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The realm of probiotics: An overview

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Abstract
Probiotics are living bacterial colonies that are incredibly beneficial to human health and are available from various sources. The sources of these probiotics were initially assumed to be of dairy origin, but various studies have elucidated the possibilities of isolation from various sources beyond that. Recent research has shown that probiotics can be isolated from unconventional sources like non dairy food wastes, which could decrease the global food waste rate, promote valorisation, and minimizes dairy consumption in lactose-intolerant individuals. This kind of probiotic generation would be much more beneficial and embraced when the government explicates stringent regulatory measures to illuminate its safety, efficacy and viability to encounter the pseudo-probiotic generation in the commercial market. The realm of probiotics has been deeply researched and has led to various advancements like pharmabiotics, postbiotics and even next-generation probiotics. The appropriate selection of probiotics and their effective delivery still remains a technological challenge. The aim of this current review is to summarize the magnitude and strategies used throughout the recent advancements in probiotics' revolution in the food and health sector.

Keywords: Postbiotic, pharmabiotic, next-generation probiotic, valorisation

Introduction

The term "probiotics" has been widely used for more than 25 years, Probiotic was coined as an opposition to the term "antibiotic". It is derived from the Greek word pro and biotos and translated as for 'life' [1]. There was a proliferation of probiotic definitions in the late 1980s and early 1990s. (Table.1) contains some of these definitions. Although all of the cited authors agreed that probiotics include live microorganisms [2]. According to the guidelines of the Food and Agriculture Organization of the United Nations/World Health Organization (FAO/WHO) endorsed by the International Scientific Association for Probiotics and Prebiotics defines probiotics as "live microorganisms that, when administered in appropriate proportions, confer a health benefit on the host" [3]. To provide benefits to the host, a probiotic strain should include the following vital properties: (a) Probiotics must benefit the host through their growth in the human body. However the specificity of the action is important, not the source of the microorganism. Indeed, it is very difficult to confirm the source of a microorganism, (b) lacking in the putative virulence genes, (c) sensitive to common antibiotics, (d) gastro intestinal (GI) tolerant, (e) catalase-negative, (f) capacity to bind to the epithelial membrane of the intestine, (g) able to compete with native gut microbiota, (h) non toxic and non pathogenic, (i) capable of inhibiting the growth and colonization of potentially dangerous microorganisms directly or indirectly, (j) To improve feed digestibility and to reduce metabolic disorders, (k) They must be safe, acid and bile tolerant [3, 16-20, 31].

Probiotic research has quickly grown up, with over 32,000 articles being published between 2002 to 2021. Proving the health benefits of probiotics such as improving gut health and experiencing various health benefits after consuming, is quite challenging. As a result, governments from different countries have taken several regulatory approaches based on the guidelines from their accrediting body to elucidate various probiotic-containing foods that was mentioned briefly in (Table.3).

Probiotic was first recorded in fermented milk where probiotics from the *Bifidobacterium* and *Lactobacillus* genera were among the first to be included in the various food products because they are Generally Recognized as Safe (GRAS) and can provide various general health benefits like supporting a healthy GI tract and boosting the immune system when administered in adequate concentration in an individual [3, 16, 28]. Probiotics are appropriate even for infants and children especially *Lactobacilli* because several investigations have illustrated that products containing *Lactobacilli* and *Bifidobacteria* are well tolerated in this age profile.

Table 1: Some of the frequently mentioned probiotic descriptions cited over the year

