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A COMPLETE REVIEW ON ANTIBACTERIAL ACTIVITY OF PROBIOTICS AND PAIRING IT WITH ANTIBIOTICS

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ABSTRACT

Probiotics are live, health promoting microorganisms which are called as "good" or "helpful" bacteria for humans. They are becoming popular at current years due to the evaluation of its beneficial activities in humans. Antibiotics are the "wonder drug" to compete with pathogenic bacteria which are life-threatening to humans. Regrettably, the microbes have become resistance to some common antibiotics. Since the antimicrobial resistance are growing day-by-day the scientific community are in the need of developing an alternative source for antibiotics. Review, we present the antibacterial effects of probiotics, their usefulness to the humans and efficacy of them to be taken along the antibiotics. It also reviews the collection of research that has proved the antibacterial activity of probiotics.

KEY WORDS: Probiotics, Antibiotics, Antibacterial effects, Bacteria.

INTRODUCTION

Probiotic is a phrase of the modern era, denotation "for life" and is in use to name bacterial association with beneficial effects on human and animal health [1]. The most commonly quoted meaning was made by Fuller (1989). The probiotics are live microbial feed supplement which beneficially affects the host animal by improving its intestinal balance. Probiotics play a major role in health-promoting "functional foods" for humans, as well as therapeutic, prophylactic growth supplements in animal production human health [2]. The probiotic strains can act as adjuncts to antibiotic therapy by reducing adverse effects, improving antibiotic function and enhancing mucosal immunity is mounting [3]. Antimicrobial resistance has been reported against almost all antibiotics discovered and it is one of the most urgent public health issue to be considered at the moment [4]. The antimicrobial or antagonistic activity of probiotics is an important property which can involve in tackling the antibacterial resistance [5].

Human helpful probiotics

The probiotic microorganisms have been used to prevent and treat a variety of human diseases for more than 100 years. Recently research of probiotics are increased. The importance of probiotics is meaningful because they have both, an application on industrial product development and a beneficial effect in human health. The action mode of probiotic microorganisms is likely to be multifactorial and seems to be specific for each strain [6]. The fact is that the intestinal microflora had metabolic functions, such as fermenting indigestible dietary residues and endogenous mucus, saving of energy, production of vitamin K, and absorption of ions. They have an important role in epithelial cell proliferation and differentiation, and the development and the homeostasis of the immune system [7].

Health benefits of probiotic bacteria to the host, and speculated mechanisms involved are [9]

1. **Resistance to enteric pathogens** has a mechanism of antagonism activity, adjuvant effect increasing antibody production, systemic immune effect, colonization resistance, limiting access of enteric pathogens (pH, bacteriocins/defensins, antimicrobial peptides, lactic acid production, and toxic oxygen metabolites).
2. **Immune system modulation** has a mechanism of

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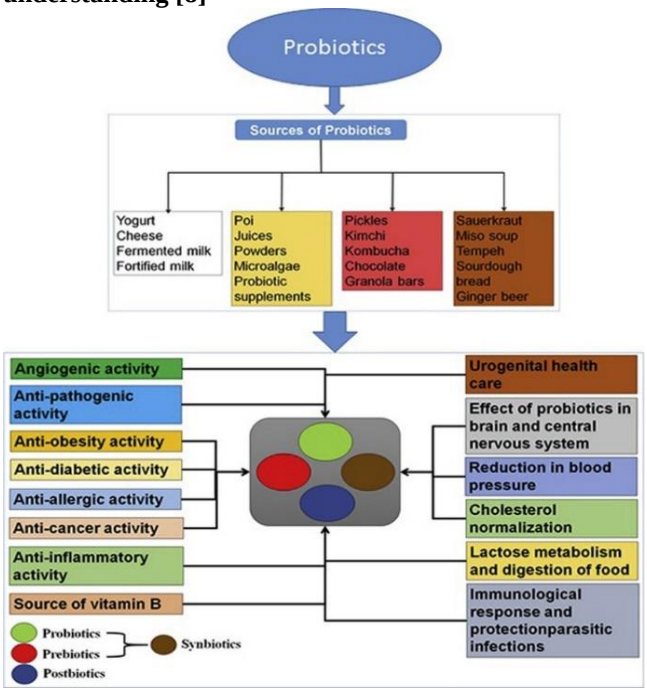
strengthening of nonspecific and antigen-specific defence against infection and tumors, adjuvant effect in antigen-specific immune responses, regulating/influencing Th1/Th2 cells, production of anti-inflammatory cytokines, decreased release of toxic N-metabolites.

