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A Revolution By Probiotic And Paraprobiotic In Food Industry: Review

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ABSTRACT

This review article focuses on the bio-food revolution arising by use of probiotics and paraprobiotic products for eliminating the deficiency and improve the human immune system to healthier state. Paraprobiotic products aid in improving the digestive system, reducing mental and nervous illnesses in humans. Probiotics and Paraprobiotics can be used as medicine which can inhibit the activation of unwanted organisms in a human system and prevent the diseases. In the production of probiotics and paraprobiotic products, live or inactivated microorganisms are used. Day to day humans come across extensive metabolic activities for which such organisms are needed by human body. In human body, microorganisms play vital role, which may be beneficial or harmful. In Food Industry the development will concentrate on enhancement of beneficial organisms and contain harmful one to avoid risk factors to human body. Therefore, the focus area of this review paper is to study beneficial microorganisms and investigated same for the manufacturing of paraprobiotic products. This study aims at functionality and scope of probiotics and Paraprobiotics in future in this area taking cognizance of past work. This review concludes that there is significant impact of probiotics and paraprobiotics products on human health. Same can be used as bio-food for eradicating imminent deficiency issues in human body.

1. Introduction

In the human body, there are numerous varieties of beneficial microorganisms are present in an external and internal area which includes skin, teeth, hand, stomach, intestine, mouth and also clothes. Even in the human gastrointestinal tract (GIT), these microorganism plays a very prominent role in digestion and also maintaining good health of human being. The human body is a host of microorganism. Those microorganisms present in the human body are mostly useful for functional activity of human beings.

Probiotics is a Greek word “Pro-Bios” means for life. This term first introduced by Kollath in 1953 and used by Lilly and Stillwell in 1965*.* The first probiotic product was fermented milk used for human consumption. At the time of 20th century, Russian scientist “Elie Metchnikoff” (Nobel Prize winner) who suggested the long healthy life of Bulgarian people after consuming the fermented milk product which decreased the toxic microbial activity (Arvind Kumar and S. Shafat, 2010). After that in the 1960s dairy industry was beginning to promote fermented milk and milk products contain *Lactobacillus acidophilus*. Commonly probiotics are defined as “live microorganism is orally taken in adequate amount to maintain good health or disease free”. It is reported that health benefits are provided due to interaction between the gastrointestinal microorganisms and immune system. Probiotic health benefits depend on the dose taken by the humans and support the immune system of the human body (Caroline N. de Almada. et al., 2016). In general, good health is provided by probiotic foods. Probiotics are classified into three categories according to the site and action of microorganisms they are, 1) Direct action on GIT microbes, 2) Direct action on epithelium and mucous layer, 3) Action on the immune system and other organs like liver, brain etc., (Rijker et al., 2010).

Probiotics are used to control diarrhea, lactose intolerance (Li et al., 2012), irritable bowel syndrome (Ducrotte et al., 2012), some type of cancer, insulin resistance (Hsieh et al., 2013), cholesterol (Bordoni et al., 2013), blood pressure (Chiang and Pan, 2012) and obesity (Arora et al., 2013). Different types of microorganisms like bacteria and yeasts which contribute the probiotic properties are used in food and clinical treatment (Amara and Shilb, 2013). In the production of probiotics and paraprobiotics mostly microbes are used which is given in Table 1. Some species are traditionally used in the production of food and beverages like fermented milk, yogurts, idli, chees, etc. In orange juice and dehydrated food contain stressful microorganism due to their low pH and water activity (Anekella and Orsat, 2013; Betoret et al., 2003; Krasaekoopt et al., 2014). At the time of production of probiotics, microorganisms are supplement after thermal treatment to avoid the chance of microbial contamination (Rokka and Rantamaki., 2010). Although, now research is focused on inactivation of probiotic microorganisms are known as paraprobiotics.