Year	Definition	Reference
1953	Probiotics, as well as vitamins, aromatic compounds, enzymes, and perhaps other substances involved in important activities, are commonly found in vegetable foods.	[1]
1954	Probiotics are opposite of antibiotics	[1]
1955	Antibiotic side effects can be prevented with probiotic therapy.	[1]
1965	A substance produced by one microorganism that encourages the growth of another.	[7]
1972	Tissue extracts which encourages the microbial growth	[7]
1973	Compounds that increase the host's resistance to infection while not inhibiting the development of microorganisms *in vitro*	[9]
1974	Organisms and substances that contribute to the microbial balance in the intestine	[9]
1992	Live microbial feed supplement that has a positive impact on the host animal by establishing microbial balance.	[11]
1992	Viable mono- or mixed cultures of living microorganisms that, when given to animals or humans, improve the qualities of the host's indigenous microflora.	[12]
1996	A live microbial culture or a cultured dairy product that has a positive impact on the host's health and nutrition.	[13]
1996	Microorganisms that, when consumed in sufficient quantities, provide health advantages beyond those provided by natural diet.	[13]
1999	Microbial cell preparations or components of microbial cells have a positive impact on the host's health and well-being	[2]
2001	A preparation or product containing sufficient numbers of viable, specified microorganisms that affect the microflora via implantation or colonization in a compartment of the host and hence have a good health effect on the host	[15]
2002	Live microorganisms that provide a health advantage to the host when given in sufficient amounts.	[3]

Acceptable Daily Intake of Probiotics (ADI)

The amount of viable cells in probiotics is usually measured in colony forming units (CFU). Many probiotic supplements that are commercially available in the market contain between 1 to 10 billion CFU per dose, but some products have up to 50 billion CFU or more. Higher CFU counts, on the other hand, do not always imply that the product is highly nutritious [30]. Probiotics do not have any specific Acceptable Daily Intake (ADI), but they must be ingested in adequate levels under medical supervision to gain their intended health effects. Considering the fact that a majority of existing clinical trials show that probiotic doses of 10-20 billion CFU per day are sufficient for immunological and digestive health, research studies evaluating the dose-response of greater CFUs and products with CFUs of 50 to 100 billion are becoming more prevalent [37, 38]. As per Natural Health Products Directorate (NHPD) and Health Canada, oral administration with no less than 10^6 CFU/g and no more than 10^{11} CFU/g (no less than 1 mg and no more than 1 gram/dose) is advised. This amount of use is consistent with dietary exposure and with the safety recognition by regulatory bodies in Japan, Europe, and Canada recognizing its safety [49]. It is also essential to remember that the effects of different probiotics might vary greatly from person to person owing to many other factors. As a result, different CFU doses of probiotics may be highly beneficial for different persons based on their health condition [29].

Route of Administration: Oral administration is the most common method of administration.

Method of preparation: Live microorganism [39]

Storage condition: Other than capsules and sachets, probiotic drinks should be stored in a tightly closed, light-resistant container in the refrigerator [42, 43].

The acceptable pharmaceutical dosage forms are limited to chewables, emulsion/suspension, powders and solution/liquid preparations [39, 41]. Many countries have many regulations on probiotics which were given in (Table 3).

The following equation was used to calculate the acceptable daily intake (ADI) for adults and children:

ADI = NOEL/Safety factor

Adults: ADI = $2.67 \times 10^{13}/100$, which is equal to 2.67×10^{11} CFU/day

Children: ADI = $2.67 \times 10^{13}/1000$, which is equal to 2.67×10^{10} CFU/day

No-observed-effect level (NOEL) was calculated from the cytotoxicity studies conducted, a reasonable and conservative safety factor or margin of safety (MOS) of 100 was used for adults and 1000 for children and the NOEL is equivalent to 2.67×10^{13} CFU.

