



Production, Cost Analysis, and Marketing of Probiotics

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Abstract

A significant focus has been given to understanding the probiotic manufacturing process at a commercial scale with different production settings, and a thorough evaluation of probiotic-product performance as well as a benefit-cost analysis is needed for the coveted future marketing. This notion is gaining the acceptance among the customers as food-makers become more commending about designing foods that create consumers' awareness in association with health, nutrition, and diet, as well as add value to food via inclusion of desirable ingredients. Probiotic products are the important topics in the functional foods all over the world, and researchers are striving hard to improve dairy products that include beneficial probiotic organisms. Such probiotic products may alter composition of microorganism in the gut, enhanced gut health. People can tolerate the milk proteins (casein) and regulate their cholesterol intake exponentially by using these probiotics. A large quantity of living microorganisms are likely to be required in the food product, which should be ingested on a regular basis to gain the benefits. All over the world, the probiotic business, especially, the dairy products yogurt and fermented milks have escalated. Many factors are responsible to fulfill consumers' expectation such as sound and scientifically proven health-promoting outcomes, accurate product information, and effective marketing strategies. Since the probiotics have demonstrated long-term success as health promoters both in human and animal health. This is to be applauded for the decision to formulate an

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effective probiotic product as the high numbers of viable organisms will be required at the time of intake. Despite the several health benefits of probiotics, research is underway by which the culture utilizes their effects is still at the earlier stage. Therefore, continuing scientific efforts have targeted to understand health-promoting effects of probiotic cultures in the cellular level as a critical obligation for ensuring probiotics' future as a functional dietary supplement. In the upcoming days, the global market for purposeful foods is anticipated to be increased considerably. Therefore, the aims of this exploration were to delve the production-processing considerations and alternate cost variables for probiotic production including all-inclusive benefit-cost analysis in global perspectives. Additionally, these insights have focused on how to gain money from microbes and probiotic marketing status as well as ensure a food microbiology-based entrepreneurship in probiotic domain.

Keywords

Probiotic · Manufacturing · Food makers · Ingredients · Global market · Microorganisms · Probiotic products · Entrepreneurship

1 Introduction

Based on the type of products, probiotics can be classified into dietary supplements, probiotics drinks, and drugs, including animal/livestock foods/feeds. Probiotic food is again sub-classified into breakfast/bakery, yogurt, infant formula, and baby food cereals including other probiotic foods. Moreover, the probiotic drinks are sub-segmented into dairy-based probiotic drinks and fruit-based probiotic drinks (Modor Intelligence, 2022).

In every step of probiotic production, process is dependent on the one before it; thus, this is challenging to determine the species and/strains which are dependent to sensitivity. Because of the cut-down method for producing cells at experiment, development work is intrinsically more closely regulated and each phase in the process has shorter pause durations, and thus, scaling up can be complicated over the times. Commercial centrifugation of cells from the spent media could require hours of time due to the large volume of cells versus minutes at lab-scale as the smaller volumes involved. These results reflect at different stresses in generally heat and absolute stress condition than those experienced at upright lab-scale centrifuge (Crittenden, 2009). In addition, there are a number of stages relating to the commercial production that are not usually involved in bench-scale production. Also, throughout commercial manufacturing, cells are likely to be exposed to a variety of pH and temperature conditions that are difficult to replicate at the lab-scale. As a result, this is critical to scale up to an intermediate level in trial to evaluate and optimize the typical production environments, and to mitigate the challenges before moving to commercial operations. The scaling up from trial to commercial basis can be difficult for the same grounds as scaling up from lab scale to pilot scale which needs further trials for commercial applications (Kurt et al., 2019). In livestock

production, cost benefit analysis would be streamlined to substantiate the usage of probiotics and the profitability at the production level to end of experimental trails. All cost items which included chicks, feed, vaccine, electricity, and casual labor were taken into consideration when estimating the total cost of production. Besides, the expense of trial ingredients was also included to the treated groups. The base cost (cost/bird) and also cost/kg live weight basis were used to calculate the cost benefit estimation (Ray et al., 2019).

In this moment, assurance of a probiotic impact, including the development of foodstuffs which contained large numbers of living organisms, needs to be explored and involved with the formation of effective probiotic items. Notwithstanding the fact that probiotics are connected with a variety of health benefits, research onto the progressions by which this culture work is still in its initial stages. As a result, persistent scientific efforts targeted to the health-promoting effects of probiotic cultures at the cellular level should be investigated as an impotent necessity to confirm probiotics' future as functional food additives (Catherine et al., 2001).

