Available online at www.jpsscientificpublications.com

Life Science Archives (LSA)

ISSN: 2454-1354

Volume – 6; Issue - 3; Year – 2020; Page: 1860 – 1874

DOI: 10.22192/lsa.2020.6.3.5

Review Article

PROBIOTICS – A POTENTIAL AGENT FOR WOUND TREATMENT

Shaimaa M. S. Zainulabdeen* and Wafaa Ayad Al-Nuaimy

Department of Biology, College of Science, AL-Muthanna University, Samawah, Iraq

Abstract

Probiotics are live microorganisms promoted with claims that they provide health benefits when consumed, generally by improving or restoring the gut flora. Immediately after wounding, microbial colonization occurs. The effects of microbial wound colonization on healing process are particularly important and therefore, based on the significant economic and social impact of wounds, so probiotics used as a new therapeutic agent in wound management are presented and analyzed. Probiotics are beneficial microorganisms, known to exert numerous positive effects on human health, primarily in the battle against pathogens. Probiotics have been associated with improved healing of intestinal ulcers, and healing of infected cutaneous wounds. The most commonly used probiotics for all studies were well-known strains of the species *Lactobacillus plantarum*, *Lactobacillus casei*, *Lactobacillus acidophilus* and *Lactobacillus rhamnosus.* All *in vitro* studies showed successful inhibition of chosen skin or wound pathogens by the selected probiotics. Most clinical studies showed slight or statistically significant lower incidence of surgical site infections, foot ulcer infection, or burn infections for patients using probiotics.

Article History

Received : 30.05.2020
Revised : 11.06.2020
Accepted: 29.06.2020

Key words: Probiotics, *Lactobacillus* sp., Wound treatment and Antimicrobial compounds.

1. Introduction

Probiotics are defined having valuable factors contributing to the health and safety of host, including humans. It is thought that consumption of abundant amount more than 10^8 Colony Forming Units (CFU) per day of probiotic will be abundant to balance the human Gastrointestinal tract (GI) micro-ecosystem by replacing damaging pathogens (Ouwehand *et al.*, 2002).

Probiotics have several benefits for health such as the immune-modulatory effect of positively stimulating both humeral and cell-mediated immunity responses. Established effect include enhancing production and circulation of serum antibodies, increasing secretion of cytokines and restoring immune function in immune- compromised hosts (Ezendam and van Loveren, 2006) and physiological effects including enhancement of intestinal motility (Saxelin *et al*., 2005). Antimicrobial effects such as competing for nutrients and adhesion locations with pathogens, lowering intestinal pH, producing short chain fatty acids, and creating extracellular bacteriocins (Gill, 2003). Lower frequency and duration of diarrhea connected to use of antibiotics

Corresponding author*: **Shaimaa M. S. Zainulabdeen
E.mail: shimaa.majeed@mu.edu.iq

LSA ISSN: 2454-1354

(Johnston *et al*., 2011) or produced by an infectious agent (Allen *et al*., 2010). Probiotics have been used for extended time in food elements for human and also to feed animals without any side effects. The excepted major principles for being accepted as probiotics are resistance to low acidity, tolerance against bile salt and to be created from human (Martin *et al*., 2004).

2. Mechanisms of Probiotics action

Mechanisms by which probiotics use healthy effects are incompletely expected. Authors include competitive inhibition with pathogenic bacteria, effects on barrier role, antagonism through the production of antimicrobial materials (organic acids, hydrogen peroxide and bacteriocins) and variety of the immune system, (Cabana *et al*., 2006; Almeghaiseeb, 2007). Mechanisms differ according to the definite strain or combination of strains used, the existence of prebiotics a non-digestible food ingredient which usefully affects the host by selectively stimulating the growth and action of one or limited amount of bacteria in the colon having the potential to improve host health (Gupta and Garg, 2009) and the condition that presence treat the patient (Devine and Marsh, 2009). Probiotic properties may be based on actions affecting microbial products like toxins, host products e.g. bile salts and food ingredients (Oeslschaeger, 2010).

Mechanism underlying probiotic properties are not completely understood, and the mechanisms cannot generalized diverse strains may differ. Most research in the space has focused on the GI tract. The claimed mechanism basic GI beneficial effects include: (I) secretion antimicrobial material, (II) competitive adherence to the mucosa and epithelium strengthening of the GI-epithelium barrier, and (IV) modulation of immune system (Collado *et al*., 2009; Reid *et al*., 2010b; Bermudez -Brito *et al*., 2012). There are several proposed mechanisms that describe how diverse probiotics work and they differ depending on the strain of probiotic used. The properties of probiotics also depend on dosage and course of administration (Upadhyay and Moudgal, 2012). Specific of these mechanisms are production of bacteriocins (Yateem *et al*., 2008; Collins *et al*., 2012). They are established as alternatives to antibiotics improve animal health and productivity (Allen *et al*., 2013). This appears to be strongly determined by the prohibition of most of the antibiotic feed spices within the European Union, because of speculated risk for creating antibiotic resistance in pathogenic microbiota (Windisch *et al*., 2008), chemical residues in animal produces, release of antibiotics in the environment (Yamamoto *et al*., 2014; Martínez-Vaz *et al*., 2014).

3. Probiotics and health implications

Lactobacilli able to inhibit the genitourinary pathogen by numerous mechanisms. Additional functions of *Lactobacilli* include competitive prohibiting of pathogens from the cell surface, co-aggregation with definite pathogenic bacteria, adherence to epithelial cells and biofilm formation based on auto aggregation and surface hydrophobicity (Dunne *et al*., 2001). Previous studies shown that auto aggregation of probiotic strains is necessary. Recent studies have simplified the importance of immunoregulatory ability of probiotics for force of preventive and beneficial effects on numerous diseases. The epithelial barrier consist of dense mucous layer containing secretory antimicrobial peptides and IgA as well dynamic functional advancements regulate permeability between cells (Ohland and Mac Naughton, 2010). There is suggestion that consumption of probiotic strains improves the integrity of intestinal barrier and the up regulation of mucin production (Devine and Marsh, 2009). The immune system approximately divided into acquired immune system, involve mainly of B and sensitized T lymphocytes, and innate immune system, involving mainly of NK cells and macrophages. Ratio of envelopment of systems differ depending on conditions of infection such species of microorganisms and amount and location of infection. Mouse studies have clarified direct activation of macrophages by probiotics increased the bactericidal effect of macrophages on pathogenic bacteria. Probiotics strains have been reported to stimulate proliferation of phagocytes such as macrophages and neutrophils

in bone marrow and spleen (hematopoietic tissues).

4. Probiotic effects on microbial toxins

One of the best important groups of bacterial virulence factors are toxins. The usefulness of certain probiotics in suppressing diarrhea most possible based on their ability to protect host against toxins. This protection can result from inhibition of toxin expression in pathogens. Certain probiotics are level able protect against cyanobacteria and fungal toxins. The basis of perceived protective effect is rather physicochemical interaction between toxin and a probiotic than metabolic inactivation, (Musa *et al*., 2009; Oelschlaeger, 2010).

