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Probiotics: The Futuristic Alternative of Antibiotics?

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ABSTRACT

Probiotics are a natural alternative to antibiotics and are generally used to treat microbial infections that cause a variety of human and animal ailments. Doctors often prescribe antibiotics to treat diseases caused by microbial systems, such as bacteria or fungi. However, their excessive and improper usage has contributed to the rise in antimicrobial resistance, dysbiosis, or imbalance of the host microbiota despite antibiotics being the most well-known life-saving drugs. Antimicrobial resistance among microorganisms has emerged as a significant danger to global health, potentially resulting in millions of deaths annually in the past and future. It is imperative that antibiotic alternatives can be found and developed in light of these global problems because there is some evidence that probiotics can fight infections, control immunological responses, and maintain overall host health by re-establishing the balance of the gut microbiota. Probiotics can act as antibiotics if the gut microflora is identified and treated with plant extracts that solely stimulate these probiotic bacteria. If the treated bacteria exhibit more efficacy than the untreated bacteria, recombinant DNA technology can increase its effectiveness; as a result, it can be a more effective substitute for such high-dose antibiotics. The present study thoroughly explains the antimicrobial resistance problems associated with antibiotic use and the possibility of using probiotics as antibiotic alternatives.

KEYWORDS

Probiotics, antibiotics, antimicrobial resistance, biotechnological strategies

Introduction

As antibiotics may either stop the growth of living organisms or kill them, they have long been used to treat bacterial infections (Kourkouta et al., 2018). However, there is now a cause for concern over the short-term efficacy of today's antibiotic repertory, owing to the spread of antibiotic resistance genes into dangerous bacteria. The World Health Organization has classified antibiotic and antimicrobial resistance as an unexpected global health danger with widespread multisector implications for food, environment, animal, and human safety owing to the worldwide spread of these diseases. By 2050, it is predicted that the number of fatalities from antibiotic-resistant pathogens will reach 10 million annually globally (Oneill, 2016). The host receives health-promoting benefits from the mammalian gut microbiota through immune system alterations, improved nutritional utilization efficiency, and pathogen elimination (Allen et al., 2014). Maintaining host health requires an overall equilibrium in the proportion of gut microbiota (Reid, 2006). Each individual has a different gut microbiota that can influence environmental and genetic factors (Aghebati-Maleki et al., 2021). One of the ecological causes of modification of the gut microbiota (dysbiosis) is the inappropriate and systematic prescription of antibiotics. This results in less microbial diversity and a deficiency of helpful microorganisms in favor of potentially hazardous germs (Petersen & Round, 2014). It is common knowledge that probiotics are "good microorganisms" instead of "bad or harmful microbes, " such as infections. Originating from the Latin "pro" and the Greek word "bios," probiotics mean "for life," while antibiotics mean "against life." A live bacterium that benefits a host when given the right conditions is the most widely used definition of a probiotic. (Hill et al., 2014). Probiotics have been shown to have antagonistic properties that prevent the growth of gut pathogens by (i) producing bioactive metabolites, such as hydrogen peroxide, organic acids, antioxidants, and antimicrobial peptides; (ii) competing with pathogens for nutrients and attachment sites; and (iii) modifying immune system functions (Vieco-Saiz et al., 2019, Azad et al., 2018).

Basics of Antibiotics

The word "antibiosis," which denotes hostile interactions between microbes, is where the etymology of the word "antibiotic" originates (Bentley & Bennett, 2003). "antimicrobials" was coined to describe natural, semi-synthetic and synthetic compounds that may stop the spread of bacteria, viruses, fungi, and parasites (Azad et al., 2018). In contrast, "antibiotics" refer to naturally produced substances that inhibit or kill bacteria (Etebu & Arikekpar, 2016). Antibiotics are low-molecular-weight compounds that can selectively kill or inhibit the growth of other species in low quantities. Both live microbes and plants produce these substances. Among these are artificially created organic substances with the same antibacterial properties (Smith et al., 1998).