Table-1

Application of Various Probiotic organisms

Sr. No.	Organisms	Product/ used in/ find in	References
1	*Lactobacillus acidophilus*	Fruit- based ice cream, Lactic acid production	Senanayake et al., 2013; Rossana liguori, 2015
2	*Lactobacillus sporogenes*	Egg production and quality of yolk cholesterol	Panda et al., 2008
3	*Lactobacillus plantarum*	starter culture in caper berry fermentation	Palomino et al., 2015
4	*Lactobacillus rhamnosus*	Naturally, in intestines prevent the growth of harmful bacteria	-
5	*Lactobacillus delbrueckii*	Bread	Plessas et al., 2008
6	*Lactobacillus reuteri*	Inhibit Some Food-borne Pathogens in UF-Feta-Cheese	Mohamadi Sani et al., 2005
7	*Lactobacillus fermentum*	Manufacture of traditional Iberian dry-fermented sausages	Moyano et al., 2011
8	*Lactobacillus lactis*	Buttermilk and cheese	Madigan M and Martinko J, 2005
9	*Lactobacillus brevis*	Sauerkraut and pickles	Pavlova et al., 2012
10	*Lactobacillus casei*	Dairy production and Yakult	Banks et al., 2004
11	*Lactobacillus farciminis*	Production of nitric oxide	Jean Fioramonti and Roquettes, 2007
12	*Lactobacillus paracasei*	Dairy product fermentation and probiotics.	Orlando et al., 2012
13	*Lactobacillus crispatus*	Hydrogen peroxide (H_2O_2) producing beneficial micro biota	Antonio and Hillier, 2003
14	*Bifidobacterium bifidum*	Mother milk	https://en.wikipedia.org/wiki/Bifidobacterium_bifidum
15	*Bifidobacterium infantis*	Produces an acid that kills harmful organisms	Edward, *2015*
16	*Bifidobacterium adolescentis*	Synthesizes various B vitamins	Arunachalam, 1999; Pompei et al., 2007
17	*Bifidobacterium longum*	Fresh milk tofu and pineapple juice	Phoem,2015
18	*Bifidobacterium breve*	Dietary supplements - capsules, powder, tablets	*www.danisco.com/dietarysupplements*
19	*Bifidobacterium lactis*	Inhibit the toxic effects of gliadin	Lindfors et al., 2008
20	*Bifidobacterium animalis*	Fermentation of Baltic Herring	Pavels Semjonovs et al., *2015*
21	*Streptococcus salivarius*	Chemical-ionization, Synthesis of a broth levan	Peter J. Simms, *1990*
22	*Streptococcus thermophilus*	Cheese manufacture	Daire Stokes et al., 2001
23	*Propionibacterium*	Acne treatment.	Ewa Jo nczyk-Matysiak et al., *2017*
24	*Leuconostoc mesenteroides*	Production de-glucose-1- phosphate and various sugar	Dols et al., 1997
25	*Bacillus clausii*	Detergent	Han-Seung Joo and Chung-Soon Chang, 2006
26	*Bacillus subtilis*	Plant growth and yield, Formation of antibiotic	Kilian et al., 2000.
27	*Bacillus licheniformis*	Starch liquefaction,	Jan Pen et al.,1992,
28	*Bacillus cereus*	Pasteurised milk, Chilled dairy products, Alkaline protease, Rice	Zwietering et al., 1996; Yamada et al.,1999
29	*Enterococcus mundtii*	Biopreservatives in Cheese and meat products, infant milk formulations as substrate	Zendo et.al.,2005; Botes et. al., 2008
30	*Enterococcus faecium*	Fermented milk product	Agerbaek et al.,1995
31	*Saccharomyces cerevisiae*	Folate biofortification	Daimmo et al., 2012
32	*Saccharomyces boulardii*	Lyophilized form of freeze-dried form, Dosage- 250 mg for twice a day for over 2 months child.	Marcia et al., 2009
33	*Candida pintolopesii, C. saitoana* and *S. cerevisiae*	Animal feeds as probiotic additives	Bovill et al., 2001; Leuschner et al., 2004

2. Practical Application

Use of Paraprobiotic is an advanced expected technique to overcome the human immune system problems. It triggers a more beneficial biological reaction in human system, which contributes to a healthy life by the proper production of metabolic cells. Thus, food technologists are working towards the implementation of paraprobiotics in the global marketplace by espousing various methods to improve the food habitats efficiencies. Paraprobiotics has potential application in food science and nutritional division such as dietary supplements, dairy products, etc. This review concludes that the probiotics and paraprobiotics products are able to improve the human health in better condition and it may be considered as a bio-food for imminent deficiency issues. Paraprobiotics products can also cure Immunomodulation and Inhibition of pathogens.