5. Production of antimicrobial compounds

Lactobacilli produce diversity of compounds that inhibitory to both Gram positive and Gram negative bacteria. These inhibitory substances include (Organic acids, Bacteriocins, Hydrogen peroxide and Biosurfactants) (Rolfe, 2000).

6. Bacteriocins of Lactic acid bacteria

Bacteriocins are antimicrobial materials of protein, some of which may contain an associated lipid or carbohydrate, prevent growth of connected or unconnected bacterial species and possibly useful for prevention of bacterial infectious diseases (Riley and Chavan, 2007; Pascual *et al*., 2008b). Bacteriocins are defined ribosomally synthesized small polypeptides utilize antimicrobial effects against closely or non-closely related bacteria. The major producer assembly for bacteriocins is

Lactic acid bacteria (LAB) that contains great diversity of microorganisms described as "Generally recognized as safe" by the US Food and Drug Administration FDA (Gulluce *et al*., 2013). Bacteriocins created by lactic acid bacteria are divided into five class based on primary arrangement, molecular mass, and molecular organization: Class I, lantibiotics; Class II, non-lantibiotic peptides (Subclass IIA pediocin-like bacteriocins with strong antilisterial activity; subclass IlB bacteriocins whose activity depends on complementary action of two peptides; subclass Ilc, dependent secreted bacteriocins), Class III large, heat labile protein bacteriocins, Class IV bacteriocins consisting of undefined mixture of protein, lipid and carbohydrate and Class V bacteriocins with circular, unmodified post transductional structure (including AS-48, gasericine A, enterocin) (Gutiérrez Merino, 2005).

Lactobacilli bacteriocins of importance because of their potential application for inhibition pathogenic bacteria that affect humans. Two *Lactobacillus* strains from human vagina, *Lactobacillus fermentum* and *Lactobacillus rhamnosus* were formerly identified and characterized as probiotics and producers of bacteriocins. In study carried out by our research group (Pascual *et al.*, 2008a,b). Bacteriocins are class of antimicrobial agents produced by LAB. All of the bacteriocins known today, Nisin is the only bacteriocin that has been given a status by FDA (Ajay *et al.*, 2010). Bacteriocins work by binding to and killing only cells with surface receptors that are recognized by that specific bacteriocin (Cascales *et al*., 2007; Chavan and Riley, 2007). Bacteriocins initially named based on the producer species such as colicins produced by *Escherichia coli*, pyocins of *Pseudomonas aeruginosa* (formerly named *pyocyania*), cloacins of *Enterobacter cloacae* and cerecins of *Bacillus cereus*,(Reeves, 1965). Fredericq (1957) created first classification, and thus nomenclature of bacteriocins focusing on the colicins of *Escherichia coli*. Fredericq (1957) grouped colicins into 17 different types (colicins A, B, C, D, E, F, G, H, I, J, K, V, S1, S2, S3, S4, and S5) based on their receptor specificity. These colicins were then further subtyped (colicin E1, E2, and E3, etc.) based on their immunity patterns, all sub-types were recognized by the same receptor, but they possessed different immunity phenotypes (Fredericq, 1957). Bacteriocins were mainly discovered in 1925 by Gratia, who observed inhibition of *Escherichia coli* S by *Escherichia coli* V almost 100 years ago. They were initially named as colicins and then their proteinaceous nature were resolved in 1957 by Fredericq, who

also demonstrated that the inhibitory activity of bacteriocins was depended on the presence of definite receptors on surface of sensitive cells (Riley and Chavan, 2007; Nes *et al*., 2007; Balciunas *et al*., 2013).

7. Microorganisms used as Probiotics

The main studied bacterial microorganisms used probiotics in thoughtful production include those derived from *Lactobacillus*, *Streptococcus* sp., *Enterococcus* sp., *Bacillus* sp., *Clostridium* sp., *Bifidobacterium* sp., *Escherichia coli* (Kruis *et al.,* 2004), *Megasphaera elsdenii* and *Prevotella bryantii* (Seo *et al*., 2010). The bacterial probiotic strains can be classified as Lactic acid bacteria (LAB), and Lactic acid utilizing bacteria (LUB). Lactic acid production and utilization in the rumen is related to feed efficiency and animal health (Seo *et al*., 2010). Yeasts and fungal probiotics such as *Saccharomyces* and *Aspergillus* respectively have given better effects in adult ruminants (Fuller, 1999; Seo *et al*., 2010).

8. *Lactobacillus* as a Probiotic

According to World Health Organization and Food and Agriculture Organization of United Nations (WHO/FAO, 2007), live microorganism that confer a health benefit to the host when controlled in suitable amounts are referred to probiotics. This definition is discussed since heat-killed strains use similar beneficial effects as live bacteria (Tanzer *et al.,* 2010). Several bacterial strains with health positive properties long to *Lactobacillus* (Collado *et al.,* 2009). The H_2O_2 making vaginal lactobacilli are reported to essential for sustainment of a healthy vaginal micro biota and it attractive to suggest that Bacterial vaginosis (BV) is caused by the lack of H_2O_2 producing *Lactobacillus* spp. (Eschenbach *et al*., 1989; Hillier *et al.,* 1992), this cannot necessarily associate causality, as LB+ were also present in women with BV (Eschenbach *et al*.,1989).

9. *Lactobacillus*

The genus *Lactobacillus* is by far largest of genera comprised in LAB. It is very heterogeneous group with unstable taxonomy, including species with large diversity of phenotypic, biochemical and physiological properties (Nigatu, 2000; Yildirim, 2001). Over 45 *Lactobacillus* species are recorded in the 1986 edition of Bergey's Manual of Systematic Bacteriology (Kandler and Weiss, 1986), and numerous more have described since then. Coeuret *et al*. (2003) recorded that *Lactobacillus* genus contains more than 80 recognized species. At the beginning of 2005, the genus *Lactobacillus* reported to include about 100 truly described species, the number of species is continually varying due to the description of new species and reclassification of others at the beginning of 2007 this genus had reached about 120 species (Blaiotta *et al*., 2008). According to Winn *et al*.(2006) *Lactobacillus* is classified as shown below:

Kingdom: Eubacteria
Phylum: Firmicutes
Class: Bacilli
Order: Lactobacillales
Family: Lactobacillaceae
Genus: *Lactobacillus*

10. General Characteristics of *Lactobacillus*

Lactobacillus is Gram - positive, non-spore forming, single cells of this species variable from long, straight or semicircular rods to coryne form Coccobacilli, ranging from 0.5 - 1.2 µm by 1 - 10 µm in size, usually occurring separately or in short chains, (Kandler and Weiss, 1986; Karthikeyan and Santosh, 2009). Most species non-motile ,the rare motile species having Peritrichous flagella (Winn *et al*., 2006) such as *Lactobacillus ghanensis* (Nielsen *et al*., 2007). Indol and H_2S not produced, catalase and gelatinase negative, microaerophilic or facultative anaerobic (Carr *et al*., 2002). The thermo bacteria are capable of growth at 45 °C or more but are unable to grow at 15 °C. The *Streptobacteria* grow at 15 °C, but most do not grow at 45 °C. The beta bacteria also grow at 15 °C (Carr *et al*., 2002). Numerous media for *Lactobacillus* have been described but best and most common one in the lab scale is deMan, Rogosa and Sharpe medium (Horn *et al*., 2005) was designed by de Man *et al*. (1960). Many LAB strains with health positive properties belong to

Lactobacillus or *Bifidobacterium* (Collado *et al*., 2009).