Antimicrobial Resistance (AMR) Issues

The resistance to and growth of microorganisms in the presence of antimicrobial drugs is known as acquired resistance (AMR) (Abushaheen et al., 2020). Antibiotic resistance is one of the greatest threats to global health. Poor cleanliness, abuse, and overuse of antibiotics are potential causes of its emergence (Aghamohammad & Rohani, 2023). Furthermore, it has been determined that animal farms may be a source of bacteria and genes resistant to antibiotics (ARBs) and Antibiotic resistance genes (ARG) (Bai et al., 2022). As a result, eating animal products treated with antibiotics poses a danger of spreading resistant germs (Ma et al., 2021). For instance, methicillin-resistant Staphylococcus aureus (MRSA) has been found in dairy farmers, cattle, and farm equipment (Papadopoulos et al., 2019). The presence of resistance genes in transposable elements, such as plasmids; reduction in antimicrobial agent uptake (efflux of the antibiotic from the cell, biofilm formation, and permeability reduction); the presence of factors that affect the target antibiotic, such as enzymes; and mutations or alterations in the antibiotic target site are the main AMR mechanisms developed by resistant pathogens (Darby et al., 2023).

The probiotic-based approach is a potentially successful tactic for stopping the spread of antibiotic-resistant microorganisms (Laich et al., 2002). Live bacteria constitute probiotics and are advantageous to humans when handled appropriately (Etebu & Arikekpar, 2016).

Table 1: Main classes of antibiotics and their sources

Antibiotics	Example	Source	Reference
Aminoglycosides	Streptomycin	*Streptomyces griseus*	**(Pissowotzki et al., 1991)**
B-Lactams	Penicillin	*Penicillium griseofulvum*	**(Laich et al., 2002)**
Glycopeptides	Vancomycin	*Amycolatopsis orientalis*	**(Jung et al., 2007)**
Lipopeptides	Daptomycin	*Streptomyces roseosporus*	**(Miao et al., 2005)**
Macrolides	Erythromycin	*Streptomyces erythreus*	**(Vieco-Saiz et al., 2019)**

Remedies for Antibiotics

With the worrying impact of AMR, it is imperative to develop novel antibiotic alternatives that are more targeted and do not negatively impact the gut microbiome. These substitutes should have the same positive benefits for such active molecules while attempting to minimize antibiotics' improper and excessive use. The alternatives include microbial-based substitute classes such as bacteriophages, probiotics, and certain vaccines and molecular substitute classes such as bacteriocins, antimicrobial peptides, medicinal plants, and nanoparticles, which directly act by inhibiting or destroying pathogens (Kunyeit et al., 2020). The latter's antibacterial processes are derived from direct or indirect actions. Bacteriophages, for example, are viruses that infect bacteria and release their genetic material, which breaks down the DNA of the bacteria and eventually kills them (Zamojska et al., 2021). Probiotics can reduce dysbiosis and bacterial infections by modulating the host's gut microbiota and immune system, or they can act indirectly by producing metabolites, such as bacteriocins, organic acids, antioxidant compounds, and nutrient-space competition.

Probiotics as a Possible Substitute for Antibiotics

According to the available data, probiotics may cure and prevent infectious diseases in human and animal health (Allen et al., 2014). For example, several clinical studies have shown that *Saccharomyces boulardii*, a probiotic yeast, reduces problems associated with Candida infections (Tegegne & Kebede, 2022). The principal antimicrobial mechanisms of probiotics include immune system modulation, mucin and tight junction protein expression enhancement, competitive exclusion, and improved intestinal barrier function.

Hypothetical Biotechnological Approach: Gut Microflora Modification

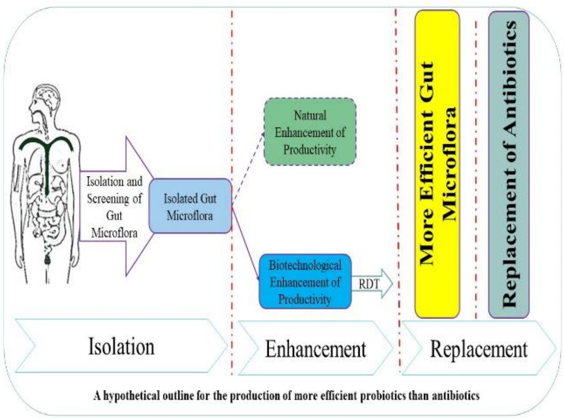

Fig. 1: The Futuristic Hypothetical Path.

