>
- [67] Cotter, P.D., Hill, C. and Ross, R.P. (2005) Bacteriocins: Developing Innate Immunity for Food. *Nature Reviews Microbiology*, **3**, 777-788.  
<https://doi.org/10.1038/nrmicro1273>
- [68] Punj, V., Bhattacharyya, S., Saint-Dic, D., Vasu, C., Cunningham, E.A., Graves, J., Yamada, T., Constantinou, A.I., Christov, K. and Chakrabarty, A.M. (2004) Bacterial Cupredoxin Azurin as an Inducer of Apoptosis and Regression in Human Breast Cancer. *Oncogene*, **23**, 2367-2378. <https://doi.org/10.1038/sj.onc.1207376>
- [69] Finnegan, M., Linley, E., Denyer, S.P., McDonnell, G., Simons, C. and Maillard, J.Y.

- (2010) Mode of Action of Hydrogen Peroxide and Other Oxidizing Agents: Differences between Liquid and Gas Forms. *Journal of Antimicrobial Chemotherapy*, **65**, 2108-2115. <https://doi.org/10.1093/jac/dkq308>
- [70] Fijan, S. (2014) Microorganisms with Claimed Probiotic Properties: An Overview of Recent Literature. *International Journal of Environmental Research and Public Health*, **11**, 4745-4767. <https://doi.org/10.3390/ijerph110504745>
- [71] Reid, G., Jass, J., Sebulsy, M.T. and McCormick, J.K. (2003) Potential Uses of Probiotics in Clinical Practice. *Clinical Microbiology Reviews*, **16**, 658-672. <https://doi.org/10.1128/CMR.16.4.658-672.2003>
- [72] Reid, G., Dols, J. and Miller, W. (2009) Targeting the Vaginal Microbiota with Probiotics as a Means to Counteract Infections. *Current Opinion in Clinical Nutrition and Metabolic Care*, **12**, 583-587. <https://doi.org/10.1097/MCO.0b013e328331b611>
- [73] Socol, C.R., de Souza Vandenberghe, L.P., Spier, M.R., Medeiros, A.B.P., Yamaguishi, C.T., Lindner, J.D.D., Pandey, A. and Thomaz-Socol, V. (2010) The Potential of Probiotics: A Review. *Food Technology and Biotechnology*, **48**, 413-434.



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