11. Sources of *Lactobacillus*

Lactobacillus are broadly distributed in diverse ecosystem and commonly create in silages (Combs *et al*., 2001), raw milk, dairy products, fermented milk (Coeuret *et al*., 2003), meat and (Bromberg *et al*., 2004), pickled vegetables, sourdoughs (De Vuyst and Vancanneyt, 2007), fermented tea leaves (Tanasupawat *et al*., 2007), beverages, sewage on plants and also in the genital, intestinal and respiratory tracts of man and animals (Savadogo *et al*., 2006). Euzéby (2014) recorded that can be found in variability of different environments ranging from foods to respiratory, GI and genital tract of humans and animals, sewage and plant material. This genus among the major of the bacterial genera with approximately 225 identified species.

12. Importance of *Lactobacillus* for Human

Lactobacillus sp. is naturally chemoorganotrophic and ferment carbohydrates to create lactic acid as main end product (Gayathri and Devaraja, 2011; Quinto *et al*., 2014). Inhabited of gastrointestinal flora can occur by diversity of microorganisms as several intestinal bacteria recognized as probiotics which live microbial feed enhancements containing potentially bacteria which have positive effect to their host health by successful its intestinal microbial balance (Ezema, 2013). They have several benefits either by attaching or by colonization in host, and beneficial for treatment antibiotic associated diarrhea, inflammation, and gastroenteritis, also probiotic bacteria acts normal treatment of urinary tract infections by lowering the medium pH and decrease opportunities for spoilage organisms to grow (Gayathri and Devaraja, 2011). *Lactobacillus* have numerous benefits, including: stops infection of pathogenic bacteria, e.g. *Escherichia coli* and *Salmonella*, helps fermentation of foods such as altered fermented milk, many industrial applications and has therapeutic properties against several infections and cancers (Abbas *et al*., 2016).

Additionally healthy, stable *Lactobacillus* population appears to protect against urogenital infections and bacterial vaginosis (Falagas *et al*., 2007). In addition to playing important role against pathogenic microorganisms, differences in composition of microbiome have linked to amount of different diseases and syndromes like obesity, circulatory disease, inflammatory bowel disease and autism are just a few examples of diseases or psychological conditions where difference in the microbiome composition has compared with healthy subjects (Turnbaugh *et al*., 2006; Marchesi *et al*., 2007; Finegold, 2008; Holmes *et al*., 2008). The two main applications of lactobacilli are starter cultures of nutrition, feed and probiotics. In fermentations, *Lactobacilli* are either present as natural contaminants, added component of a former batch or added as a pure or mixed culture. The purpose to affect flavor and texture and to improve the safety and shelf-life of ending product. Examples of fermented products inoculated with *Lactobacilli* include meat products, dairy products, vegetables and silage (Hammes and Hertel, 2006).

13. Exopolysaccharide

Certain lactic acid bacteria (LAB) produce Exopolysaccharides (EPS), either Capsular polysaccharides (CPS) that are tightly associated with the cell surface or slime EPS that are secreted into the extracellular environment. EPS from LAB can be divided into Homopolysaccharides, which are polymers composed of one type of monosaccharide, and Heteropolysaccharides (HePS), which are polymers of repeating units that are composed of two or more types of monosaccharides. A large biodiversity of HePS from LAB exists regarding their composition and structure, Molecular mass (MM), yield and functionalities. Further, polymer formation is strongly influenced by culture conditions. Recently, the molecular genetics of HePS biosynthesis have been studied for different LAB species. Several glycosyl transferases involved in the assemblage of the HePS repeating units have been discovered. EPS can act as viscosifying, stabilizing, gel-forming, and water-binding agents in various foods. Additionally, they have been

claimed to display properties beneficial to health. Little attention has been paid to CPS formation by food grade LAB. Exploration of the biodiversity of wild LAB strains is the most suitable approach to search for a desired EPS phenotype.

14. Biosynthetic pathways leading to EPS synthesis in LAB

A key intermediate linking the anabolic pathways of EPS production and the catabolic pathways of sugar degradation appears to be Glucose-6-phosphate, in which the flux of carbon bifurcates between the formation of fructose-6-phosphate toward the products of Glycolysis, biomass and ATP formation and toward the biosynthesis of sugar nucleotides, the precursors of EPSs (Fig. 1). Phosphoglutcomutase (PGM), the enzyme involved in the conversion of Glucose-6-phosphate to Glucose-1-phosphate, potentially has an important role in the divergence of flux between these catabolic and anabolic pathways. (Hugenholtz and Kleerebezem, 1999; Degeest and De Vuyst, 2000).Glucose-1-phosphate serves as a branch point for the formation of the sugar nucleotides UDP–glucose and dTDP – glucose *via* the action of UDP–glucose pyrophosphorylase and dTDP – glucose pyrophosphorylase, respectively. Note that these sugar nucleotides are used to form a variety of polysaccharides in the cell and hence the enzymes associated with their formation are shared (often termed 'housekeeping enzymes'). Conversion of galactose to Glucose-1-phosphate *via* Galactose-1-phosphate (the Leloir pathway) is possible if the system is present in the cell.

The subsequent stage of EPS synthesis in LAB - assembly of the monosaccharide repeating unit was achieved by several EPS - specific enzymes, as identified initially in *Streptococcus thermophilus* (Stingele, 1996) and in *Lactobacillus lactis* NIZO B40 (Van Kranenburg *et al.*, 1997). This repeating unit is assembled on a C55 – isoprenoid - lipid carrier molecule, which is attached to the cytoplasmic membrane of the cell (Van Kranenburg *et al*., 1999).

15. Interference of *Lactobacillus plantarum* with *Pseudomonas aeruginosa in vitro* and in infected burns

Pseudomonas aeruginosa infection is often difficult to eradicate because of resistance to many antibiotics and disinfectants (Hancock, 1998; McDonell and Russell, 1999). Consequently, this organism is an emerging therapeutic problem (Luzzaro *et al*., 1870) and is one of the most serious complications seen in burn wounds (Rumbaugh *et al*., 2000). The probiotic *Lactobacilli* have been used mainly to treat gastrointestinal disorders (Marteau, 2002). However, their ability to secrete acids, bacteriocins and other by-products that may neutralize infection caused by pathogens, and the fact that they are considered to be harmless microorganisms that regulate the host's inflammatory and immune responses, mean that *Lactobacilli* may be useful for the treatment of clinical infections in other parts of the body, such as recurrent bladder infections caused by *Escherichia coli*, vaginosis caused by anaerobic microbes, wound infections caused by *Staphylococcus aureus*, and others (Perdigo´n *et al*., 1998; Hessle *et al*., 2000; Valde´z *et al*., 2001; Reid, 2001; Harder, 2002; Gan *et al*., 2002).