Unconventional Sources of Probiotics

To comprehend the growing demand for health supplements, probiotics are being employed in the form of capsules, drinks, yogurt, and other products. Many studies are focusing on Lactic Acid Bacteria (LAB) isolation from fermented dairy milk products, meals, fruits, vegetables, animals, and feces of breast-fed newborns, among other sources [32-36]. *Lactobacilli* are naturally present in dairy products such as cheeses, yogurts, fermented milks, and raw milk, and it is also present in non dairy source of food products such as fruits, vegetables etc, which can be taken as a supplement to benefit the consumer's health. Probiotics are increasingly being used for human and animal health. Human probiotics are often obtained from dairy foods, however animal probiotics are frequently obtained from the animals' own digestive tracts. People who are lactose intolerant are increasingly choosing probiotics from sources other than milk products. Non-dairy fermented foods and beverages such as fresh fruits and vegetables, food wastes, breast-fed newborn feces, and human breast milk, are some of these unconventional sources of probiotic. Probiotic microorganisms can also be screened from non-intestinal sources, such as from grains, fruit juice, food processing waste could benefit the whole environment in turning the waste product to wealth in many ways and it is also cost effective [52]. Probiotic generation from the non-dairy food waste benefits the environment in many ways, waste product utilization is called valorization hence the valorization of waste food products for probiotic production is highly appreciable. The use of probiotics from "unconventional sources," as opposed to "conventional ones," is likely to grow. One of the reasons why alternate probiotic sources have become more popular is to minimize dairy consumption in lactose-intolerant people [56]. PCR-based techniques, 16S rRNA sequencing, and DNA fingerprinting techniques such as ribotyping and Pulsed Field Gel Electrophoresis (PFGE) are currently employed for identification [55]. Probiotic strains currently in use should be placed in an internationally recognised culture collection/repository. (Table 2) shows the isolation of *Lactobacilli* from various unconventional sources, as well as their proposed action in our bodies [44].

Table 2: Isolation of probiotics from different sources

Sources of probiotics and Media	Strains isolated and their health properties	References
Kefir grains	*Lactococcus lactis* strain DPC3147, isolated from kefir grains, developed a bacteriocin (lacticin 3147) with antibacterial activity against *Escherichia coli, Listeria monocytogenes, Salmonella typhimurium,* and *Salmonella enteritidis* and that can be successfully used in the treatment of vaginal infections. The enzyme β-galactosidase is found naturally in kefir grains that helps to reduce lactose levels and hence it is used in the treatment of lactose intolerance in a specific population.	[45]
Human Stool culture (MRS agar)	*L. plantarum* E2C2 and *L. plantarum* E2C5 obtained from the healthy human stool samples. These probiotics obtained from the sample have many potentials in managing the specific metabolic disorders such as hyperoxaluria.	[46]
Papaya juice (MRS agar)	*L. acidophilus* and *L. plantarum* is found as probiotic in papaya pulp which is used for vegetarians or consumers who are allergic to lactose present in probiotic dairy products	[47]
Banana, apple, and grape (MRS agar)	*L. plantarum* and *L. mesenteroides have great* potential to be used in therapeutics and as food biopreservatives obtained from the fruit source which has various health benefits towards consumers.	[48]
Pineapple waste (MRS broth)	After bananas, pineapple is the second most consumed and produced fruit, accounting for more than 20% of global tropical fruit production. Pineapple waste is made up of leftover pulp, peels, and skin from the pineapple processing industry. For the manufacturing of lactic acid bacteria, pineapple waste is used as a carbon source. *Lactobacillus* usage in probiotic manufacturing has been increasing rapidly. This type of waste-based probiotic production would be ideal in terms of both economic and environmental impact. This bacteria maintains gut health.	[50]
Soybean waste (MRS broth)	*Lactobacillus* isolated from solid waste produced in soy milk production could be used as a starter for the manufacturing of functional meals manufactured from soybeans. Lactic Acid Bacteria isolated from solid waste of soybean milk production were all *Lactobacillus* with the *plantarum* strain being the most common. Soy milk is one of the most popular functional foods, especially among lactose-intolerant individuals.	[51]
Sugarcane bagasse (MRS media)	*Lactococcus lactis produces* 10.85 g/L lactic acid. Sugarcane bagasse, a byproduct of the sugar production industry used as preservative in food, pharmaceutical applications etc.	[52]
Non-dairy, non-fermented beverages and foods such as fresh fruits, vegetables and the feces of breast-fed infants. (MRS agar)	Many potential probiotics were isolated from a variety of sources, including non-intestinal sources and non-dairy fermented food products, such as traditional fermented foods, fermented drinks, vegetables, and fruit juices *L. plantarum* isolated from fermented idli batter and many *Lactobacillus, Pediococcus* and *Lactococcus* species were obtained but were primarily *Lactobacillus* species.	[52]
Turmeric residue, simple medium supplemented with the inexpensive nitrogen source through SSCF.	*Lactobacillus paracasei* produced 97.13 g/L lactic acid from turmeric waste during curcuminoid production. This low-cost l- and d-lactic acid synthesis based on renewable biomass has a lot of industrial potential. As a result, there has recently been a lot of interest in producing lactic acid from low-cost, renewable biomass resources, with high lactic acid concentration, yield, and productivity.	[53]
Chili stalks (MRS Agar)	Chili stalks which are considered as waste products could be used to extract a probiotic that is used in lactose fermentation, which acts as a source of non-dairy lactic acid bacteria production. This type of probiotic source would bring a revolution in the field which serves as a low-cost, eco-friendly, considered as agricultural leftover, readily available non-dairy starter as well as a good source of probiotics, making it an desirable product considering its multiple health benefits and suitable for lactose intolerant individuals.	[54]