Food manufacturers will be continuing to develop new diets, resulting in more food ingredients being linked to health claims. In the near future, sport-related items, fortified foods and drinks, and dairy products, for example, yogurts, cheese, ice cream, and milks containing prebiotics and probiotics are all likely to be incorporated. Although the market for the functional ingredients is favorable, scientific validation is essential for future expansion as well profitability issues. In present time, since most of antimicrobials are found to be ineffective globally, thus, antimicrobial resistance (AMR) is escalating at an alarming rate as Neu (1994), which have serious impact on health and overall development throughout the world. Therefore, multisectoral actions are to be needed to obtain the Sustainable Development Goals (SDGs) (WHO, 2021). Given the situation, very high concern about antibiotic uses (AMU) use and antimicrobial resistance (AMR), therefore, alternative options for pathogen suppression, such as probiotics and prebiotic including organic acids, herbal product, are becoming more demanding. The World Health Organization (WHO) advocates to increasing efforts towards prevention of disease by enhancing immunization with vaccination including global initiatives to lessen the use of antibiotics in food animal production (Kabir, 2009; Kamruzzaman et al., 2005) including human health perspectives.

Probiotics have also been recommended as an alternative to antibiotics in livestock (Canganella et al., 1996; Fuller, 1986; Gardiner et al., 1999; Underdahl et al., 1982) and poultry productions (Arif et al., 2021; Edens et al., 1997; Gardiner et al., 1999; Islam et al., 2014).

2 Historical Aspects

Historically, usually the fermented foods are connected with the exploration and understanding of probiotics or useful microbial agents, and it is thought that we are using the probiotics since the first edible stuff experienced from the fermentation process. The International Scientific Association for Probiotics and Prebiotics

(ISAPP) gave the definition of a fermented food as “foods made through desired microbial growth and enzymatic conversions of food components” (Marco et al., 2021). The fermented food items like beer, kefir, cheese, wine, and bread have a long the past, and their usage can be carried back to hundreds of years, even earlier to Egyptian and Middle-Eastern civilization.

Numerous preliminary approaches of treatment, such as bacterial interference, serum therapy, and the activation of macrophages to kill germs, may be worth to reconsidering (Bengmark, 1998). In this regard, several probiotic strains have been demonstrated to reduce the growth of enteropathogens such as *Salmonella enteritidis*, enterotoxigenic *Escherichia coli*, and *Serratia marcescens* (Gonzalez et al., 1993; Drago et al., 1997) and may have therapeutic potential in vitro. The recent data indicate that *Lactobacillus* GG has antagonistic activity against *Salmonella typhimurium* C5 infection both in vitro and in vivo (Hudault et al., 1997), which makes the groundwork for the clinical application of probiotics through pathogen suppression. Also, probiotics’ immunostimulatory characteristics (Marteau & Rambaud, 1993) have likely to increase the host’s resistance to disease, potentially reducing the need for antibiotics. In addition to their role in human health maintenance, new evidence suggests that some probiotic strains, particularly *Lactobacillus* strains, may protect the urogenital tract from microbial infections, and that probiotic microorganisms can reduce the risk of infections associated with the use of medical devices (Reid et al., 1994, 1995, 1998).

Table 1 represents the time-line summary on the discovery of probiotics which gives a primary understanding of the idea of probiotics, prebiotics, paraprobiotics, postbiotics, and synbiotics that evolved in 1905 and continuing its advancement as of date (Cuevas-González et al., 2020; Hill et al., 2014; Lee & O’Sullivan, 2010; Lilly & Stillwell, 1965; Mackowiak, 2013). However, robust efforts are ongoing for development of new probiotics considering benefits both in human and animal health.

In most recent years, the probiotics have been documented as multifaceted benefits as functional ingredients, such as anticancerous (Górska et al., 2019; He et al., 2019; Mendoza, 2019), prophylactic and antigenotoxic, (Chandel et al., 2019), antioxidative (Mishra et al., 2015), anti-inflammatory (Plaza-Díaz et al., 2017; Posocco et al., 2018), antiosteoporotic (Lee & Kim, 2020), antihypertensive (Rai et al., 2017), and antidiabetic prospects (Wang, Bai, et al., 2020; Wang, Shang, et al., 2020). There is unanimous consensus on the positive impact of probiotics on psychological state of the well-being via alteration of sleep, cognitive reactions, and mental condition (Marotta et al., 2019).

3 Production and Processing

3.1 Detection of Strains

Strain identification is the first pivotal step in the probiotics production process. The strain selection exclusively be influenced by the objectives for producing a particular probiotics supplement which have significant health claims. When you intend to

Table 1 Time line for successful development of probiotics, prebiotics, synbiotics, postprobiotics, and postbiotics (adapted from Gao et al., 2021)

