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Mini Review

Harnessing Microbes for the Benefit of Man

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Abstract

Microorganisms reside in and around humans and are sometimes pathogenic. However, most of the microbes in the air or in our body, which exist as commensals or symbionts, benefit us in some form or other. We depend heavily on these beneficial microbes for our optimum health. The purpose of this review was to delineate and summarize the various applications of microbes for the benefit of mankind. In many areas, the biochemical properties and metabolic end products of microbes are now being channelized for improving human health and quality of life. The author collated data from various published articles and tried to present a holistic viewpoint of this aspect of the application of microbes for the betterment of human health and public health as well.

Introduction

Microbes outnumber us humans by many times. A fraction of microorganisms cause many diseases in man. However, they are also beneficial to us in many ways, like producing vitamins and strengthening the immune system [1]. Our body has more microbial cells that live on and in our body as commensals and symbionts.

There are good and bad microbes. For example, probiotics are “good bacteria” because they impart numerous health benefits to man and also disallow the adherence of pathogens in our gut. On the other hand, “bad” microbes are the pathogenic bacteria that cause many infections, many of which lead to tremendous morbidity and mortality, or may also turn out to be oncogenic. Examples of such bad microbes are *Shigella* spp., *Salmonella* spp., and *Vibrio* spp., which infect us by the feco-oral route, and *Streptococcus pneumoniae* which infects us via the aerosol route and may cause pneumonia and other infections.

Some of the beneficial aspects of microbes are listed as under

A. Probiotics: Probiotics are live microorganisms which when ingested in small amounts, impart many health benefits to the host. *Bifidobacterium* spp. (a Gram-positive rod), *Lactococcus* and *Lactobacillus* spp. (a microaerophilic Gram-positive non-sporulating bacillus) are very good examples of probiotics [2]. *Bifidobacterium* spp. is in fact, the first bacterium to colonize the human gut. Among yeasts,

Saccharomyces cerevisiae var. *boulardii* is an excellent probiotic. Probiotics displace the pathogenic microorganisms from the gut and also synthesize short-chain fatty acids which help in the nourishment of the enterocytes. Lactobacilli in the gut also helps produce Vitamin K, Vitamin B12, GABA, and serotonin which serve vital functions in the human body. Probiotic bacteria in the gut produce SCFA (short-chain fatty acids) that also boost the secretion of IgA in the gut lumen, which helps fight gut infections.

Killed probiotic bacteria can also be eaten and are also beneficial, and are termed paraprobiotics.

Bacteriocins, the most important metabolites produced by probiotics can act as novel therapeutic agents, and have shown strong evidence in terms of fighting pathogens, potential as antimicrobial agents, and also show anticancer activity. Figure 1 shows an image of curd, used popularly as food and as a probiotic.



Figure 1: Yogurt (curd) as a probiotic food. Source of image: Author.

B. Fecal microbial transplant: Here stool from a healthy donor, containing the beneficial or commensal bacteria, is transplanted in the gut of the diseased person. This is helpful for curing IBD (Inflammatory bowel disease) and IBS (Irritable bowel syndrome) where there is a loss of normal resident microbial flora of the gut. It replenishes the lost microbial population in the gut. Gut flora from a healthy person's gut can be transplanted into the gut of a person with IBD. Fecal transplant has also been successfully used to cure and treat *Clostridium difficile* infection of the gut.

C. As sources of antibiotics: Molds like *Penicillium notatum* and *P. chrysogenum* produce the beta-lactam antibiotic Penicillin, which has revolutionized the treatment of infections. It was a chance discovery by Alexander Fleming, way back in 1928. Penicillin kills bacteria by hampering cell wall formation. The filamentous fungus *Micromonospora purpurea* produces the aminoglycoside antibiotic Gentamicin [3]. The Gram-positive spore-bearing bacillus *Bacillus subtilis* is noted for the production of Bacitracin, a powerful topical antibiotic. Similarly, *Pseudomonas fluorescens* can produce Mupirocin, another topical antibiotic used on skin and mucosa, which has been found to be active against *Staphylococcus aureus*. These molecules are produced by bacteria or fungi for their own protection and to kill competing microorganisms in the natural environment. Recent research has found many other antibiotics and anthelmintics from soil bacteria, which are discussed in the following sections.

D. As sources of antifungal agents: Filamentous Gram-positive bacteria like *Streptomyces nodosus* act as sources of antifungal agents like Amphotericin B [4]. This compound has also now been modified as liposomal Amphotericin B and is also useful as a potent therapeutic option against *Leishmania donovani* causing visceral leishmaniasis.

E. As sources of therapeutic enzymes: Serratiopeptidase, an enzyme used medicinally, reduces oedema after inflammation due to infections and trauma and is obtained from *Serratia* spp. It acts by breaking Tyr-Tyr (Tyrosine-Tyrosine) and other amino acid linkages. A detailed discussion on this can be found later.

