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Article

Anti-microbial and anticarcinogenic activity of Postbiotics: a review

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ABSTRACT

Modern world is marked by several lifestyle and non-communicable diseases and cancer is perhaps the most common of them all, taking the proportions of a pandemic. There is a complex relationship between postbiotic compounds and human health, as numerous studies have shown. Postbiotics appear to be important mediators of the intricate and direct relationship between these variables. The word "postbiotics" describes a group of biological micro- and macromolecules that, when taken in sufficient quantities, have a variety of positive health benefits on the host. Due to their anti-proliferative, anti-inflammatory, and anti-cancer capabilities, postbiotics may be able to regulate the efficiency of cancer treatment and lessen the negative effects of conventional medicines in cancer patients, according to several reports. Postbiotics have since drawn considerable scientific interest due to their distinctive properties and are regarded as a novel option for adjuvant therapy in patients with cancer. The antimicrobial and anticarcinogenic activity of postbiotics will be summarised in this review paper.

Introduction

Postbiotics are useful bioactive substances (Moradi et al. 2020**)** that are produced in a matrix during fermentation and have potential applications in health promotion. The term "postbiotics" as a catch-all for all synonyms and terms those are connected to these components of microbial fermentation. Thus, metabolites, short-chain fatty acids (SCFAs), microbial cell fractions, functional proteins, extracellular polysaccharides (EPS), cell lysates, teichoic acid, peptidoglycan-derived muropeptides, and pili-type structures are just a few of the various components that can be found in postbiotics (Żółkiewicz et al. 2020).

The utilisation of beneficial microbes or probiotic as they are better known in the food industry promote new insights. According to FAO/WHO study, probiotics are 'live microorganism that confers a health benefit to the host when administered in sufficient quantities' **(**Katarzyna et al. 2014). Advantageous intestinal bacteria like *Bacteroides, Fusobacterium, Eubacteria, Peptococcus, Peptostreptococcus, Bifidobacterium, Escherichia & Lactobacillus* **(**Shin et al. 2019; Vasquez et al. 2019) have been studied extensively in this regard. Noteworthy, multiple beneficial advantages have been highlighted such as improved lactose intolerance, mitigation of complications of cancer, decrease in blood cholesterol, building up of stronger immunity, reduction in some alimentary tract symptoms, synthesis of vitamins B & K as well as keeping the body metabolism healthy **(**Rad et al. 2020; Ansari et al. 2020). The good effects of probiotics are employed in body by supplements of foods & pharmaceutical metabolites. Due to these numerous health benefits these probiotics are being highly accepted by people (Abbasi et al. 2021). Authors have highlighted that, it has enormous antimicrobial, antioxidant effects besides carrying anticarcinogenic properties (Angelin & Kavitha, 2020; Ragul et al. 2020). Moreover, probiotics supress growth & activity of pathogenic microbes during food preservation (Chetwin et al., 2019; Barros et al. 2020). Vivarelli et al. 2019 have reported that, probiotics are foremost anticarcinogenic compounds that have been proved by mice trial or human trial. In spite of all these advantages the utilisation of these live microbes has been somewhat halted. One of the challenges is its viability. In supplements, live microbes do not provide same advantages to people of different age groups and physiological conditions at all times. Negative effects of live microbes may also create biasness regarding immunity, Crohn's disease, some alimentary tract disease etc. These have been observed especially in the case of pregnant mothers, expectant women, infants, adolescents, some adults, geriatric people (Devirgiliis et al. 2013). Another challenge is the exposure of probiotics to antibiotic resistance & their transmission capability. Genes which are involved in causing virulence & supress ability of harmful microbes reside in intestine. Accumulation of harmful microbes in intestinal microbiota, therefore promotes antibiotic resistance which may be involved in causing multiple problems of health (Ogier & Serror, 2008). So, Researchers have observed this serious problem & they are continuously trying to remove these challenges by coming up with solutions through research. It has been noted that the utilisation of 'Postbiotics' is alternative of 'Probiotics' and this is one of the greatest solutions to the challenges faced. Postbiotics are functional bioactive compounds that develop by probiotics-mediated fermentation, such as organic acid, bacteriocins, carbonic substances & enzymes (Mathur & Singh, 2005). This review conveys efficacy of postbiotics to stave off cancer.