Growth of *Pseudomonas aeruginosa* was inhibited fully by the *Lactobacillus plantarum* T and AF preparations, while the NF preparation resulted in 97 % inhibition. The *Pseudomonas aeruginosa* quorum-sensing molecules N-(3-oxododecanoyl)-L-homoserine lactone and N-butyryl-L-homoserine lactone are important for the control of elastase rhamnolipid and the formation of differentiated biofilm (Gambello and Iglewski, 1991; Costerton *et al*., 1999; Rumbaugh *et al*., 2000; Sauer *et al*., 2002). The findings of their study were agreed with previous data, in that direct inhibition of AHL activity and blockage of their synthesis (indirect assay) decreased virulence factor production and resistance to antimicrobial agents. The same inhibition profile of the T, AF and NF preparations was obtained for elastase and biofilm production with different concentrations of *Pseudomonas aeruginosa*. This inhibition was not dependent on the growth of *Pseudomonas*

aeruginosa, as this was negligible at 1 hour. Recent investigations have demonstrated that quorum-sensing molecules play no role in early biofilm formation, but are important in the later stages (Sauer, 2002).

The acid *Lactobacillus plantarum* growth medium itself had some inhibitory activity, but the greatest inhibitory effect was observed with the T and AF preparations. In order to investigate the *in vivo Lactobacillus plantarum* inhibitory effect, a burned-mouse model of *Pseudomonas aeruginosa* infection was treated with whole cultures of *Lactobacillus plantarum*. At day 10, treatment with *Lactobacillus plantarum* (group BPs + Lp) enhanced *Pseudomonas aeruginosa* phagocytosis by tissue phagocytes significantly, and led to a decrease in apoptosis. Concomitantly, there was a decrease in the bacterial counts in skin, liver and spleen. The effect of the treatment was more pronounced on day 15, with macroscopically diminished purulent exudates, a more diffuse inflammatory cell infiltrate, and fast regeneration and tissue repair. It has been shown in animal models of infection that the ability of *Pseudomonas aeruginosa* to colonise the host, as well as its capacity to induce inflammation and cause death, is attenuated in the absence of the complete las and rhl quorum-sensing systems (Rumbaugh *et al*., 1999). The direct inhibition of AHL activity and blockage of their synthesis by *Lactobacillus plantarum* and its by-products could decrease significantly the production of virulence factors and resistance to antimicrobial agents. Previous studies have demonstrated that 3O-C12-HSL regulates the immune response and stimulates the inflammatory response directly, since it induces the expression of COX2, prostaglandin E2 and other cytokines, as well as chemokines such as interleukin-1a, interleukin-6, interferon-c, tumour necrosis factor-a, MIP-2, MIP-1B and IP-10 (MIP-2 is mainly a chemotactic factor for PMNs) (Smith *et al*., 2002). Production of AHL molecules *in vivo* by *Pseudomonas aeruginosa* has been demonstrated in infected mice (Wu *et al*., 2000), and the production of pro-inflammatory cytokines is exacerbated by *Pseudomonas aeruginosa* infection of burned wounds (Rumbaugh *et al*., 2001).

In immunocompetent individuals, the induction of inflammation is beneficial, but in immunodeficient subjects, who mount a potent inflammatory response, such induction would produce significant tissue destruction and the ability to combat the infection would be reduced severely (Wu *et al*., 2000). It has been demonstrated that interleukin-18, another inflammatory cytokine, inhibits *Pseudomonas aeruginosa* infection (Schultz *et al*., 2003). However, the interaction of *Lactobacilli* with fibroblasts, epithelial cells and inflammatory cells produces a very different pattern of cytokines and chemokines in comparison with pathogenic bacteria (Blum *et al*., 2002; Hessle *et al*., 2000). Perhaps these antagonisms confer on *Lactobacilli* the anti-inflammatory activity reported previously (Blum *et al*., 2002; Perdigo´n *et al*., 1998; Ashahara *et al*., 2001). The cells contained in the whole-cell culture preparation of *Lactobacillus plantarum* (T) would have an ability to interfere with the infective capacity of *Pseudomonas aeruginosa* cells by inhibiting the excessive PMN influx induced by the pathogen and allowing effective bacterial clearance. Moreover, *Pseudomonas aeruginosa* has a toxic effect on phagocytes (Dechaeux *et al*., 2000) and *Lactobacillus* protects them from the apoptosis caused by pathogens (Valde´z *et al*., 2001). While this therapy is not as effective as some novel antibiotics, such as novospirin-10 or protegrin-1, in the *Pseudomonas aeruginosa* burned wound infection model (Steinstraesser *et al*., 2002), the apparent activity of *Lactobacillus plantarum* and its by-products deserves further investigation for possible use in topical wound treatments.