F. As sources of other drugs like statins: Molds like *Aspergillus terreus* are natural sources of hypocholesterolemic agents like statins. In fact, the isolation of natural statins like compactin, mevastatin, and lovastatin from *A. terreus* can be termed one of the greatest achievements of industrial microbiology [5]. Statins are a class of drugs that inhibit HMG-CoA reductase and thus lower cholesterol production. The statins were initially discovered in fungi, and for many years fungi were the only source for the statins. Among the statins, mevastatin was the first to be studied as a fungal secondary metabolite, later followed by lovastatin (also called monacolin K or mevinolin).

G. As sources or catalysts in the preparation of beverages and fermented products: Yeasts like *Saccharomyces* spp. help in the production of wines and other fermented beverages and foods like bread and idli. This is because of their ability to produce gas and acid from carbohydrates by means of fermentation. This also produces the fluffy feel of bread and idli, owing to the gas formation. Yeasts can break down pyruvic acid to produce ethanol, which is useful in beer brewing and winemaking.

H. As sources of pigments and antioxidants: Prodigiosin produced from *Serratia marcescens* is a bright red, non-diffusible pigment that acts as a natural antibiotic and antioxidant. It can also be produced by other bacteria like *Hahella chejuensis*, *Zooshikella rubidus*, *Pseudomonas magnesorubra*, and *Vibrio gazogenes*. It also has strong anticancer and immunosuppressant properties [6]. *Serratia* spp. was named so, as a tribute to Italian physicist Serafino Serrati. It has been shown that prodigiosin works due to the presence of a methoxy group in its molecule. Moreover, the enhanced inhibitory activity of prodigiosin along with metal ions, viz., Zn^{2+} , Al^{3+} , and Cu^{2+} has been noted against methicillin-resistant *Staphylococcus aureus*.

I. Biodegradation of waste: Bacteria like *Pseudomonas putida* help degrade organic matter of biomedical and other types of waste [7]. It is thus used in waste disposal sites and Oxidation ponds. Microorganisms are considered to be the sole biological source for degrading hydrocarbons. Bacterial species have been reported to degrade hydrocarbon.

J. Source of packaging and other materials: Biopolymers are among the most investigated biodegradable materials for developing food packaging materials because of their remarkable properties, including renewability, abundance, non-toxicity, biodegradability, biocompatibility, and functionality. Pullulan, a tough fibrous biopolymer material derived from the mold *Aureobasidium pullulans*, a nonpathogenic fungus, can be used as packing and binding material for industrial purposes. It is also useful as a thickener and stabilizer [8]. Biopolymers are now potential candidates to meet current packaging demand and serve as a good alternative to petrochemical-based, non-biodegradable packaging materials. Among available biopolymers, pullulan is a microbe-derived biopolymer that has been extensively used for many purposes.

K. Application of bacteria in vector control: Gram-positive spore-bearing bacteria like *Bacillus thuringiensis* can be used in stagnant water bodies to kill larvae of mosquitoes [9]. The bacterium secretes specific proteins known as "cry proteins" that are toxic to insects, which have also been elaborated later on [10]. A gene of this bacterium is also used to make genetically modified crops like Bt-brinjal and Bt-tomato which are naturally resistant to pest attack.

L. As normal microbial flora of the vagina in females of reproductive age group, Lactobacilli maintain healthy epithelial lining of the vagina and also vaginal pH. Any loss or alteration of Lactobacilli in the vagina and overgrowth of Gram-negative bacilli and anaerobes may lead to Bacterial vaginosis, which is characterized by foul-smelling vaginal discharge [11]. This disease may also affect the developing fetus in pregnant women.

M. In molecular biology: The heat-stable Taq polymerase enzyme from the bacterium *Thermus aquaticus* has enabled the development of the Polymerase Chain Reaction which is used to amplify specific portions of DNA. PCR is now used extensively in research, clinical diagnostics, and forensic analyses [12].

N. Microbes, when attenuated or killed, can serve as sources of vaccines. Vaccines are the immunogenic components of microbial antigens. Examples of live attenuated vaccines are the Oral Polio vaccine and of killed vaccine is the IPV or Injectable Polio vaccine [13].

O. Thermotolerant bacteria like *Geobacillus stearothermophilus* act as a biological control in sterilization processes like autoclaving. *Bacillus subtilis* and *C. tetani* are used as biological controls for dry heat sterilization methods, like hot air ovens.

P. Microbes can also be directly consumed as food, like yogurt (containing probiotic bacteria) and mushrooms. Mushrooms are basidiomycetous fungi that are sometimes edible (especially white button mushrooms) and are rich in protein, low in calories, and devoid of cholesterol [14].