3. **Infection caused by *Helicobacter pylori*** has a mechanism of competitive colonization inhibition of growth and adhesion to mucosal cells, which decreases the gastric *H. pylori* concentration.
4. **Small bowel bacterial overgrowth** has a mechanism of influence the influencing the Lactobacilli activity of overgrowth flora, decreasing toxic metabolite production, normalizing of a small bowel microbial community, and antibacterial characteristics.

Fig-1 Complete uses of probiotics with proper understanding [8]



Probiotic as antibiotics

The latest study to investigate probiotics concludes that regular use may reduce the need for antibiotics [6]. The antagonistic activity of one microorganism against other is caused by the competitive exclusion, immune modulation, stimulation of host defense system, production of organic acid or hydrogen peroxide that lowers pH & Production of antimicrobial such as bacteriocins, production of signaling molecules that trigger changes in gene expression.

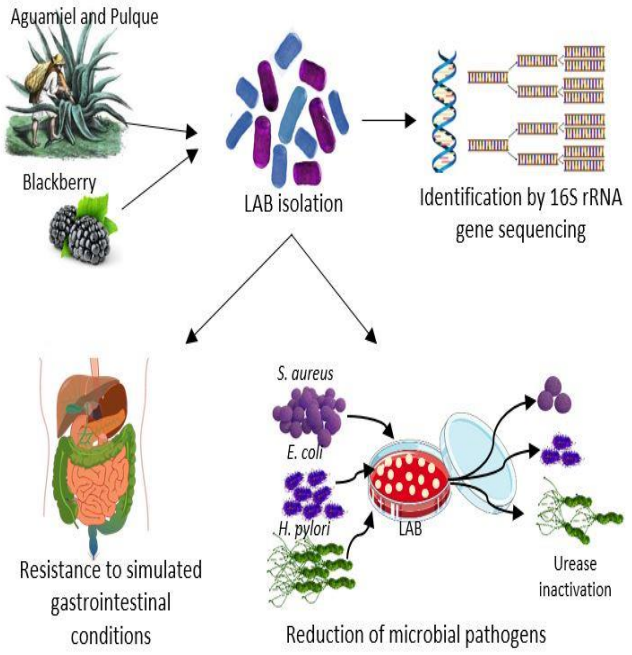
Beneficial microorganisms produces some antibacterial like lactic acid, acetic acid, formic acid, phenyllactic acid, benzoic acid as well as other organic acids, short chain fatty acids, hydrogen peroxide, carbon dioxide, acetaldehyde, acetoin, diacetyl, bacteriocins like inhibitory substances and others . The most common bacteriocins include lacticin, lactocin, pediocin, pisciolin, enterocin, reuterin, plantaricin, enterolysin and nisin [5].

Probiotics exhibits anti-pathogenic activity which is considered as most beneficial because unlike classic antibiotics, disturbance or alteration in the composition of the complex population of the gut microbiota is inhibited. The influence of probiotics on the survival of *Salmonella enterica, Serovar typhimurium* and *Clostridium difficile* in an *in vitro* model has investigated and postulated that probiotics inhibit pathogens by the production of short-chain fatty acids (SCFAs), such as acetic, propionic, butyric and lactic acids [8]. Various oral bacterial strains produce the fatty acid, which may inhibit some bacterial colonization and/or emergence, or in some cases inhibit existing species and enable pathogens to emerge in the microbial biofilms [11].