16. References

1) Abalos, A., Pinazo, A., Infante, M. R., Casals, M., García, F and Manresa, A. (2001). Physicochemical and antimicrobial properties of new rhamnolipids produced by *Pseudomonas aeruginosa* AT10 from soybean oil refinery wastes. *Langmuir*, 17: 1367 - 1371.
2) Abbas, H., Mohammed, S., Shawkat, D and Baker, Y. (2016). Effect of *Lactobacillus* sp. Crude Bacteriocin (CB) and Cell-Free Supernatant (CFS) against *Escherichia coli* Growth and Adherence on Vaginal Epithelial Cell Surface. *International Journal of Advanced Research in Veterinary Science*, 4(1): 614 – 620.
3) Allen, S. J., Martinez, E. G., Gregorio, G. V and Dans, L. F. (2010). Probiotics for treating acute infectious diarrhoea. *Cochrane Database System Reviews*, 11.
4) Allen, H. K., Levine, U. Y., Looft, T., Bandrick, M and Casey, T. A. (2013). Treatment, promotion, commotion: Antibiotic alternatives in food-producing animals. *Trends Microbiology*, 21: 114 - 119.
5) Allesen Holm, M., Barken, K. B., Yang, L., Klausen, M., Webb, J. S., Kjelleberg, S., Molin, S., Givskov, M and Tolker Nielsen, T. (2006). A characterization of DNA release in *Pseudomonas aeruginosa* cultures and biofilms. *Molecular Microbiology*, 59: 1114 - 1128.
6) Almeghaiseeb, E. S. (2007). Probiotics: an overview and their role in inflammatory bowel disease. *Saudi Journal of Gastroenterology*, 13 (3): 150-152.
7) Ashahara, T., Nomoto, K., Watanuki, M and Yokokura, T. (2001). Antimicrobial activity of intraurethrally administered probiotic *Lactobacillus casei* in a murine model of *Escherichia coli* urinary tract infection. *Antimicrobial Agents and Chemotherapy*, 45: 1751 - 1760.
8) Bermudez Brito, M., Plaza Diaz, J., Munoz Quezada, S., Gomez Llorente, C and Gil, A. (2012). Probiotic mechanisms of action. *Annals of Nutrition and Metabolism*, 61: 160 - 174.
9) Blaiotta, G., Fusco, V., Ercolini, D., Aponte, M., Pepe, O and Villani, F. (2008). *Lactobacillus* strain diversity based on partial *hsp* 60 gene sequences and design of PCR – restriction fragment length polymorphism assays for species identification and differentiation. *Applied Environmental Microbiology*, 74(1): 208 - 215.
10) Blum, S., Haller, D., Pfeifer, A and Shiffrin, E. J. (2002). Probiotics and immune response. *Clinical Reviews of Allergy and Immunology*, 22: 287 - 309.
11) Boles, B. R., Thoendel, M and Singh, P. K. (2005). Rhamnolipids mediate detachment of *Pseudomonas aeruginosa* from biofilms. *Molecular Microbiology*, 57: 1210 - 1223.
12) Cabana, M. D., Shane, A. L., Chao, C and Hemker, M. O. (2006). Probiotics in primary care pediatrics. *Clinical Pediatrology*, 45: 405 - 410.
13) Caiazza, N. C., Shanks, R. M and O'Toole, G. A. (2005). Rhamnolipids modulate swarming motility patterns of *Pseudomonas aeruginosa*. *Journal of Bacteriology*, 187: 7351 - 7361.
14) Carr, F. J., Chill, D and Maida, N. (2002). The lactic acid bacteria: a literature survey. *Critical Reviews in Microbiology*, 28(4): 281 - 370.
15) Chen, S. Y., Wei, Y. H and Chang, J. S. (2007). Repeated pH-stat fed-batch fermentation for rhamnolipid production with indigenous *Pseudomonas aeruginosa* S2. *Applied Microbiology and Biotechnology*, 76: 67 - 74.
16) Coeuret, V., Dubernet, S., Bernardeau, M., Gueguen, M and Vernoux, J. P. (2003). Isolation, characterization and identification of *Lactobacilli* focusing mainly on cheeses and other dairy products. *Lait*, 83: 269 – 306.
17) Collado, M. C., Isolauri, E., Salminen, S and Sanz, Y. (2009). The impact of

probiotic on gut health. *Current Drug Metabolism*, 10: 68 - 78.

18) Collins, B., Caitriona, M., Guinane, P. D and Cotter, C. H. (2012). Assessing the contributions of the Lia S histidine kinase to the innate resistance of *Listeria monocytogenes* to nisin, cephalosporins, and disinfectants. *Applied Environmental Microbiology*, 78(8): 2923 - 2929.

19) Costerton, J. W., Stewart, P. S and Greenberg, E. P. (1999). Bacterial biofilms: a common cause of persistent infections. *Science*, 284: 1318 - 1322.

20) Costerton, B. (2004). Microbial ecology comes of age and joins the general ecology community. *Proceedings of National Academy, USA* 101: 16983 -16984.

21) Costerton, W. J., Lewandowski, Z., Caldwell, D. E., Korber, D. R and Lappin Scott, H. M. (1995). Microbial biofilms. *Annual Reviews in Microbiology*, 49: 711 - 745.

22) Davey, M. E., Caiazza, N. C and O'Toole, G. A. (2003). Rhamnolipid surfactant production affects biofilm architecture in *Pseudomonas aeruginosa* PAO1. *Journal of Bacteriology*, 185: 1027 - 1036.

23) Dechaeux, D., Toussaint, B., Richard, M., Brochier, G., Croize, J and Attree, I. (2000). *Pseudomonas aeruginosa* cystic fibrosis isolates induce rapid, type III secretion-dependent, but Exo U independent, oncosis of macrophages and polymorphonuclear neutrophils. *Infection and Immunology*, 68: 2916 - 2924.

24) Devine, D. A and Marsh, P. D. (2009). Prospects for the development of probiotics and prebiotics for oral applications. *Journal of Oral Microbiology*, 19: 145 - 149.

25) Déziel, E., Gopalan, S., Tampakaki, A. P., Lépine, F., Padfield, K. E., Saucier, M., Xiao, G and Rahme, L. G. (2005). The contribution of MvfR to *Pseudomonas aeruginosa* pathogenesis and quorum sensing circuitry regulation: multiple quorum sensing-regulated genes are modulated without affecting *lasRI*, *rhlRI* or the production of *N*-acyl-*L*-homoserine lactones. *Molecular Microbiology*, 55: 998 - 1014.

26) Domka, J., Lee, J and Wood, T. K. (2006). YliH (BssR) and YceP (BssS) regulate *Escherichia coli* K-12 biofilm formation by influencing cell signaling. *Applied Environmental Microbiology*, 72: 2449 - 2459.

27) Dunne, C., O'mahony, L., Thornton, G., Feeney, M., Daly, C., O'Sullivan, G and Collins, J. K. (2001). *In vitro* selection criteria for probiotic bacteria of human origin: Correlation with *in vivo* findings. *American Journal of Clinical Nutrition*, 73: 386 - 392.

28) Eschenbach, D. A., Davick, P. R and Williams, B. L. (1989). Prevalence of hydrogen peroxide producing *Lactobacillus* species in normal women and women with bacterial vaginosis. *Journal of Clinical Microbiology*, 27: 251 -256.

29) Evans, K., Passador, L., Srikumar, R., Tsang, E., Nezezon, J., and Poole, K. (1998) Influence of the Mex AB – Opr M multidrug efflux system on quorum sensing in *Pseudomonas aeruginosa*. *Journal of Bacteriology*, 180: 5443 -5447.

30) Ezema, C. (2013). Probiotics in animal production. *Journal of Veterinary Medicine and Animal Health*, 5(11): 308 - 316.

31) Ezendam, J and Van Loveren, H. (2006). Probiotics: immunomodulation and evaluation of safety and efficacy. *Nutrition Reviews*, 64(1): 1 - 14.

32) Falagas, M. E.; Betsi, G. I. and Athanasiou, S. (2007). Probiotics for the treatment of women with bacterial vaginosis. *Clinical Microbiology and Infections*, 10(5): 13657 - 13664.

33) Finegold, S. M. (2008). Therapy and epidemiology of autism - *Clostridium* spores as key elements. *Medical Hypotheses*, 70(3): 508 - 511.

34) Gallagher, L. A and Manoil, C. (2001). *Pseudomonas aeruginosa* PAO1 kills

Caenorhabditis elegans by cyanide poisoning. *Journal of Bacteriology*, 183: 6207 - 6214.