3. Mechanism of probiotics

Probiotic mechanisms which includes improvement of the epithelial wall, better linkage to intestinal mucosa, and hindering the pathogen adhesion, prohibiting of pathogenic microorganisms, creation of anti-microbial substances and modification in functional activity of the immune system. Probiotics microorganism used to hold intestinal mucus and epithelial cells has considered as one of the most essential assortment principles in bio food. Linkage of intestinal mucosa may avoid the removal of probiotic cells and allowing temporary colonization, immune modulation, and competitive pathogens rejection. Various different techniques used in the bond analyses of probiotics. The more cooperative tests are assessing the linkage to epithelial cell and intestinal mucus. Endogenous bacteria attached to epithelial cells and intestinal mucosa (Yuan Kun Lee and Seppo Salminen, 2009).

4. What is Paraprobiotics?

As per FAO/WHO, probiotics use live microorganism, viable, culturable, and immunologically active microorganism which gives health benefits to the human beings (Adams, 2010; Ananta and Knorr, 2009). The term 'Paraprobiotics' defined as the use of inactivated microorganism or cell fraction to confer a health benefit to the consumer (Taverniti and Guglielmetri, 2011) also referred as "*inactivated probiotics*" and "*ghost probiotics*" (Tsilingiri and Rescigno, 2013; Tsilingiri et al., 2012). The term "*postbiotics*" also proposed defined as "non-viable microbial products or metabolic byproduct from probiotic microorganism that cause biological activity in host". Therefore, "paraprobiotics" are also called as "postbiotics" (Patel and Denning, 2013). Production of paraprobiotics required inactivated microorganism, for that several methods are used. In those methods, microorganism becomes partially non-viable due to its physiological changes in microorganism. Sometime, it becomes completely non-viable because of different cell structures like DNA break, cell membrane and cell envelope damages in microorganism. This has been determined by the viability of microorganism using fluorescent dyes which show the viability, characteristics, and differentiates biological parameter like intracellular activity, cytoplasmic enzymes and integrity of the membrane. The main dye used in determination of cell viability like Carboxy fluorescein diacetate (cFDA), Fluorescein diacetate (FDA), Hydroethidine, propidium iodide (PI) and SYTO-9 (Ananta and Knorr, 2009; Doherty et al., 2010).

5. Inactivation method of microorganism

Paraprobiotics contain bacteria concentrations between 1×105 to 1×1014 per doses (Raz and Rachmilewitz, 2005). Inactivation of probiotic microorganism can be carried out by various methods are used to produce paraprobiotics product. Commercial methods like Thermal treatment (TT), (Chiu et al., 2013) High pressure processing (HPP), (Ananta and Knorr, 2009) Ultraviolet rays (UV), (Lopez, et al., 2008; Van Hoffen et al., 2010) Irradiation (I), (Kamiya et al., 2006) Sonication (S), (Shin et al., 2010) and other methods like Pulsed Electric Field (PPE), Ohmic heating, supercritical CO2, Drying, and change in pH. This method can cause destruction of the microorganism.

6. Methodology

6.1. Thermal Treatment

Most common methods for inactivation of microorganism for the production of paraprobiotics is thermal treatment. In this method, heat is applied on microorganism for a specific period. This time period varies from organism to organism according to their stability and characteristics like the type of microorganism, vegetative cell or spores, growth medium, growth stage, prior exposition, stress, pH, water activity, mode of heating etc., (Juneja and Sofos, 2002). This treatment is based on thermal resistance of microorganism, which is given by two parameters D and Z value. The D value represents the time required to reduce 90% of microbial population at a specific temperature and the Z value represents the temperature range for a reduction in the D value (Awuah et al., 2007).