Research based evidence for antibacterial activity of probiotics

1. The probiotics has some antibacterial activity and there are few researches which has proved it. The followings are the information extracted from the researches done on the antibacterial activity of probiotics. Few collected *Lactobacillus* isolates were used against the pathogens to check the antimicrobial activity and the method used was agar-well diffusion method [12].
2. Fourteen isolates of different probiotic strains from cheese and fermented products of two *Lactobacillus spp*, eleven Bifidobacterium *spp*, and one *Streptoococcus spp*, were used against several human *(Staphyllococcus aureus* and *Eschericia coli*) and plant (*Rhizoctonia solani* and *Fusarium oxysporum*) pathogens by examining their *in vitro* antimicrobial properties. The agar-well diffusion method was used to prove the antibacterial activity [13].
3. The evaluation of the antimicrobial activity of four *Lactobacillus species (Lactobacillus bulgaricus, Lactobacillus casei, Lactobacillus plantarum* and *Lactobacillus Fermentum)* were experimented against intestinal pathogenic to investigate the inhibitory activity against four bacterial enteric pathogens *(Escherichia coli, Staphylococcus aureus, Shigella dysenteriae* and *Salmonella paratyphi A)* was done in this study. The medium used was MRS medium (de Man, Rogosa and Sharpe medium). The results obtained as the enteropathogens growth was stopped in the presence of all *Lactobacillus* and inhibition zone was found between 12 and 32 millimeter. They concluded that these four *Lactobacillus* strains had potential antimicrobial compounds against human enteric pathogens and should be further studied for their human health benefits [14].

4. The antimicrobial effect of probiotic bacterial strains isolated from different natural sources against two pathotypes of pathogenic *E. Coli* was determined in this study [15].
5. About 26 *Lactobacillus* and *Bifidobacterium* strains were tested for its antibacterial activity. Ten strains with antimicrobial activity against two pathogens was determined. The study concluded that these probiotics may play an important role in the food industry as starter cultures, co-cultures or bioprotective cultures, to improve food quality and safety or as probiotic therapeutics, appropriate for clinical practice [16].
6. That study shows that several *Lactobacillus* strains exhibit antibacterial activity against carbapenam-resistant *enterobacteriaceae*. They also conclude by saying that further studies are required [17].
7. Antimicrobial Activity Production of antimicrobial substances is one of the main probiotic properties for strain selection. In this study, 60% of the isolates had inhibitory activity against E. coli and S. aureus. Few showed low antibacterial activity and few showed high activity [18].
8. The conclusion made in that study are given below. They are,
   i. Probiotics Oral Administration Increase the Numbers of Paneth Cells at the Base of the Intestine Crypt.
   ii. Probiotics Oral Supplementation Increases the Antimicrobial Activity in Intestinal Fluids.
   iii. The Antimicrobial Activity Induced by Oral Probiotics Is Also Effective in Aging Mice.
   iv. Oral Administration of Probiotics Does Not Modify Large Intestine Microbiota [19].



9. Probiotic yogurt containing strains of *L. fermentum, L. acidophilus*, and *Bifidobacterium*; and EOs of peppermint, basil, and zataria was manufactured with viable probiotic counts up to the acceptable range and appropriate antimicrobial activity during 28 days was obtained in that study [20].
10. Pure probiotic strains were isolated from commercial probiotic products and tested for their antimicrobial and anti-biofilm activities against *C. sakazakii* and positive results were obtained in that study [21].
11. The results of that study showed that the antimicrobial property of the probiotic broth was significantly increased and showed good bacteriostatic activity against on *Staphyllococcus aureus, Escherichia coli* and *Candida albicans*. To overcome the problem of resistance in pathogenic microbes Selenium metal was incorporated into probioticts supplement. The antimicrobial activity was enhanced [22].
12. The combination of different probiotic strains to complete the inhibition growth of bacteria and spores were tested. As a result of the conducted studies strains of *Bacillus subtilis* and *Bacillus spp*. had high antimicrobial activity. It's important for the application of these probiotic strains in foods to extend the shelf life. *Bacillus* probiotics strains were used for the production of functional foods (yogurt; bioyogurt; bread with extended shelf - life; raw - dried meat products; cheeses; organic preservation of cosmetic creams) [23].
13. Evaluation of antimicrobial efficacy of probiotic *Lactobacillus* strains isolated from dairy products was the objective of that research and obtained good results [24].
14. Their work demonstrates the inhibitory activity of lactic acid bacteria consortium against multi drug resistant clinical isolates and concluded that the study showed the potential of the whole broth and cell lysate of the combination of *L.acidophillus, L. plantarum*, and *L. casei var. rhamnosus* as a better inhibitor towards MDR clinical isolates [25].
15. In this work, the study was conducted to evaluate the antibacterial effectiveness of probiotics lactobacilli group and *Bifidobacterium* against *Enterococcus faecalis* and *Candida albicans* in both planktonic stage and biofilm stage and concluded that the probiotic therapy represents a potential antimicrobial treatment option that should be developed further. It also shows that probiotics offer potential benefits for root canal therapy and that further *in vitro* and *in vivo* studies are warranted to determine the full potential of bacterio therapy in endodontics [26].
16. The work of them were the spent culture supernatant (SCS) of the probiotic *lactobacillus rhamnous GG* has been reported to exert antibacterial activity against *salmonella thyphimurium* and concluded that obtained strong antimicrobial activity of *L.rhamnous GG*

against *salmonella* was mediated by lactic acid under growth condition [27].