Next-generation probiotic

Monostrain and multistrain/multispecies probiotics are the two types of probiotics available. Due to the symbiosis among strains, multiple studies have demonstrated good health effects when multistrain probiotics are administered [57]. They have been shown to decrease pathogen growth and atopic dermatitis, suggesting that they could be used to treat other disorders such as Inflammatory bowel disease (IBD). Ecologic® Tolerance/Syngut™ is another multispecies probiotic that was created utilizing four different probiotic strains (*Bifidobacterium lactis* W51, *L. acidophilus* W22, *L. plantarum* W21, and *Lactococcus lactis* W19). This consortium's strains have been shown to improve gut barrier function, reduce post-immunological induced stress, decrease Th2, and increase IL-10 levels, all of which are useful in patients with food intolerance [58]. Multispecies probiotics also decreased high sensitivity C-reactive protein (hs-CRP) and increased plasma glutathione (GSH) in diabetic patients [59, 60]. They manipulate the intestinal flora with multispecies probiotics that reduce bacterial translocation, morbidity, and mortality in a rat model of acute pancreatitis.

Next-generation probiotics, which include members from *Clostridium* clusters IV, XIVa and XVIII, *F. prausnitzii*, *Akkermansia muciniphila*, *Bacteroides uniformis*, *Bacteroides fragilis*, and *Eubacterium hallii* [61-64]. Preclinical trials of these next-generation probiotics found positive results for inflammatory and metabolic illnesses [61, 65]. New methodologies are also required for the production of new probiotic products utilizing human-derived microorganisms. This means that these strains must come from the major groups of the gut microbiota, be identified as safe, and have potential positive effects demonstrated. For example, *Faecalibacterium prausnitzii* is a *Clostridium* cluster IV extreme oxygen sensitive (EOS) bacterium that accounts for 3–5% of total fecal bacteria and is one of the most common groups in human feces [79, 80]. Because *F. prausnitzii* strains have been shown to have anti-inflammatory capabilities, they can be investigated in mouse models to see if they have any therapeutic benefits before moving on to human trials. A successful alternate technique for the treatment of CDI is fecal microbiota transplant (FMT) or fecal bacteriotherapy. When other antibiotic treatments fail, FMT can resolve both CDI and rCDI [67], with a success rate of 90% [68, 69]. FMT is now being evaluated as a viable treatment for ulcerative colitis [70], irritable bowel syndrome [71], and metabolic syndrome [72] due to its efficacy. Some patients do not respond to FMT, due to the fact that only specific bacterial phylotypes can be therapeutic when transported properly [73]. As a result, the efficacy of FMT in the treatment of gastrointestinal problems remains controversial [74]. Nausea, vomiting, fever, stomach pain, and diarrhea are some of the side effects of FMT [73, 75]. There is a scarcity of data on the long-term effects of FMT. FMT can cause disease by passing undetected or unmonitored risk factors such as viruses, bacteria, or even allergies to the FMT recipient. To solve this problem, researchers created a synthetic bacteria cocktail with a well-defined natural history to replace FMT [76]. To replace FMT, other microbiome therapies of chosen fecal bacteria could be created [77]. For example, a stool substitute made up of 33 pure intestinal bacteria taken from a healthy donor and used in the treatment [78]. As a result, the term "RePOOPulate" was coined to describe the gut microbiome. Studies recommended that replacing FMT with "RePOOPulate" could be effective to treat rCDI. Additional validation is needed for this infection to be completely resolved with this technique. There are several advantages by using this synthetic stool substitute. The synthetic bacterial cocktail's assembly is highly repeatable, allowing for standardization and upscaling. Furthermore, because the bacterial mixture can be rendered pathogen and virus-free, patient safety can be ensured [78]. These findings show that multispecies communities, like the one used in the RePOOPulate study, are more efficient than single-strain or mixed cultures of probiotic bacteria but these new generation probiotic should accomplish several requisites including safety requirements and well established beneficial effects on the host before being considered as probiotics.