In paraprobiotics, thermal treatment results in an increased the cell smoothness or roughness which result in immune modulating properties. If, high temperature is applied it results in more roughness. Researchers said that heat treatment improve or reduce the effect of paraprobiotics. The authors reported that decrease in body weight and viral load in the lungs of mice has infected by the flu virus. This has been cured by supplementing the paraprobiotics organism, i.e., *L. gasseri (*treated at 90º C for 5 min) is used for inactivation of flu virus. Other animals are treated by same paraprobiotic organism treated at 70º C for 30 min and suspended in saline solution (NaCl). More diversity in heat inactivation condition of probiotics results in production of paraprobiotics. The time and temperature vary from 5 to 60 min at 60 to 121º C at specific condition depends on the microorganism used in paraprobiotics (Kawase et al., 2012; Ou et al., 2011).

6.2. Ionizing radiation

Application of electromagnetic waves or electron is known as Ionizing radiation on probiotics for inactivation to produce paraprobiotics. The radiation sources are gamma rays emitted from radioisotopes Co60 and Cs137, high energy electron and X-rays. The amount of radiation absorbed is measured in Grays (Gy) (Farkas and Mohacsi-Farkas, 2011; Ibrahim, 2013). The 2-10 kGy refer to ionizing radiation (Farkas, 1998). Treatment up to 10 kGy is considered as safe ionizing radiation (Farkas, 2006; Mansur, et al., 2014). In this method, microorganism inactivation takes place by damaging the nucleic acids directly or indirectly. Absorption of radiation energy per target molecule takes place in direct damage, and in indirect damage interaction between reactive species formed by radiolysis of water like hydroxyl radical (Manas and Pagan, 2005). But, now a day production of paraprobiotics from ionizing radiation is banned. Because of the few drawbacks in ionizing radiation, they are over usage/over exposure of organisms in ionizing results in production of toxic biological products due to change in DNA or RNA structure. The 1,2 M rad using a cesium 137 source at 8 Gy/min for overnight is a more effective treatment of Colitis in animal (Raz and Rachmiewitz, 2005). Cobalt 60 source for 20 h at 8.05 Gy/min used to inactivate *L. reuteri* (5×109 bacteria/ml in MRS broth).

6.3. Ultraviolet rays

The UV rays are categorized under non-ionizing radiation and it has germicidal property (Lado and Yousef, 2002). Electromagnetic spectrum ranges from 200 to 400 nm are considered under UV rays. It also contains short ranges from 200 to 280 nm, medium from 280 to 320 nm and long UV waves from 320 to 400 nm. Mostly, short wave is used for inactivation of microorganism. Some of the major advantages which encountered in UV methods are applied to disinfect the air, surface, water, etc., It also inactivates the vegetative bacterial cell and spores (Gayan et al., 2013). It has minimum loss of sensory qualities without toxic effect takes place. Low energy is required as compared to other methods (Gayan et al., 2014). This method used for inactivation of microorganism by protein denaturation and production of DNA photoproduct, i.e., Pyrimidine dimer formed between adjacent pyrimidine on the same DNA strand and interrupt DNA transcription or translation may cause mutagenesis and death of cell occur (Franz et al., 2009). The production of paraprobiotics required to expose 5 to 30 min in UV.

6.4. High Hydrostatic Pressure

In this method, high pressure is applied at varying times on microorganism for inactivation. This is the anticipated new technology in the food industries for inactivation of microorganism. The HHP is employed at different ranges of pressure, i.e., 100 to 1200 MPa, but direct pressure is not applied on microorganism due to the fluid medium is getting transferred or spill out from the reactor. By direct pressure method may cause damages or demises the microorganism (Chawla, et al., 2011; Rendueles et al., 2011). Microorganism are inactivated by the homogenization process in that high pressure is applied which varies from 30 to 350 MPa. Inactivation microorganism happened by increasing the pressure and shear stress leads to rupture of microbial cell (Diels and Michiels, 2016). The pressure ranges from 20 to 180 MPa is used to reduce the microbial growth and suppress protein synthesis. At 180 MPa pressure, cell lose their viability and above 300 MPa irreversible protein denaturation takes place and inactivate the vegetative cell and bacteriophages (Lado and Yousef, 2002). Enzymes required high pressure to inactivate. Comparison between thermal inactivation and high-pressure inactivation is 60 to 75℃ for 15-300s and 400 to 600 MPa at 37 ℃ for 10 min respectively for cells of *L. rhamnosus* in phosphate buffer solution (PBS) at concentration of 109 CFU/ml. If above 400 MPa high pressure leads to lethal effect on cell (Ananta and Knorr, 2009).