Probiotics and antibiotics

Most of the antibiotics prescribed in clinical practice are natural products that originate from *Streptomyces spp*, which were first used as agricultural probiotics. Antibiotics and probiotics has promising effects on gut flora they can modify the gut microbiota. The effect of a probiotic species on the digestive flora depends on the strain and is largely determined by bacteriocin production [28]. Some of the evidence suggests a protective effect of probiotics in preventing Antibiotics-Associated Diarrhoea (AAD) and among the various probiotics *Lactobacillus rhamnosus* or *Saccharomyces boulardii* provides the positive results while the likelihood that adverse events are very rare [29]. Probiotics work efficiently as an adjunctive therapy (given along with standard antibiotics vancomycin or metronidazole) for *Clostridium Difficile* Infections, CDI it produces several proteases that directly degrade *C. difficile* toxins or increase the immune response to *C. Difficile* toxins [30].

Advantages

Multiple mechanisms of action possible, *In situ* delivery vehicle, safe in diverse patient populations**,** diversity of potential organisms**,** aids natural body defences**,** lack of significant drug interactions & ease of administration and Inexpensive.

Disadvantages

Strain specific effects, heterogeneous trials, risks in immuno compromised & lack of quality control regulations.

The approach of probiotics in the prevention of antibacterial resistance

There is an experiment done to prove that probiotics had a useful potential inhibitory effect on the growth of the pathogens. The inhibitory zones of probiotics were greater than those of antibiotics as well as combination of antibiotic + probiotic was concluded from that study [31]. Probiotics can help to prevent and treat disease through several mechanisms.

1. **Direct interaction:** Probiotics interact with the disease-causing microorganisms directly and making it harder for them to cause the disease.
2. **Competitive exclusion:** Probiotics directly compete with the disease and developing the microorganisms for nutrition or enterocyte adhesion sites.
3. **Modulation of host immune response**: Beneficial microbes interact with and strengthen the immune system and help prevent disease [32].

The mechanisms which are mentioned below gives deeper view that, how probiotics work in tackling the antibacterial resistance:

(1) They may exclude pathogens from the host by competing for nutrients,

(2) Some may produce chemicals against the pathogens.

(3) Some may mimic the oligosaccharide receptors of the host cells used by pathogens to enter the cells.

(4) They may block the ligand-receptor contact, which helps in host pathogen interaction.

When taken orally, probiotics can neutralize toxins and interfere with gut pathogens and finally wipe out the infection from the gut region [33].The use of probiotics to address the global problem of emerging antibiotic resistant microorganisms is a “double - edged” sword – with both beneficial effects and associated risks as depicted [34].

Hence so far probiotics can be used as partial replacement or adjunct to antibiotic treatment and thereby help treating multidrug resistant UTIs but the role of probiotics in preventing drug-resistant infections in humans has not yet been established. The Centre for Disease Control and Prevention (CDC) is actively researching the subjects [35].

There are some drawbacks to this approach:

1. There is the possibility of resistance transfer from the probiotic to human bacterial pathogens, either directly or indirectly via the commensal flora.
2. The probiotics can acquire resistance genes from human commensals by themselves.
3. In case of immune compromised patients the infections may cause due to the probiotic itself, a rare occurrence mainly developing in, the presence of a multi resistant strain could result in the availability of only a limited number of antibiotics to treat the patient.
4. It should however be stressed that, at the very least, viable microorganisms used as feed additives, should not contribute to the genetic pollution by resistance determinants [36].

CONCLUSION

There are many evidences for the antibacterial activity of probiotics however further researches are required to explore and the consumption of probiotics will surely leads to the healthy life. These probiotics were identified to play a major role in addressing the life-threatening antibacterial resistance. This review may support the upcoming researches in probiotics to prove its antibacterial activity.

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