Moreover, RePOOPulate consists of a more phylogenetically diverse community including strains with more beneficial health effects that can be the candidates for next generation probiotics. The composition of Stool Substitute (RePOOPulate) includes the following strains of probiotic: A*cidaminococcus intestinalis, Bacteroides ovatus, Bifidobacterium adolescentis* (two different strains), *Bifidobacterium longum* (two different strains), *Blautia producta, Clostridium cocleatum, Collinsella aerofaciens, Dorea longicatena* (two different strains), E*scherichia coli, Eubacterium desmolans, Eubacterium eligens, Eubacterium limosum, Eubacterium rectale* (four different strains), *Eubacterium ventriosum, Faecalibacterium prausnitzii, Lachnospira pectinoshiza, Lactobacillus casei/paracasei, Lactobacillus casei, Parabacteroides distasonis, Raoultella sp, Roseburia faecalis, Roseburia intestinalis, Ruminococcus torques* (two different strains), *Ruminococcus obeum* (two different strains), *Streptococcus mitis.*

Regulatory challenges

Regulatory statements and challenges may vary in different countries. The FDA should approve the product that is Generally Recognized as Safe (GRAS) in the United States. In the United States, however, if a probiotic is used as a dietary supplement, it is considered as "food" and should be regulated under the Dietary Supplement Health and Education Act (DSHEA). If the probiotic was thought to have a therapeutic purpose, the FDA would have to verify that the probiotic medicine was safe and effective before it could be licensed. According to the Japanese regulations, probiotic products fall into different categories of foods and Foods for Specific Health Uses (FOSHU). Efficacy claims for probiotic products are not allowed on the label until the product has received clearance from the Ministry of Health and Welfare (MHLW) to be classified as FOSHU, which requires efficacy and safety validation [96]. The term probiotics is being misused by producers who market products that do not have beneficial properties. Bacterial products that do not give any beneficial results are called pseudo-probiotic products [97]. These pseudo probiotic foods are the outcome of the umbrella concept, where a potential probiotic species is utilized in numerous formulations as a minor ingredient, but the product is marketed on that species despite its small contribution. Manufacturers seek the advantages of this concept and push the results of probiotic products to manufacture other less potential products. This compromises the market of the actual product because pseudo probiotic products have similar specifications but limited or no efficacy, blurring the consumer's vision due to the unregulated nature of the probiotic market. This leads to health issues and many other problems and questions in terms of quality [98]. Consumption of multispecies probiotics was linked to an increase in mortality in patients with severe and acute pancreatitis [99]. Because a probiotic treatment involves its direct consumption, there are two primary safety issues linked with them. The first step is to determine whether mono or multi-strain probiotics have any negative effects on consumer health [100]. Second, during the creation of the probiotic, a high standard of quality must be maintained to ensure that it is free of contamination and that the correct strain composition is maintained [101]. Along with the live bacteria, some dead bacteria and their fragments form during the synthesis of probiotics, which are inseparable, but they are low and normally avoided during safety inspections. The details of these dead microorganisms are not stated on the product labels, and the producers completely ignore them. As a result, clinicians are unaware of these "hidden elements" and may ignore the product's true effectiveness [102].