6.5. Sonication

Ultrasound is used to inactivate microorganism. It is a physical method to break the intermolecular attraction. Ultrasound frequency is more than an outpost of human audition (more than 16 kHz) (Gibson et al., 2008). In this method, gas bubbles are produced in liquid media after explosion of bubbles the temperature and force is created per unit area. Inactivation depends on the nature of ultrasound wave, time, and type of microorganisms used (Butz and Tauscher, 2002). Physical and chemical change takes place because of intracellular cavity. Inactivation of microorganism takes place due to breaking of cell membrane, cell wall, DNA damage and free radical production (Birmpa, et al., 2003). In sonication, *Bifidobacterium longum* is inactivated by placing in saline solution at 108-109 CFU/ml for 5 min and reduces the cholesterol level (Shin et al., 2010).

6.6. Other methods for inactivation

6.6.1. Pulse electric field- High or low voltage is applied to the microorganism placed in between two electrodes for inactivation (Gongora et al., 2004). The electric field in between is 2 to 87 kV/cm. It is used for inactivation of enzymes, spores, yeast, gram positive vegetative cell and gram-negative bacteria (Devlieghere et al., 2004; Gongora-Nieto et al., 2002).

6.6.2. Ohmic heating- It is also known as joule heating. Heating is occurring by passing the electric current in it. Organisms have well electrical resistance property due to that it capable to produce heat within it. In this process, it reduces the entry of energy and thermal damage (Pereira and Vicentre, 2010).

6.6.3. Supercritical CO2 Technology- High concentration CO2 is used at critical temperatures and pressure. The critical temperature is 31.1℃ and pressure is 7.38 MPa. It is more profitable, because of CO2 is cheap, environmentally safe, non-toxic, and use below 20 MPa pressure (Efaq et al., 2015; Garcia et al., 2007; Yuk and Geveke, 2011).

6.6.4. Dehydration- In this process, removal of water from microorganism take place. Therefore, water activity decreases and microorganism growth is stopped. Removal of water by lyophilization, spray drying and osmosis are used. In lyophilization, the microorganism is frozen and placed in a vacuum and spray drying which results in powder form. The drying temperature used for spray dryer is 150-180 ℃ so, the decline of microorganism occurs.

6.6.5. pH-microorganism grows in specific pH it may be above or below the neutral level of microorganism. Therefore, changing the pH will result in inactivation of cells (Foerst et al., 2011; Ananta et al., 2005; Peighambardoust et al., 2011).

7. Application of Paraprobiotics

7.1. Immunomodulation

A chemical agent that modifies the immune response or the functioning of the immune system is known as immunomodulation. Immune system divided into innate and adaptive system. Innate system works with the help of white blood cells. Adaptive system works with the help of lymphocytes B and *T.* (Bermudez-Brito et al., 2012; Oelschlaeger T.M. 2010*). Paraprobiotics* act on the immune system and alter them. *L. gasseri* TMC0356 and *L. plantarum* L-137 paraprobiotics show vitro immunomodulation effect. *L. plantarum* L-137 help in stimulating the production of IL-12p40 (Miyazawa et al., 2011)

7.2. Inhibition of pathogens

Paraprobiotics protect the host against infection. Protection mechanism is direct inactivation of pathogens by the production of lactic acid, bacteriocin, etc. (Bermudez-Brito et al.,2012) *L. plantarum* b240 protect from the infection of *Salmonella enterica sarovar, Typhimurium* (Ishikawa et al., 2010) and *Ln. mesenteroides* 1RM3 protect from irruption and infection by *Listeria monocytogenes* (Nakamura et al., 2012), *L. plantarum* L-137 protected from H1N1 flu virus and *L. plantarum* 062 also (Maeda et al., 2009).