35) Gallagher, L. A., McKnight, S. L., Kuznetsova, M. S., Pesci, E. C and Manoil, C. (2002). Functions required for extracellular quinolone signaling by *Pseudomonas aeruginosa*. *Journal of Bacteriology*, 184: 6472 - 6480.

36) Gambello, M and Iglewski, B. (1991). Cloning and characterization of the *Pseudomonas aeruginosa* lasR gene, a transcriptional activator of elastase expression. *Journal of Bacteriology*, 173: 3000 - 3009.

37) Gan, B. S., Kim, J., Reid, G., Cadieux, P and Howard, J. C. (2002). *Lactobacillus fermentum* RC-14 inhibits *Staphylococcus aureus* infection of surgical implants in rats. *Journal of Infectious Disease*, 185: 1369 - 1372.

38) Gayathri, D. A and Devaraja, T. N. (2011). *Lactobacillus* sp. as probiotics for human health with special emphasis on colorectal cancer. *Indian Journal of Science and Technology*, 4(8): 0974 - 6846.

39) Gill, H. S. (2003). Probiotics to enhance anti-infective defences in the gastrointestinal tract. *Best Practice and Research Clinical Gastroenterology*, 17(5): 755 - 773.

40) Gupta, V and Garg, R. (2009). Probiotics. *Indian Journal of Medical Microbiology*, 27(3): 202 - 209.

41) Hammes, W and Hertel, C. (2006). The genera *Lactobacillus* and *Carnobacterium*. In: The Prokaryotes. pp. 320-403.

42) Hancock, R. E. (1998). Resistance mechanisms in *Pseudomonas aeruginosa* and other non-fermentative gram-negative bacteria. *Clinical Infectious Disease*, 27: 93 - 99.

43) Harder, B. (2002). Germs that do a body good. *Science News*, 161: 72 - 77.

44) Hassett, D. J., Charniga, L., Bean, K., Ohman, D. E and Cohen, M. S. (1992) Response of *Pseudomonas aeruginosa* to pyocyanin: mechanisms of resistance, antioxidant defenses, and demonstration of a manganese-cofactored superoxide dismutase. *Infection and Immunology*, 60: 328 - 336.

45) Hessle, C., Andersson, B and Wold, A. (2000). Gram positive bacteria are potent inducers of monocytic IL-12 while Gram negative bacteria preferentially stimulate IL-10 production. *Infection and Immunology*, 68: 3581 - 3586.

46) Hillier, S. L. (1992). The relationship of hydrogen peroxide-producing *Lactobacilli* to bacterial vaginosis and genital microflora in pregnant women. *Obstet Gynecology*, 79: 369 - 373.

47) Holder, I. A., Neely, A. N and Frank, D. W. (2001). Type III secretion or intoxication system important in virulence of *Pseudomonas aeruginosa* infections in burns. *Burns*, 27: 129 - 130.

48) Holmes, E., Loo, R. L., Stamler, J., Bictash, M., Yap, I. K., Chan, Q., Ebbels, T., De Iorio, M., Brown, I. J and Veselkov, K. A. (2008). Human metabolic phenotype diversity and its association with diet and blood pressure. *Nature*, 453(7193): 396 - 400.

49) Horn, S. J., Aspmo, S. I and Eijsink, V. G. H. (2005) Growth of *Lactobacillus plantarum* in media containing hydrolysates of fish viscera. *Journal of Applied Microbiology*, 99: 1082 - 1089.

50) Jander, G., Rahme, L. G and Ausubel, F. M. (2000). Positive correlation between virulence of *Pseudomonas aeruginosa* mutants in mice and insects. *Journal of Bacteriology*, 182: 3843 - 3845.

51) Johnston, B. C., Goldenberg, J. Z., Vandvik, P. O., Sun, X and Guyatt, G. H. (2011). Probiotics for the prevention of pediatric antibiotic - associated diarrhea. *Cochrane Database System Reviews*, 11: 555 - 562.

52) Kandler, O and Weiss, N. (1986). Genus *Lactobacillus*. In: Bergey's Manual of Systematic Bacteriology, Vol. 2. (edited by Sneath, P. H. A.; Mair, N. S. and Hold,

J.G), William and Wilkins Co., Baltimore, USA.

53) Karthikeyan, V and Santosh, S.W. (2009). Isolation and partial characterization of bacteriocin produced from *Lactobacillus plantarum*. *African Journal of Microbiology Research*, 3(5): 233 - 239.

54) Klemm, P., Hancock, V., Kvist, M and Schembri, M. A. (2007). Candidate targets for new antivirulence drugs: selected cases of bacterial adhesion and biofilm formation. *Future Microbiology*, 2: 643 - 653.

55) Lamont, I. L., Beare, P. A., Ochsner, U., Vasil, A. I and Vasil, M. L. (2002) Siderophore mediated signaling regulates virulence factor production in *Pseudomonas aeruginosa*. *Proceedings of National Academy of Science, USA* 99: 7072 - 7077.

56) Lang, S. (2002) Biological amphiphiles (microbial biosurfactants). *Current Opinion in Colloid and Interface Science* 7: 12-20.

57) Latifi, A., Winson, M. K., Foglino, M., Bycroft, B. W., Stewart, G. S., Lazdunski, A and Williams, P. (1995). Multiple homologues of LuxR and LuxI control expression of virulence determinants and secondary metabolites through quorum sensing in *Pseudomonas aeruginosa* PAO1. *Molecular Microbiology*, 17: 333 - 343.

58) Lugtenberg, B. J., Dekkers, L and Bloemberg, G. V. (2001). Molecular determinants of rhizosphere colonization by *Pseudomonas. Annual Reviews of Phytopathology*, 39: 461 - 490.

59) Luzzaro, F., Mantengoli, E and Perilli, M. (1870). Dynamics of a nosocomial outbreak of multidrug resistant *Pseudomonas aeruginosa* producing the PER-1 extended-spectrum beta lactamase. *Journal of Clinical Microbiology*, 39: 1865 - 1871.

60) Lyczak, J. B., Cannon, C. L and Pier, G. B. (2002). Lung infections associated with cystic fibrosis. *Clinical Microbiology Reviews*, 15: 194 - 222.

61) Marchesi, J. R., Holmes, E., Khan, F., Kochhar, S., Scanlan, P., Shanahan, F., Wilson, I. D and Wang, Y. (2007). Rapid and noninvasive metabonomic characterization of inflammatory bowel disease. *Journal of Proteome Research*, 6(2): 546 - 551.

62) Marteau, P. R. (2002). Probiotics in clinical conditions. *Clinical Reviews of Allergy and Immunology*, 22: 255 - 273.

63) Martin, R., Langa, S., Reviriego, C., Jimenez, E., Marin, L. M., Olivares, M., Boza, J., Jimenez, J., Fernandez, L., Xaus, J and Rodriguez, J. M. (2004). The commensal microflora of human milk: new perspectives for food bacteriotherapy and probiotics. *Trends in Microbiology*, 114(15): 121 - 127.