Table 3: Comparison of probiotic regulations between different countries and regions

Country/region	Accrediting body	Regulation	References
United States	U.S. Food & Drug Administration (FDA)	Depending on the intended usage of the product, it is classified as dietary supplements, foods, or drugs. Because of their classification, probiotic foods are subject to additional requirements. If a probiotic is used as a dietary supplement, it is considered as "food" and regulated under the Dietary Supplement Health and Education Act (DSHEA)	[22]
European Union	European Food Safety Authority (EFSA)	Probiotics are categorized as health claims under Regulation No. 1924/2006, implying health benefits when consumed. Europe implemented a regulatory commission on functional food science in Europe (FUFOSE).	[23]

		EFSA adopted Qualified Presumption of Safety (QPS) to ensure the premarket safety assessment of foods and food supplements.	
Canada	Health Canada	Validating health claims on strain-specific evidence, clear and specific statements on probiotic benefits, and the documentation on the strain added to food product	[21]
Brazil	Agência Nacional de Vigilância Sanitária - Brazilian Health Regulatory Agency (ANVISA).	In Brazil the strains are approved on a case-by-case basis, based on Resolution No 18/1999, and they must demonstrate their safety, efficacy and the health advantages.	[29]
Asia-Pacific	Ministry of Health, Labor and Welfare (Japan) and State Administration for Public Regulation (China)	Food items containing probiotics in Japan are required to include health claims such as enhancing Gastro intestinal (GI) health and other health benefits when consumed in adequate quantities. Japan acts as a global market leader, where probiotics are considered as both foods and drugs. According to the Japanese regulations, probiotic products fall into different categories of foods and Foods for Specific Health Uses (FOSHU)	[26]
Australia/New Zealand	Food Standards Australia and New Zealand (FSANZ)	Probiotic-containing products are evaluated on a case-by-case basis in accordance with the Standards 1.2.7 rule. Composition, safety, health claim, and history of use in other countries are all required for risk evaluation.	[25]
India	Indian Council of Medical Research (ICMR)	Probiotics have strain-specific effects. It's essential to know a strain's identity in order to link it to a specific health effect and to conduct proper surveillance and epidemiological investigations.	[27]
Malaysia	Food Safety and Quality Division (FSQD), The Drug Control Authority, NPCB and the Committee for the Classification of Food-Drug Interface Products	The regulatory bodies that enforce regulations on food and drugs are (FSQD), The Drug Control Authority, The National Pharmaceutical Control Bureau (NPCB). Malaysian regulations are based on CODEX and have complicated regulatory requirements for functional foods; however, currently there are no distinct guidelines for the probiotic category.	[30]

(Table. 3) shows the regulations that are followed in different countries to prevent the development of pseudo probiotics. On the other hand, medical physicians typically prescribe brands as per their names, where there will be high risk in developing these kinds of pseudo probiotics. Probiotics are not acceptable for their pharmaceutical names, and the trademark rules for manufacturing these items are beyond our control. The terms used by US patent and trademark offices do not need a trademark for a specific probiotic preparation, therefore a single trademark can cover a variety of products. This allows the possibility of selling a new probiotic product without any proper testing and marketed under a well-known brand. Any changes in the composition of a probiotic must be noted on the label, as required by law, so that consumers and clinicians may make better decisions on consuming the product [106]. The selection of probiotics and their effective delivery remains a technological challenge in sustaining the viability of the probiotic culture in the formulated product where microencapsulation is believed to be the solution [108].

Recent development in probiotic - pharmabiotic

The term "probiotic" had devolved into a marketing tool rather than a scientific descriptor. Finally, experts landed on the word 'pharmabiotic,' which refers to human-derived bacterial cells or the products that should have a pharmacological impact in health or disease. Pharmabiotics, or probiotics as pharmaceuticals having general health claims must include probiotic microorganisms that provide a general or specific health claim against various diseases. For eg; bacteriocins are used as pharmabiotics in case of incorporating a potent bacteriocin produced by strains of *Lactococcus lactis* into the teat seals that were effective in preventing mastitis in dairy cattle [107]. Pharmabiotics should be beneficial and safe for internal use. The only requirement for safety is that these strands must be genetically identified and must meet safety standards of the regulatory authority before use [105]. The APC Microbiome Ireland SFI Research Center, founded as the Alimentary Pharmabiotic Center (APC) is a research center working on the human microbiome for developing more pharmabiotics that benefits human health [107].

