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Can Bacteriocins Curb the Emergence of Antibiotic Resistant Pathogenic Bacteria in the Globe?

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Abbreviations: ARPB: Antibiotic Resistant Pathogenic Bacteria; LAB: Lactic Acid Bacteria; GRAS: Generally Recognized as Safe

Commentary

The global clinical medicine, on facing the bacterial antibiotic resistance emergence problem, is at the antibiotic invention crisis. The bacterially (good commensal bacteria) formed bacteriocins (which are non-toxic as well as non-immunogenic and bacterial resistance to which is deemed weak), hardly produce adverse effect on the host, and potentially impede and evade the infection with antibiotic resistant pathogenic bacteria (ARPB), in humans. This unlocks an improved vista in developing novel treatment regime utilizing the 'acquiescent to bioengineering' bacteriocins to be useful alone in place of antibiotics or in combination with antibiotics.

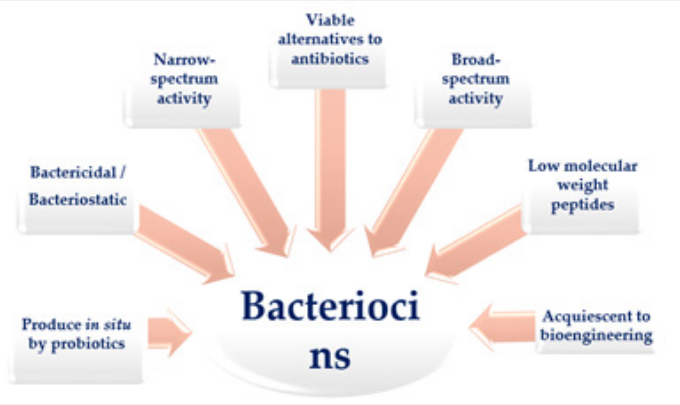

Figure 1: Bacteriocin properties (data source: Tacconelli et al. [2]; Cotter et al. [5]; Garcia-Bayona and Comstock [14]; Angelakis et al. [20]). The nontoxic and non-immunogenic natures of such antimicrobial peptides authenticate their acceptability as protein antibiotics in balancing the antibiotic resistance crisis.

Antibiotics —the magic bullets— remain the gold standard therapeutics, since their introduction in clinical medicine, for the treatment of life-threatening bacterial infections to humans. However, the use, misuse and overuse of antibiotics, not only in clinical practices, in agriculture and food industries too, led to the emergence of ARPB, in the community as well as in healthcare settings, and that the bacterial antibiotic resistance is a global emerging health crisis, which, therefore, imperatively needs the development of newer effective antimicrobials (target-specific narrow spectrum, not only the broad spectrum) to curb the ARPB dissemination [1-3]. Probiotics, in the form of lactic acid bacteria (LAB), mainly the lactobacilli, might be the suitable candidates of biotherapeutics in order to combat the unchecked emergence and dissemination of ARPB [4, 5]. Because of their antagonistic property against bacterial pathogens, including the antibiotic resistant individuals: spoilage, food-borne and pathogenic bacteria [6], by producing antimicrobial substances (hydrogen peroxide, lactic acid and bacteriocin) the LAB are regarded as living medicines as well as the 'army bacteria' having the GRAS (generally recognized as safe) status [7]. The bacteriocins (ribosomally synthesized antimicrobial peptides of low molecular weight) are effective alternatives to

the conventionally used antibiotics, possessing the capacity to display narrow as well as broad antibacterial spectra [5,6], and decolonizing property. Such low molecular antimicrobial peptides act as bacteriostatic as well as bactericidal agents, based on the bacteriocin class or the kind of target bacterial pathogens [8]. As has been reported [5, 9-11], the LAB bacteriocins act by disrupting the bacterial cell membrane integrity or act within the cell targeting the metabolism of protein, RNA or DNA, and the evidence on chances of emergence of bacteriocin-resistant bacteria is meager [3,5,12]. The properties that bacteriocins possess and for which these are valued candidates of biotherapeutics for the treatment of ARPB infection to humans are depicted in Figure 1.

The bacteriocins act synergistically (with antibiotics) and target explicitly [5,6,13,14]. Bacteriocins as well as the source probiotic microorganisms provide growth inhibitory effect against life-threatening infection causing gram-positive (*Bacillus cereus, Enterococcus faecalis, Listeria monocytogenes, Staphylococcus aureus, Streptococcus pyogenes*), and gram-negative (*Acinetobacter baumannii, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa*, and *Proteus spp*.) ARPB; those might be useful as biomedicines, in a rotational order with antibiotics, in order to minimize the antibiotic selection pressure in the given niches [4,15,16]. Genetic modification of probiotic microorganisms might strengthen the probiotic functionality (activity and stability) in order to deal with the dawdling discovery of newer antibiotics and to combat the escalating emergence of ARPB too. Moreover, the genetically modified bacteriocins, diffocins: Avidocin-CDs, are found safe to be used in the treatment and prevention of Clostridium difficile infections specifically, which neither disrupt the normal gut microbiota nor exorcise the Avidocin-CD decolonizing capacity [3].

Finally, the replacement of antibiotics with living therapeutics, probiotics or the bacteriocins they synthesize, be capable of saving the twentieth century's wonderful discovery of 'magic bullet' from its mislaying within a practice of 'imprudent antibiotic usage' in the twenty first century [17], and, before it is excessively late, the global awareness on the consequences of antibiotic overuse is an urgent need [18]. On the other side, the LAB antimicrobial peptides are required to be bio-engineered for selective use of bacteriocins against ARPB infections as the narrow-spectrum biotherapeutics with decolonizing capacity [19,20].

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