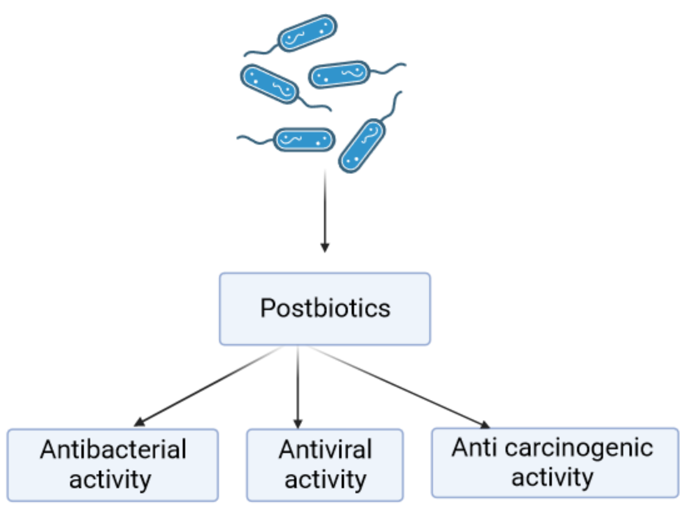

Figure: 1 *different activities of postbiotics*

Properties of Postbiotics

Extensive literature has reviewed that, Postbiotics are the compounds produced by the fermentation of probiotics. These may be developed by imbibing particular fibre to probiotic microbes (Rad et al. 2020). Crucial postbiotics are short chain fatty acids (SCFA) that are formed by carbohydrate fermentation (Yordshahi et al. 2020).

In accordance with Bomfim et al. 2020, the two known procedures which generate postbiotic are natural processes like fermentation & experimental procedures. Postbiotics have multiple beneficial effects of probiotics. They also have strong immunity, hypersensitivity, antimicrobial activity, antioxidant effect, anti-obesity, anti-diabetes, anti-hypersensitivity, antiproliferation, anticancer effect & so on (Homayouni Rad et al. 2021).

Moradi et al. (2020) reported that postbiotics, since not microorganisms, are not prone to as much bias as probiotics. They are safe for human consumption, can promote longer shelf life of foods and have other beneficial effects as well. It is important to note that, effects of postbiotic depends directly upon the type of probiotic which is used to produce the postbiotic compounds & also the chemical nature of postbiotic itself.

Some effects of postbiotics & their mechanism

Antibacterial functions of postbiotics

Suppression of the activities of infectious microbes & food spoilage or infestation are the good effects of postbiotics. In modern & scientific community, postbiotics are available as antibiotics & preservatives. Antibacterial effects are fabricated on the basis of

a. The type of probiotics from which postbiotics are developed.
b. The variety of target microbes. For example, Gram negative is very much resistant to the effect of postbiotic components as compared to gram positive organisms.
c. The effectiveness of postbiotics **(**Moradi et al. 2020).

Postbiotics have strong antimicrobial effect because it blocks intestinal epithelium & attaches to receptors which are required by harmful microbes to alter gene expression of host & also change surrounding environment (Nataraj et al. 2020). Authors have said that, *Lactobacillus plantarum* and its postbiotic effect is very much crucial as postbiotic because it stop the adherence & interfering capacity of *Listeria monocytogenes* **(**Moradi et al. 2019).

Postbiotics developed from probiotics like *L. casei, L. acidophilus* can increase gut IgA level in small & large intestine which block enteric infestations generated pathogens like *E. coli, S. enteritidis* **(**Humam et al. 2020). Supernatants of *Bifidobacterium & Lactobacillus* cultures have also good antibacterial efficacy that has been experimented by invitro studies to stop the interference of *E. coli* into enterocytes. Supernatants are very much effective for gene expression, cell barrier, & have effective antibacterial properties (Safar et al., 2019**)**. Acetate is developed from *Lactobacilli* which mitigate E. coli 0157:H7 activity (Bhat et al. 2019).

