

Highlights on the Usefulness of Probiotic Lactobacilli: A Review Based Study

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ABSTRACT

Probiotics are the live microorganisms that when applied sufficiently the hosts get beneficial effects. The lactic acid bacteria constitute such group of beneficial bacteria, among which lactobacilli have been studied largely in terms of the probiotic authenticity for human consumption around the world. This communication updates, based upon the available published data, the physiological stressors tolerance and antibacterial capacity as well as the safety profiles of lactobacilli, including the strains available from different natural sources, intended to be used as probiotics, because of the increasing interest on probiotic consumption by the people around the world.

Keywords: Lactobacilli, probiotics, antagonistic activity, bacteriocin, fermented food

1. INTRODUCTION

Among the lactic acid bacteria (LAB), the species of the genus *Lactobacillus*, comprise the major strains/members of the gut microbiota of humans (and other vertebrates), entailing in the process of fermentation of foods, thus improving the quality and safety of food as well as the wellbeing of the consumers. The microorganisms of such kinds are 'generally recognized as safe' (GRAS) and can be used as probiotics, safely and scientifically (Fuller, 1989; Mandal et al., 2012). Such probiotic microorganisms are adapted to two different environmental conditions: the extra-intestinal environment such as food, and the gut of humans in terms of

colonization/survival and persistence, exercise diverse pressure of selection related to their growth rate and carbohydrate metabolism. The food isolates of *Lactobacillus reuteri* accomplish of maintaining host-specific physiological characters and are recognized as probiotics (Zheng et al., 2015; Yang et al., 2015; Sieladie et al., 2011). Here, it is important to note the consensus definition of probiotics: "live microorganisms that, when administered in adequate amounts, confer a health benefit on the host" (Hill et al., 2014).

Since the probiotic lactobacilli strains are commonly applied with food system and consumed orally, and their passageway set up from the mouth cavity to the lower intestinal lumen, the strains are required to conquer various physical as well as chemical stressors such as acid (low-pH) and bile in the gastrointestinal tract for survival and so as to confer the beneficial effects (Yadav et al., 2016). Many authors, from various parts of the globe, justified the probiotic features of LAB strains isolated from different sources, time to time. The probiotic characteristics of various *Lactobacillus* strains considering various tests, together with the acid (low-pH) tolerance and antibiotic susceptibility have been explored by Srinu et al. (2013).

2. Physiological stressors tolerance of probiotics

In normal physiology, human intestinal bile salts concentration varies

between 0.3% and 0.5% (Zavaglia et al., 1998; Dunne et al., 2001), and therefore, bile salts tolerance of probiotic lactic acid bacteria within such concentration is physiologically significant, while the standard pH level for probiotic testing relies at 3 (Liong and Shah, 2005). Among the *Lactobacillus* strains isolated from traditional dairy products, a few have been reported to survive at pH 2.0 and display growth in 0.2% bile salt, as per the report of Amraii et al. (2014). On the basis of their findings, a direct screening technique, can exclude the growth of acid (low pH)-sensitive lactobacilli, for the selection of prospective probiotic strains from locally available natural sources. Nevertheless, a few reports are available on probiotic validation of naturally obtained LAB strains from locally available sources including our part of the globe (Halder and Mandal, 2015; Halder et al., 2017; Mandal and Halder, 2018; Halder and Mandal, 2018), and it is not feasible to corroborate the specific properties of a given probiotic bacterial strain and to generalize the same for other strains of probiotic bacteria. So that it is imperative to explore scientifically the probiotic properties of LAB, such as lactobacilli (and enterococci), from different locally available niches in different regions of the world including our parts in India.

3. Antagonism to bacterial pathogens

The FAO/WHO (2007) recommended that the probiotics must hold the capacity to demonstrate the antagonistic activity against bacteria causing life-threatening infection to humans. The research works in relation to discoveries of beneficial bacteria like the probiotic lactobacilli, as protective as well as curative agents for the elimination and control of potential pathogenic bacteria is being increased globally (Al-Madboly and Abdullah, 2015). The lactobacilli (from locally available sources) have been studied because of their incredible capacity to inhibit the growth of microbial pathogens. Currently, the antibiotic treatment options

are insufficient ever since the increasing rate of emergence of antibiotic resistant pathogenic bacteria (gram-negative as well as gram-positive) globally. Alternative to the antibiotics, which constitute the mainstay of all therapy against bacterial infections (VanBoeckel et al., 2014), probiotic lactobacilli have been established to be appropriate for biotherapy with demonstrated antibacterial activity (Iyapparaj et al., 2013; Sing et al., 2017). Thus, in order to check the bacterial antibiotic resistances, by putting in place an appropriate and/or alternative treatment protocol, precise characterization of antagonistic activity of locally isolated LAB strains is an emergent as well as imperative issue, since bacterial resistance to multiple antibiotics have been marked as the global public health crisis (Martinez, 2008). The scientific documentation on the antibacterial activity of probiotic LAB strains is scanty within and from our part of the globe (Mahalot and Mandal, 2018; Halder et al., 2021), and therefore, it is imperative to explore extensively the antibacterial properties of LAB strains, intended to be used as probiotics, from every possible locally available niches including our region (Malda, West Bengal, India).

4. Probiotics in combating antibiotic resistant pathogenic bacteria

The use of probiotics in India dates back to thousands of years with the use of yoghurt (curd) as a beneficial food supplement in almost each and every household, and currently many commercial probiotic products are being marketed globally. Because they antagonize the pathogenic bacteria in the human gastrointestinal tract, or in the food through multifunctional ways: by elaborating antimicrobial substances, such as H₂O₂, organic acids, mainly lactic acid, and bacteriocins (Abdel-Daim et al., 2013, Halder et al., 2021), by contending for nutrients and adhesion sites, or by restricting the spread (of microbial

pathogens) within the colonized body (DiCerbo et al., 2015).