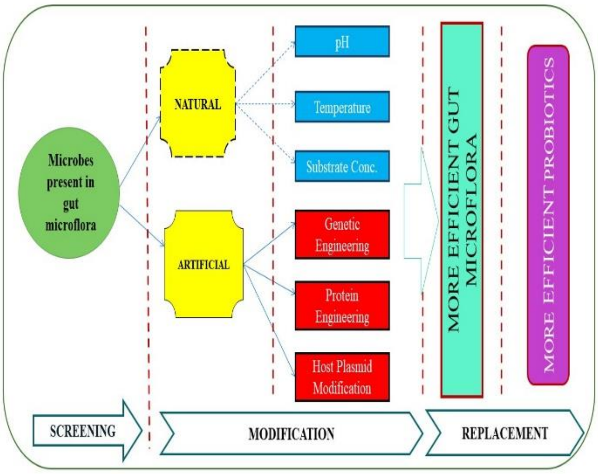

Fig. 2: Possible biotechnological modification flow

The paper suggests a hypothetical approach to enhance gut microflora to obtain the desired Probiotics. The process of such modification is presented in the picture given above. At first, microbes from the human gut are to be isolated to obtain pure cultures on different media accordingly to form single colonies. The colonies thus obtained are to be subjected to further screening to check for their protein expression levels (Helmy et al., 2023). Next, strategies are to be devised to alter their chemistry. The strategies involved in modifying the microbes can be either natural or artificial. Natural techniques can include changing the parameters and applying stress conditions like pH, temperature, substrate concentration, etc. On the other hand, artificial or biotechnological approaches can consist of genetic engineering, protein engineering, and host plasmid modification (Raheem et al., 2021). Genetic engineering techniques can be used to alter the gene makeup of the isolated microbes. The genes responsible for the expression of the targeted proteins can be modified by changing a single base pair, deleting a part of the DNA, or adding a new segment of nucleotides in the DNA. Another alternative technique for enhancing the probiotic microorganisms' efficiency is protein engineering. Here, the proteins encoded by the successfully screened microorganisms will be first analyzed through in-silico processes in the dry lab. Modifications will occur in the protein's active site where the protein-ligand interaction occurs (Silva et al., 2020; Weber et al., 1985). The desired variants are to be then modified through the wet lab processes. Host plasmid modification is yet another critical approach in modern-day biotechnology. Several artificial plasmids that perform efficiently upon insertion into many host organisms are already available in the market. This technique can be used to introduce the gene of interest isolated from the microbes into the choice of host-microbe.

Conclusion

Overuse and inappropriate use of antibiotics lead to an increase in incidences of pathogen resistance and dysbiosis, which pose a serious risk to the health and welfare of people and animals. Because probiotics are living, multifunctional microorganisms with many more properties and activities than antibacterial chemicals, they seem like solid alternatives. Probiotics offer additional modes of action against infections, including space exclusion and nutrition competition, in addition to their ability to generate various antibiotic-like antimicrobial metabolites and immunomodulation activities. These multi-action processes raise the possibility of using probiotics in place of antibiotics by reducing the likelihood of pathogen-acquired resistance. Furthermore, probiotics can be used as antimicrobials against viruses in addition to bacteria. If successfully isolated, screened, and modified, microbes from the gut can prove to be efficient probiotics. The probiotics may be used to replace high-toxicity chemotherapeutic agents in the near future. Many studies and clinical trials have demonstrated their effectiveness in suppressing pathogens, both human and animal, and this data supports their potential uses in illness prevention, infection treatment, and enhancing immunological function, growth performance, and nutrition efficiency. Notwithstanding these benefits, maintaining cell viability and optimizing dosage are still practical obstacles to attaining high specificity and quick treatment times with probiotics as opposed to antibiotics. Hence it can provide the proper action against several diseases by improving the patient's immune status and competing with pathogens, inhibiting their growth and thus conferring a stable health status.

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