Many synthetic microbial communities intended for transplantation are developed that should be able to meet manufacturing, mode of action, and safety requirements [81, 82]. For example, Seres Health developed SER-109, a new biological agent that promotes resistance to pathogenic invaders like C. difficile by restoring the equilibrium in the gut microbiome [83]. Seres health also developed SER-287 for the treatment of IBD (Inflammatory Bowel Disease) and in specific ulcerative colitis [84]. RBX2660, a mix of live human microorganisms produced by Rebiotix, is a commercially available treatment for recurrent CDI [85]. In addition, new formulations containing *Clostridia* classes IV and XIVa strains were created to control the immune response. Vedanta Biosciences, Johnson and Johnson produced the first community of 17 strains (VE202), which has proven to be an effective therapeutic for auto-immune disorder [86-89]. On the other hand, non-dairy sources of probiotics made from food waste are emerging gradually. Every year, over one-third of the food produced for human use, roughly 1.3 billion tonnes, is lost or discarded. Globally food waste is estimated to be around 30% for cereals, 40-50% for root crops, fruits, and vegetables, 20% for oilseeds, meat, and dairy, and 30% for fish globally each year. Waste product utilization is called valorization, hence the valorization of waste food products for probiotic production along with elucidating the efficacy and safety standards is embraced.

Postbiotic - A revolution in probiotic

Postbiotics are bioactive compounds produced when probiotics, the beneficial bacteria in your gut, feed on prebiotic foods in your colon, such as fibers [90]. Despite the fact that these bioactive compounds are probiotic bacteria's waste products, they have a variety of health benefits for your body. This is because many of the health advantages linked with prebiotics and probiotics actually come from the production of postbiotics. Prebiotics and probiotics are combined in synbiotics. Postbiotics are not considered synbiotics and they do not contain any live microorganisms, they have similar mechanism and similar effectiveness like probiotics. In the case of postbiotics, the issue of dose standardization, which is a significant challenge in the creation of probiotics, does not exist in the postbiotic. In comparison to probiotics, postbiotics have a longer shelf life, are easier to store and transport, and have a lower requirement for maintaining a low temperature. In modern medicine, postbiotics are an appealing therapeutic and preventive technique. Such postbiotics, according to current evidence, exhibit pleiotropic effects, including immunomodulatory, anti-inflammatory, antioxidant, and anti-cancer capabilities etc. Some of these properties are in clinical use. Other developing health advantages have been linked to postbiotics, but more research is needed to determine the scope of these effects:

Allergies may be alleviated: According to research, 34 adolescents with the disorder supplementing with a postbiotic for 8–12 weeks dramatically reduced the severity of atopic dermatitis (eczema). The placebo group, on the other hand, showed no improvement [91].

Weight loss may be aided: A few studies suggest that postbiotics, such as short-chain fatty acids, can help people lose weight by decreasing hunger signals [92, 93]. It's possible that it can help reduce the risk of heart disease. Butyrate appears to help decrease blood pressure and repress genes involved in cholesterol synthesis in animal studies. Many developments are sprouted in the field of postbiotics, but describing its efficacy and safety is quite challenging [94, 95]. Though these probiotics or postbiotics are not categorized as drugs, they do provide various human health advantages and can also help with major pathological disorders like IBD and hepatic encephalopathy. There is a lack of safety and legal protection for the genuine manufacturers whose goals are to classify, evaluate, and standardize the various novel probiotics utilizing the most up-to-date research and development methods in the absence of legal guidelines [106].

Conclusion

Currently postbiotic, pharmabiotic, next-generation probiotic, non dairy sources of probiotic have been emerging which are safe for the majority of the population, however negative effects can arise in some circumstances. As a result, more stringent controls in determining the safety, efficacy, development and distribution of medically useful probiotics are required. Specifically, valorization of food waste especially from the non dairy source for the production of probiotics is highly recommended because they are eco friendly, easily available, cost effective, highly preferable by vegans, and suitable for lactose intolerant individuals. This kind of probiotic production from the discarded food product could reduce global food waste and would be highly encouraged bringing probiotics' future prospects to the next level.

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