According to literature, Postbiotics are very much effective against gram positive microorganism as antibacterial postbiotics may not pervade the gram-negative microbe's outer membrane. *Lactobacillus plantarum* UG1 have good antibacterial activity in gram positive bacteria as compared with gram negative microbes. The results had highlighted that, gram negative organisms have a persistent capacity of resistance against probiotics (Korotkyi et al. 2019**)**.

- *Organic acid as a postbiotics*

This foremost postbiotic component is organic acid act as antibacterial compound **(**Aljumaah et al., 2020). Probiotic microbes generate few crucial acids like citric acid, acetic acid, tartaric acid. Moreover, lactic acid, acetic acid tartaric acid, malic acid, citric acid supresses activity of pathogenic microbes with low p^H value (Mani-López et al. 2012).

Rad et al. (2020**)** noted that the reducing action of lactic acid is a result of its effect on cell membrane of bacteria. Antibacterial mechanism of organic acids was due to the effect of its capacity of decreasing intracellular pH & lowering integrity of membrane.

- *Bacteriocin as a postbiotics*

Bacteriocins have antibacterial efficacy which can be used in developing fermented food products that helps to stop the activity of pathogens & furthermore it is resistant to p^H & heat (Gálvez et al. 2007**)**. It shows advantageous effects on cytoplasmic membrane. Bacteriocins are attached through such sensitive substances like bacterial peptide that helps to stop the development of spores of harmful microbes in cell membrane (O'Connor et al. 2020).

- *Fatty acid as a postbiotics*

Postbiotics can act as convenient replacement to antibiotics because they carry efficient antibacterial properties. Short cain fatty acids are developed from saturated & unsaturated carbon chain linked to carboxylic group. Lauric & myristic acids have strong antibacterial capacity. These types of postbiotic mechanisms involved here are enhanced membrane permeability, disarranged electron transport chain, also disturbance of the structural & enzymatic functions as well as functional modifications of protein enzymes (Yoon et al. 2018).

- *Peptides as a postbiotics*

This kind of postbiotics stop the manipulation of harmful microbes by pleiotropic mechanism like debasement of microbial membrane & stop the production of macromolecules (Waghu & Idicula-Thomas, 2020). Peptides are generated by mainly ribosomal bacteria (Rad et al., 2020). Bacteria generally hold peptides. In cell membrane, most of the peptides are present which may be used as postbiotics. (Hanson et al. 2019; Karimi et al. 2020).

Zasloff (2002) reported that antibacterial peptides can act by causing leaking out of cellular components, blocking sensitive compounds of microbes & also generating detrimental procedures like present hydrolase activity which have detrimental effects on cell & form excessive acids in bacterial membrane.

Antiviral properties of postbiotics

Postbiotics, the bioactive compounds produced by probiotics, have gained attention for their potential health benefits, including antiviral properties. Research suggests that these compounds may exhibit direct antiviral activity or modulate the host immune response to enhance antiviral defenses (Aghebati-Maleki et al. 2021).

Wu et al. (2020) reported that postbiotics prevent reverse transcriptase activity, stop host cell perforation, and inhibit the absorption of viruses. The type of probiotic used on postbiotic extracts and the type of virus it contains greatly influence the antiviral qualities of postbiotics. Researchers have demonstrated that Plantaricin has favourable sites on SARS-CoV2.

As a postbiotic, plantaricin inhibits the manipulation of infection by controlling T cells' ability to produce immunity, produces IFN-γ, and lowers proinflammatory cytokines **(**Aguila et al. 2020).

- *Organic acid as a postbiotics*

Chemicals such as organic acids, acetoin, intermediate compounds, and pyrrole compounds are often produced in the postbiotic after bacterial fermentation. For instance, acetoin plays a key role in both the synthesis of amino acids and the flavour of food (Xiao et al. 2012**)**. By binding organic acid to the virus's glycoprotein (S), probiotics can develop organic acid's antiviral potential and prevent the virus from shutting down the angiotensin converting enzyme (ACE2) (Gurung et al. 2020**)**.

- *Fatty acid as a postbiotics*

This type of postbiotics (like lauric acid, myristic acid) has extensive antiviral capacity and very much active to supress virus enlargement (Mali et al. 2020). By binding organic acid to the virus's glycoprotein (S), probiotics can develop organic acids that prevent the virus infection (Churchward et al. 2018; Desbois, 2012).