Recent microbe-derived molecules discovered beneficial for humans and also the significance of these findings

a. Probiotic bacteria like *Lactobacillus* spp. release compounds like butyric acid and propionic acid, which exert purported beneficial effects like protection of gut epithelial integrity and stimulation of release of IgA. They have also now been used to treat successfully, dental caries and headaches. Nowadays yeast-based probiotics are also important and have an advantage over bacterial probiotics, in that they will never develop resistance to oral antibacterials.

b. Pyocyanin, the blue-green water-soluble phenazine pigment released by *Pseudomonas aeruginosa*, can inhibit many bacteria as well as *Candida* spp. but not all bacteria [15].

c. Taq polymerase produced by *Thermus aquaticus*, a non-flagellated Gram-negative bacterium, has found its application in PCR (Polymerase chain reaction) assays. *T. aquaticus* is ubiquitous in hot springs and hydrothermal vents. Its DNA polymerase is quite heat-stable and is most active around 70 °C.

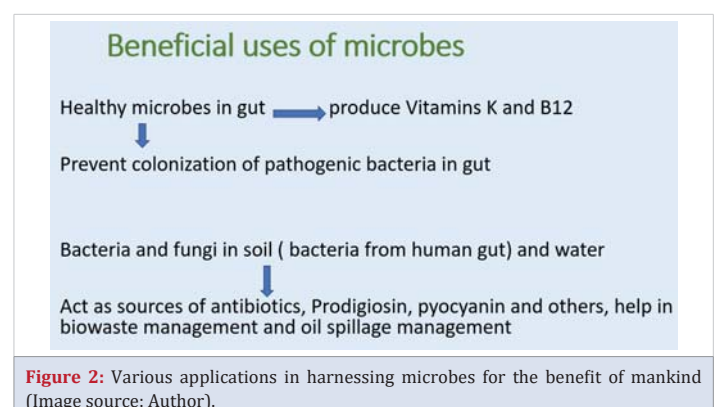
d. *Bacillus thuringiensis*, an aerobic spore-bearing Gram-positive bacillus, releases insecticidal crystal pore-forming proteins, known as Cry toxins. These Cry toxins interact with many insect midgut proteins, thereby leading to the formation of a pre-pore oligomer-like structure. Then occurs membrane insertion, with the final killing of the insect midgut cells by virtue of osmotic shock. This property has been applied to kill larvae of *Anopheles* mosquito in water collections for control of malaria [16].

e. *Serratiopeptidase* is derived from cultures of *Serratia* spp. which is found in soil, water, and human gut. Clinical studies have reported its effectiveness in reducing swelling and edema. It also aids in metabolizing scar tissues in the body and is particularly helpful for curing post-traumatic swelling, fibrocystic breast disease, and bronchitis [17]. This molecule is a powerful anti-inflammatory analgesic, anti-edemic, anti-atherosclerotic, and topical rapid-acting drug.

The various applications in harnessing microbes for the benefit of man are also depicted in the schematic diagram below (Figure 2).

Discussion

Thus there are many listed beneficial uses of different microorganisms, mainly bacteria and fungi. Humans have harnessed the profound medicinal and other applications of microbes to an appreciable extent. The list of beneficial uses of microbes for man is pretty long and this article has just tried to provide a highlight. This also stresses the fact that both humans and microbes depend on each other heavily for their survival and well-being. A healthy microbiome supports and maintains our health, but when this microbiome is disturbed in some way, it has been linked to hundreds of ailments like cancers, IBD (Inflammatory Bowel Disease), autoimmune and cardiovascular diseases [18]. Research and development are now underway in many areas of beneficial application of microbes for mankind, in medical, core as well as industrial microbiology. Microbes have been used to derive natural antibiotics like Penicillin (from the mold *Penicillium notatum* and *P. chrysogenum*) and Tetracycline (from the



fermentation of *Actinomyces* spp.). Chlortetracycline was produced by *Streptomyces aureofaciens* [19]. Recently, Anthelvencins A and B, pyrrolamide metabolites produced by *Streptomyces venezuelae* ATCC 14583 and 14585. Isolated in 1965, have been shown to possess anthelmintic and also moderate antibacterial activities [20]. Now it has also been reported that bioinformatic analysis of metagenomes, which are the collective genes of a microbial community, can reveal hitherto unknown bacterial metabolites that may function as antibiotics [21]. Nevertheless, we must also remember that such harnessing of microbes for the benefit of man will have its own inherent limitations, like in the case of probiotics taken orally. Such probiotic bacterial strains may cause bloating in some, and living bacterial strains may also be harmful to people with compromised immune systems [22]. The cellular toxicity, in man, of products like pyocyanin and prodigiosin, derived from bacteria, also have to be studied in more detail. The author feels that further research is needed in these aspects, with dedicated funding, and much more needs to be explored, since these things may turn out to be of tremendous public health importance in the future.

Conclusion

Microorganisms are not always harmful but many a time they are beneficial to the human host. With the passage of time more and more beneficial uses of microbes in man are being unfolded.

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