64) Martínez Vaz, B. M., Fink, R. C., Diez Gonzalez, F and Sadowsky, M. J. (2014). Enteric pathogen plant interactions: Molecular connections leading to colonization and growth and implications for food safety. *Microbes and Environment*, 29: 123 - 135.

65) Mashburn, L. M and Whiteley, M. (2005). Membrane vesicles traffic signals and facilitate group activities in a prokaryote. *Nature*, 437: 422 - 425.

66) McDonell, G and Russell, D. (1999). Antiseptic and disinfectants: activity, action, and resistance. *Clinical Microbiology Reviews*, 12: 147 - 179.

67) Musa, H. H., We, S. L., Zhu, C. H., Seri, H. I and Zhu, G. Q. (2009). The potential benefits of probiotics in animal production and health. *Journal of Animal and Veterinary Advances*, 8: 313 - 321.

68) Nielsen, D. S., Schillinger, U., Franz, C. M. A. P., Bresciani, J., Amoa - Awua, W., Holzapfel, W. H and Jakobsen, M. (2007). *Lactobacillus ghanensis* sp. a motile lactic acid bacterium isolated from Ghanain cocoa fermentations. *International Journal of Systemic and Evolutionary Microbiology*, 57: 1468 - 1472.

69) Nigatu, A. (2000). Evolution and numerical analyses of RAPD and API 50 CH patterns to differentiate *Lactobacillus plantarum, Lactobacillus fermentum, Lactobacillus rhamnosus, Lactobacillus sake, Lactobacillus parabuchneri, Lactobacillus gallinarum, Lactobacillus casei, Weissella minor* and related taxa isolated from kocho and tef. *Journal of Applied Microbiology*, 89: 969 - 978.

70) Ochsner, U. A and Reiser, J. (1995). Autoinducer - mediated regulation of rhamnolipid biosurfactant synthesis in *Pseudomonas aeruginosa*. *Proceedings of Natural Academy of Science, USA,* 92: 6424 - 6428.

71) Oelschlaeger, T. (2010). Mechanisms of probiotic actions - A review. *International Journal of Medical Microbiology*, 300: 57 - 62.

72) Ohland, C. L and Mac Naughton, W. K. (2010). Probiotic bacteria and intestinal epithelial barrier function. *American Journal of Physiology*, 298: G807 - G819.

73) Park, S. Y., Heo, Y. J., Choi, Y. S., Déziel, E and Cho, Y. H. (2005). Conserved virulence factors of *Pseudomonas aeruginosa* are required for killing *Bacillus subtilis*. *Journal of Microbiology*, 43: 443 - 450.

74) Perdigon, G., Valdez, J and Rachid, M. (1998). Antitumor activity of yogurt: study of possible immune mechanism. *Journal of Dairy Research*, 65: 120 - 138.

75) Pesci, E. C., Milbank, J. B. J., Pearson, J. P., McKnight, S., Kende, A. S., Greenberg, E. P and Iglewski, B. H. (1999). Quinolone signaling in the cell to cell communication system of *Pseudomonas aeruginosa*. *Proceedings of National Academy of Science,* 96: 11229 - 11234.

76) Potera, C. (1999). Forging a link between biofilms and disease. *Science,* 283: 1837 - 1839.

77) Pukatzki, S., Kessin, R. H and Mekalanos, J. J. (2002). The human pathogen *Pseudomonas aeruginosa* utilizes conserved virulence pathways to infect the social amoeba *Dictyostelium discoideum*. *Proceedings of National Academy of Science, USA,* 99: 3159 - 3164.

78) Rahme, L. G., Stevens, E. J., Wolfort, S. F., Shao, J., Tompkins, R. G and Ausubel, F. M. (1995) Common virulence factors for bacterial pathogenecity in plants and animals. *Science,* 268: 1899 - 1902.

79) Rahme, L. G., Tan, M. W., Le, L., Wong, S. M., Tompkins, R. G., Calderwood, S. B and Ausubel, F. M. (1997). Use of model plant hosts to identify *Pseudomonas aeruginosa* virulence factors. *Proceedings of National Academy of Science, USA,* 94: 13245 - 13250.

80) Reid, G. (2001). Probiotic agents to protect the urogenital tract against infection. *American Journal of Clinical Nutrition*, 73: 437S - 443S.

81) Reid, G. (2012). Microbiology: categorize probiotics to speed research. *Nature*, 485: 446 - 446.

82) Reid, G., Younes, J. A., Van der Mei, H. C., Gloor, G. B and Knight, R. (2013). Relationship between lactocin 705 and membranes: speculations on antimicrobial mechanism. *Applied Environmental Microbiology*, 73(2): 415 - 420.

83) Ren, D., Bedzyk, L. A., Thomas, S. M., Ye, R. W and Wood, T. K. (2004) Gene expression in *Escherichia coli* biofilms. *Applied Microbiology and Biotechnology,* 64: 515 - 524.

84) Rolfe, R. D. (2000). The role of probiotic cultures in the control of gastrointestinal health. *Journal of Nutrition,* 130: 396S - 402S.

85) Rumbaugh, K., Griswold, J. A and Hamood, A. N. (2000). The role of quorum sensing in the *in vivo* virulence of *Pseudomonas aeruginosa*. *Microbial Infections*, 2: 1721 - 1731.

86) Rumbaugh, K. P., Griswold, J. A., Iglewski, B. H and Hamood, A. N. (1999). Contribution of quorum sensing to the virulence of *Pseudomonas aeruginosa* in burn wound infections. *Infection and Immunology*, 67: 5854 - 5862.