- *Peptides as a postbiotics*

Peptides are a type of postbiotics that are produced by the microbiota. Antimicrobial peptides (AMP) are peptides that produce pores in bacterial membranes or hinder the formation of the bacterial wall (Severino et al. 2017).

- *Hydrogen peroxide*- Aljumaah et al. 2020, have reported that, it is very commonly produced by all type of bacteria however it is observed in aerobic culture of catalase negative microbes & their substances of lactic acid bacteria. It removes infections by interchange with bacteria, virus, fungi, enzymes, nucleic acids thereby stop cloning & contamination (Bidra et al. 2020).

Antioxidant activity of postbiotics

Postbiotic has potentiality to stop the activity of free radicals that damage the activity of nucleic acid, carbohydrate, protein, lipid. Especially, antioxidant enzymes like catalase, peroxide dismutase (SOD), glutathione peroxidase (GPx) have efficient activity to stop the function of free radicals (Homayouni et al., 2020). *Lactobacillus plantarum RG14, RG11* strains make type of postbiotic enzyme this enhances antioxidant capacity of glutathione peroxidase in serum & rumen fluid & also escalate the activity of hepatic superoxide dismutase (Izuddin et al. 2020), *Lactobacillus plantarum* forms postbiotic enzyme which increases the good enzymatic activity (Lin et al., 2020), *Lactobacillus plantarum R111* produce postbiotic enzyme that, also enhances GPx, CAT, GSH & fall heat stress marker (Humam et al., 2020). *Lactobacillus* have efficient action on catalase that provide relief from inflammation, infection or other stresses (Humam, et al., 2019). Authors have proved that genetically modified *Lactobacillus lactis* have enormous anticarcinogenic property in colon (Humam et al. 209). Noteworthy, *Lactobacillus fermentum* generate much antioxidant enzyme (Wegh et al. 2019).

- *Glutathione peroxidase as a postbiotics*

This enzyme has crucial function to hold microbes in secure zone from oxidative damage. It converts peroxide to alcohol & supress generation of the free radicals (Brigelius & Flohé, 2020). Ungati et al. (2019) reported that this enzyme has multiple isoenzymes these are encrypted by multiple genes. GPx-1 has hydrogen peroxide which act as substrate observed in cytoplasm of mammalian tissues (Chen et al. 2019).

Antitumor activity of postbiotics

Postbiotics have anticancer effects through apoptosis, anti-proliferative, and anti-inflammatory actions as well as by altering the immune system and composition of the gut microbiota (Cuevas-González et al. 2020). Yang et al. (2020) reported that *Lactobacillus paracasei* improve postbiotic efficacy against colorectal cancer. These probiotic strains have blocking capacity of cell wall protein in human carcinoma & cell development.

Luang-In et al. (2020) reported that *L. plantarum* I-UL4 is affixed to human breast cancer cells MCF-7 via a protein postbiotic function. *Lactobacillus paracasei K5* is a kind of protein postbiotic act upon colon cancer of human. It has aggregated that efficient antiproliferative functions & strong apoptotic effects. Which is proved by analysis quantitatively & confocal, microscopic fluorescent & linking function of postbiotics **(**Chondrou et al. 2020**)**.

Anticarcinogenic activity of Postbiotics

The use of postbiotics as a supplement to cancer treatment and prevention has a close relationship to the host immune system's response and function. Various studies have validated the possible function of postbiotics in cancer prevention and treatment, specifically in cases of gastrointestinal (GI) cancer **(**Schwartz et al. 2019; Klemashevich et al. 2014**).**

Zhong et al. (2014**)** reported that several mechanisms, such as gut microbiota modification and beneficial microbiota dominance, enhanced immune system function and response, and significant antioxidative and anti-proliferative properties, are responsible for the anticarcinogenic effect of LAB.

Conclusion:

In conclusion, postbiotics is a new idea that recognises the significance of microbial metabolites in the upkeep of health. To determine the ideal dosage and frequency of postbiotic supplement administration for cancer patients, randomised double-blind clinical trials are required. Based on various research studies it was found that the typical SCFA, butyrate, which is produced by the intestinal metabolism of fibre or added as tributyrin, prevents the development of cancer and specifically promotes death in tumour cells.

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