Therefore, novel *Lactobacillus* probiotics can be used as non-antibiotic drugs in treatment of bacterial infection to humans, or can be used in combination with antibiotics in combating the infection caused by multidrug resistant pathogenic bacteria (Fayol-Messaoudi et al., 2005). However, the scientific basis supporting their (locally available commercial probiotics and probioticated foods) use lacks substantial published data in India, excepting a few from our part of the globe (Halder and Mandal, 2015; Halder et al., 2017; Mandal and Halder, 2018; Halder and Mandal, 2018). Thus, based upon the public and scientific interest on probiotics, an evaluation of the current state of understanding on probiotic features of lactobacilli, which are unstudied and naturally or commercially available, is required.

The emergence of multiple antibiotic resistant pathogenic bacteria in the community as well as in healthcare settings is a potentially serious threat to public health (Agtini et al., 2005). Since the infection with MDR bacterial pathogens is common in India, preparation of alternative treatment protocol of bacterial diseases with *Lactobacillus* probiotics may be of help for the mankind. An evaluation of the current state of knowledge about probiotics with respect to identifying prospective probiotic organisms, with improved activity, reliable efficacy and scientific validity for use in humans is required, and since the clinical application of any antimicrobial agent is based on the *in vitro* findings, evaluation of their antibacterial effect, and study of the interaction between antibiotics and probiotic and antibiotics and bacteriocin (antimicrobial peptides of low molecular weights) is mandatory. Therefore, the one possible prospect to reduce the ARPB (antibiotic resistant pathogenic bacteria) infections to humans is to set up LAB strains, or to utilize bacteriocins produced by them (Dobson et al., 2012, Halder et al.,

2021), as protein antibiotics (alone or in combination with antibiotics).

A paradigm shift in the treatment of infectious disease is necessary to prevent antibiotics becoming obsolete and, where appropriate, alternatives to antibiotics need to be considered. There is some evidence that probiotics such as lactobacilli strains are useful in the prevention and treatment of human infection with MDR bacteria including the ESKAPE (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Enterobacter* spp.) group (Ramsamy et al., 2018; Cotter et al., 2013; Wright, 2007). Moreover, an evaluation of the conventional method of lactobacillus identification combined with genetic approaches will improve the existing knowledge of lactobacilli species identification and strain (Halder et al., 2021).

5. Probiotics safety concern

It has been reported that the probiotic microorganisms, which were basically isolated from local niches, must be safe as well as non-pathogenic, thus suitable for human consumption. Therefore, the uncharacterized LAB isolates are needed to be screened for haemolytic, gelatinase and DNase activities (Halder et al., 2017). Additionally, the probiotic LAB strains can be antibiotic sensitive so as to be incompetent to disseminate the resistance property to the pathogenic bacteria in the same ecological niches, or the antibiotic resistance among them be innate and non-transferable (Jose et al., 2015, Halder et al., 2017). The isolated LAB strains are required to be investigated for lysozyme tolerance as well, since the stressors to the probiotic microorganisms commence to exhibit the hostile functionality in saliva because of lysozyme action (Mathara et al., 2008). It has been reported that the LAB isolated from cow-milk and goat-milk had sensitivity to the majority of the antibiotics tested, and resistances were investigated for all isolates to methicillin, for *Lactobacillus*

sp. G1 and *Lactobacillus* sp. C1 isolates to vancomycin, while to trimethoprim for *Lactobacillus* sp. G1 and *Lactococcus* sp. G2 (Mahalot and Mandal, 2018). Since the good LAB strains have not even been waived from transferable antibiotic resistance phenomenon, many authors have documented the status of various resistances to antibiotics for safety profiling of native LAB isolates (Mourad et al., 2006; Georgieva et al., 2015). Therefore, the unstudied isolates of LAB from different sources within a given locality, are required to be characterized for safety profiling by excluding the chances of gelatin liquefaction, DNase and haemolytic activities, and non-transferability of antibiotic resistances among the isolates.

In addition to the above, some adverse effects that are linked to the use of probiotic lactobacilli (*L. rhamnosus*, *L. casei*, *L. paracasei*) include bacteraemia, sepsis, infective endocarditis and liver abscess among immunocompromised (including HIV) patients, in people with different underlying medium conditions: ulcerative colitis, diabetes mellitus and colitis (Castro-Gonzalez et al., 2019).

6. CONCLUDING REMARKS

Overall, though there have been ample research worldwide on the beneficial role of probiotics, and probiotic characterization, the information on safety profiling and studies on probiotic-antibiotic as well as antibiotic-bacteriocin combinations against multidrug resistant bacteria is meagre. Therefore, the probiotic potentiality assessment of locally isolated and unstudied lactobacilli strains takes an account of testing for identity confirmation, physiological stressors tolerance, functionality, and safety profiling as well, and before *in vivo* application, *in vitro* testing is mandatory in authenticating the preferred outcome (Gareau et al., 2010). Currently some such scientific data are available from our part of the globe, and still more studies are needed to be carried out from our locality, with precise

objectives, in order to investigate the observable facts as mentioned above, in tackling the emergence as well as dissemination of antibiotic resistant bacteria and the life threatening infections caused by them in local niches, in order to get health benefits by the consumers at least in our part of the globe (Malda, India).

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