8. Additional use of Paraprobiotics

Some of the other function of paraprobiotics are Recovery of intestinal injuries, Reduction of bacterial translocation and preservation of the intestinal barrier, Treatment of diarrhea, Reducing lactose intolerance, Cholesterol reduction, Respiratory diseases, Improvement in alcohol induced liver diseases, Inhibition of growth of cancer, Treatment of atopic dermatitis, Modulation of response to visceral pain, Treatment of colitis, Suppression of some age associated manifestations, and Inhibition of dental caries. **Table 2** describes the various paraprobiotics Microorganism/Product for that the Concentration, Inactivation methods and Condition of inactivation.

Table-2

Preparation of paraprobiotics Microorganism/Product, Concentration, Inactivation methods, Condition of inactivation, and Reference List

Microorganism/ Product	Concentration	Method of inactivation	Condition of inactivation	Reference
Bifidobacterium breve Yakult (BbrY) and *Bifidobacterium bifidum* Yakult (BbiY)	--	Heat	100 º C for 30 min	Kamilya et al., 2015
Bifidobacterium longum SPM1207	10^8-10^9 CFU/ml	Sonication	Sonication for 5 min	Shin et al., 2010
Capsules containing *L. acidophilus* LB	5 billions/ capsule	Heat	_	Xiao et al., 2002
E. faecium JWS 833	--	Heat	110 º C for 15 min	Choi et al., 2012; Sawada et al., 2016
Fermented Milk containing *L. gasseri* CP2305	1×10^{10} bacterial cells per container	Heat	95 º C for 30 min	Sawada et al., 2016.
L. acidophilus (LAP5, LAF1, LAH7)	1×10^{10} CFU/ml	Heat	100 º C for 30 min	Lin et al.,2007.
Lactobacillus brevis SBC8803	1.45×10^9 CFU/mg	Heat	121 º C for 20 min	Segawa et al., 2008
L. brevis SBC8803	_	Heat	121 º C for 20 min	Ueno et al., 2011.
L. casei CRL 431	10^9 cells	Heat	80 º C for 30 min	Villena et al., 2009.
L. gasseri OLL2809	5×10^8 cell/mg	Heat	75 º C for 60 min	Sashihara et al., 2008.
L. plantarum 06CC2	_	Heat	Boil for 1 hr.	Takeda et al., 2011.
L. plantarum b240	_	Heat	121 º C for 15 min	Ishikawa et al., 2010
L. reuteri	1×10^9	irradiation heat	80 º C for 20 min., Cobalt 60 source for 20 hr. at 8.05 Gy/min	Kamiya et al., 2006.
L. rhamnosus GG	10^6,10^8, and 10^{10} CFU/ml; 10^8 CFU/L	Heat	80 º C for 20 min.	Bloise et al., 2010; Li et al., 2009.
L. lactis G50	0.5 g/Kg (w/w)	Heat	100 º C for 30 min	Kimoto-Nira et al., 2009
Leuconostoc mesenteroides 1RM3	9 log CFU/ml	Heat	100 º C for 10 min	Nakamura et al., 2012.

Skimmed milk supplemented with *L. rhamnosus* HN001	10^9 microorganism/day	Heat	100 º C for 15 min	Gill and Rutherfurd, 2001
Supplementation with *L. casei* GG	10^{10-11} CFU/g	Heat	85-100 º C for 10 min	Kaila et al., 1995
Tablets containing *L. gasseri* 0LL2809	1×10^{10} cells/tablet	Heat	75 º C for 60 min	Gotoh et al., 2009.
Yogurt containing lactic acid bacteria (*L. bulgaricus, S. thermophilus, L. acidophilus*) (Mix-LAB)	1×10^7, 1×10^8 and 1×10^9 cells/ml	Heat	65 º C for 60 min	Zeng et al., 2015.

9. Conclusion

Evidence show in this review paraprobiotics acts as probiotics but, mechanism of action is different and give health benefit to human being, cannot cause infection and harmful diseases to the body. It also gives the nutrition to the body. It secretes various enzymes and acids, which is involved in metabolic reaction and it also decreases the deficiency of vitamins and minerals. The production of paraprobiotic product is cheap and easy. In paraprobiotics, modified microorganism is used. The improvement of paraprobiotics as constituents and their application in food and beverages is important. At the time of processing probiotics are not survive but paraprobiotics are survive.

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