87) Rumbaugh, K. P., Colmer, J. A., Griswold, J. A and Hamood, A. N. (2001). The effects of infection of thermal injury by *Pseudomonas aeruginosa* PAO1 on the murine cytokine response. *Cytokine*, 16: 160 - 168.
88) Sauer, K., Camper, A. K., Ehrlich, G. D., Costerton, J. W and Davies, D. G. (2002). *Pseudomonas aeruginosa* display multiple phenotypes during development as biofilm. *Journal of Bacteriology*, 184: 1140 - 1154.
89) Saxelin, M., Tynkkynen, S., Mattila Sandholm, T and de Vos, W. M. (2005). Probiotic and other functional microbes: from markets to mechanisms. *Current Opinion in Biotechnology*, 16(2): 201 - 211.
90) Schultz, M. J., Knapp, S and Florquin S. (2003). Interleukin-18 impairs the pulmonary host response to *Pseudomonas aeruginosa*. *Infection and Immunology*, 71: 1603 - 1634.
91) Schuster, M., Lostroh, C. P., Ogi, T and Greenberg, E. P. (2003) Identification, timing, and signal specificity of *Pseudomonas aeruginosa* quorum controlled genes: a transcriptome analysis. *Journal of Bacteriology*, 185: 2066 - 2079.
92) Singh, P. K., Schaefer, A. L., Parsek, M. R., Moninger, T. O., Welsh, M. J and Greenberg, E. P. (2000). Quorum sensing signals indicate that cystic fibrosis lungs are infected with bacterial biofilms. *Nature*, 407: 762 - 764.
93) Smith, R. S., Harris, S. G., Phipps, R and Iglewski, B. H. (2002). The *Pseudomonas aeruginosa* quorum sensing molecules N-(3-Oxododecanoyl) homoserine lactone contributes to virulence and induces inflammation *in vivo*. *Journal of Bacteriology*, 184: 1132 - 1139.
94) Smith, R. S and Iglewski, B. H. (2003). *Pseudomonas aeruginosa* quorum-sensing systems and virulence. *Current Opinion in Microbiology*, 6: 56 - 60.
95) Soberón Chávez, G., Lépine, F and Déziel, E. (2005). Production of rhamnolipids by *Pseudomonas aeruginosa*. *Applied Microbiology and Biotechnology*, 68: 718 - 725.
96) Stanghellini, M. E and Miller, R. M. (1997). Biosurfactants: their identity and potential efficacy in the biological control of zoosporic plant pathogens. *Plant Disease*, 81: 4 - 12.
97) Steinstraesser, L., Tack, B. F and Waring, A. J. (2002). Activity of novospirin G10 against *Pseudomonas aeruginosa in vitro* and infected burns. *Antimicrobial Agents and Chemotherapy*, 46: 1837 - 1844.
98) Stewart, P. S and Costerton, J. W. (2001). Antibiotic resistance of bacteria in biofilms. *Lancet*, 358: 135 - 138.
99) Stoodley, P., Sauer, K., Davies, D. G and Costerton, J. W. (2002). Biofilms as complex differentiated communities. *Annual Reviews of Microbiology*, 56: 187 - 209.
100) Sutherland, I. W. (2001). The biofilm matrix-an immobilized but dynamic microbial environment. *Trends in Microbiology*, 9: 222 - 227.
101) Tan, M. W., Rahme, L. G., Sternberg, J. A., Tompkins, R. G and Ausubel, F. M. (1999). *Pseudomonas aeruginosa* killing of *Caenorhabditis elegans* used to identify *Pseudomonas aeruginosa* virulence factors. *Proceedings of National Academy of Science, USA*, 96: 2408 - 2413.
102) Tanzer, J. M., Thompson, A., Lang, C., Cooper, B., Hareng, L. and Gamer, S. (2010). Products. *Food Microbiology*, 27: 698 - 709.
103) Torres, A. G., Perna, N. T., Burland, V., Ruknudin, A., Blattner, F. R and Kaper, J. B. (2002) Characterization of Cah, a calcium-binding and heat-extractable autotransporter protein of enterohaemorrhagic *Escherichia coli*. *Molecular Microbiology*, 45: 951 - 966.
104) Tsuda, M., Miyazaki, H and Nakazawa, T. (1995) Genetic and physical mapping of genes involved in pyoverdin production in *Pseudomonas aeruginosa* PAO. *Journal of Bacteriology*, 177: 423 - 431.

105) Turnbaugh, P. J., Ley, R. E., Mahowald, M. A., Magrini, V., Mardis, E. R and Gordon, J. I. (2006). An obesity-associated gut microbiome with increased capacity for energy harvest. *Nature*, 444(7122): 1027 - 1131.

106) Upadhyay, N and Moudgal, V. (2012). Probiotics: A review. *Journal of Clinical Outcomes and Management*, 19: 76 - 84.

107) Valdez, J. C., Rachid, M., Gobbato, N., Perdigon, G. (2001). Lactic acid bacteria induce apoptosis inhibition in *Salmonella typhimurium* infected macrophages. *Food, Agriculture and Immunological Research*, 13: 189 – 197.

108) Wagner, V. E., Bushnell, D., Passador, L., Brooks, A. I and Iglewski, B. H. (2003). Microarray analysis of *Pseudomonas aeruginosa* quorum - sensing regulons: effects of growth phase and environment. *Journal of Bacteriology*, 185: 2080 - 2095.

109) Wagner, V. E., Frelinger, J. G., Barth, R. K and Iglewski, B. H. (2006). Quorum sensing: dynamic response of *Pseudomonas aeruginosa* to external signals. *Trends in Microbiology*, 14: 55 - 58.

110) WHO. (2007). Guidelines for the evaluation of probiotics in food: report of a joint WHO working group on drafting guidelines for the evaluation of probiotics in food, London, Ontario, Canada. 2002.

111) Willcox, M. D., Zhu, H., Conibear, T. C., Hume, E. B., Givskov, M., Kjelleberg, S and Rice, S. A. (2008). Role of quorum sensing by *Pseudomonas aeruginosa* in microbial keratitis and cystic fibrosis. *Microbiology*, 154: 2184 -2194.

112) Windisch, W., Schedle, K., Plitzner, C. and Kroismayr, A. (2008). Use of phytogenic products as feed additives for swine and poultry. *Journal of Animal Science*, 86(14): E140 - E148.

113) Winn, W. C., Allen, S. D., Janda, W. M., Koneman, E. W., Procop, G. W., Schreckenberger, P. C and Woods, G. L. (2006). Koneman's Color Atlas and Textbook of Diagnostic Microbiology.6th ed, Lippincott Williams and Wilkins, Philadelphia, USA.

114) Wu H., Song Z and Hentzer M. (2000). Detection of N-acyl homoserine lactone in lung tissue of mice infected with *Pseudomonas aeruginosa*. *Microbiology*, 146: 2481 - 2493.

115) Yamamoto, S., Nakano, M., Kitagawa, W., Tanaka, M., Sone, T., Hirai, K and Asano, K. (2014). Characterization of multi-antibiotic-resistant *Escherichia coli* isolated from beef cattle in Japan. *Microbes Environment*, 29: 136 - 144.

116) Yateem, A., Balba, M. T., Al-Surrayai, T., Al-Mutairi, B and Al-Daher, R. (2008). Isolation of lactic acid bacteria with probiotic potential from camel milk. *International Journal of Dairy Science*, 3(4): 194 - 199.

117) Yildirim, Z. (2001). Isolation and identification of an antimicrobial substance producing *Lactobacilli*. *Global Journal of Pharmacology*, 26(4): 303 – 306.

Access this Article in Online

Quick Response Code	
Website	**www.jpsscientificpublications.com**
DOI Number	**DOI: 10.22192/lsa.2019.6.3.5**
Thomson Reuters Researcher ID	**L – 5547 – 2016**
ISI Impact Factor	**4.206**

How to Cite this Article:

Shaimaa M. S. Zainulabdeen and Wafaa Ayad Al-Nuaimy. 2019. PROBIOTICS – A potential agent for Wound treatment. *Life Science Archives*, 6(3): 1860 – 1874.

DOI: 10.22192/lsa.2019.6.3.5