Year	Discovery	Reference
1905	Detection of lactobacillus in yogurt and its connection with the longevity and gut performance	Mackowiak (2013)
1906	Detection of Bifidobacterium in feces of infants and their role in protection against organisms in the intestine and prevention of childhood diarrhea	Lee and O'Sullivan (2010)
1960	The term probiotic was first introduced as "substances produced by the one microorganisms which stimulates the growth of another microorganisms"	Lilly and Stillwell (1965)
1974	The definition of the term "probiotic" was corrected as growth promoting animal feed supplements	Parker
1989	The definition of the term "probiotic" improved as "microbial feed supplement which beneficially affect the host animal by harmonizing its microbial balance"	Mackowiak (2013)
1989	The most updated definition of probiotic is "live microorganism that when administered in adequate amounts, confer a health benefits to the host" introduced	WHO (2021)
2013	A probiotic recently defined as a substance selectively utilized by the host microorganisms conferring health benefit in symbiotic condition. The definition was further revised and grammatically corrected as "live microorganisms which when administered adequate amount confer a health benefit to the host"	International Scientific Association for Probiotics and Prebiotics (ISAPP)
2015	Non-viable microbial cells or supernatants (paraprobiotics or interactive probiotics), microbial metabolites, and growth promoting elements (postbiotics) have also emerged	Mackowiak (2013)

make a supplement to favor digestion, to boost health of your immune mechanism, prove a healthy response to infrequent stress, or further (Nutra Science, 2022).

Since each strain has particular features, they confirm specific benefits. A few strains help healthy immunity, whereas others assist lactose digestion. This is unnecessary to depict that for manufacturing highest quality supplements, raw materials contained excellent-grade probiotics are needed. The identified strains should live within the gut to validate the effectiveness of the probiotics. The commonly applied probiotics are generated under the genus *Lactobacillus*, is a group of lactic acid producing beneficial bacteria that consist of around 400 probiotic species in the human body (Healthline, 2022). Other genus like *Bifidobacterium*,

Bacillus, and *Streptococcus* are commonly used for probiotic production (Nutra Science, 2022).

3.2 Nutritional Prerequisites

The dietary requirements for growth and performance, the nutritional capacity of the environment in which the microbe was adapted and from which probiotics was sourced and is typically connected with the complexity of these auxotrophies, and nutrient demand (Hebert et al., 2004). Understanding the nutritional requirements of the microbe and establishing a particular fermentation medium that promotes growth including improving the cells' ability to survive, and respond to the stresses imposed by the manufacturing process is vital to producing a high-performance final product. Identifying strain-dependent dietary requirement necessitates a multidisciplinary, empirical knowledge-based approach. For probiotic preparation, LAB and *bifidobacteria* are demanding microbes in these regards. Around 20 amino acids are auxotrophic in LAB and *bifidobacteria*, and they have food requirements that must be met from the outside environment in order to grow. The ability to assess the genome (genomics), gene expression (transcriptomics), protein expression (proteomics), and metabolism (metabolomics) of strains provides important knowledge which is useful for the assessment of strain-dependent nutritional needs and capabilities, and the final performance of the manufactured product (Siewerts et al., 2010; Siragusa et al., 2014; Smokvina et al., 2013).

Using these methods to understand the composition of intricate basic ingredients allows researchers to match critical fermentation media ingredients for the nutritional needs of the species and/or strain development, allowing them to squeeze the media and process to improve species and strain performance while also lowering manufacturing costs and increasing efficiency. Thus, there is a wealth of empirical data that can be collected with the proper skills and innovative ideology. When combined, these approaches were found to be extremely powerful for understanding species and strain dependencies, species and strain sensitivities, nutritional needs, and nutritional limitations, and therefore, high-performance strains to be successfully developed and manufactured that meet customer expectations.

3.3 Raw Materials with Special Requirements for Growth Media

The raw ingredients used to make probiotics and other dairy starter cultures must be carefully selected and monitored. However, there may be need for the media coverage from the client and/consumer in addition to the organisms' development requirements (Kurt et al., 2019).

3.4 Fermentation and Processing of Raw Materials

The raw material for producing probiotics can be obtained from around the world. Probiotics are specially manufactured to conserve wholesomeness and excellence. Culture of bacteria could take up to 6 weeks of duration. This could not be shortened the cultivation time when the cultures are developed. Every time, detailed strain ID records are specific in the material received from supplier. Therefore, this is needed to be dependent on a specific supplier as others could not afford you with the desired strain with IDs. Likewise, other resources may not be instantly obtainable in the essential quantity with the agreement manufacturer, which may further delay from submission of a request to supply of products.

All the equipment and nutrients should be decontaminated to remove any undesirable contamination. The strain to be included to the media is in a big tank. The strain reproduces in the nutritious and warm component bath till it confirms the desired count colony-forming units (CFU). The metabolites are also generated during the process as a byproduct of the bacteria's metabolism (Nutra Science, 2022).

Fecal microbiota and fermented products with indefinite microbiota cannot be considered as probiotic (Hill et al., 2014). If there is no cell count level of a probiotic strain in a food product, this could not be assured the health benefits. However, this is to be needed a minimal CFU of 10^6 – 10^8 CFU/g is recognized as an adequate number which can ensure probiotic benefits (Champagne et al., 2011).

The fermentation medium is so important in the production of probiotics; however, several modifications in the raw materials can have a significant impact on growth and performance. The supplier's modifications to raw materials could be the result of cost reductions from the process improvements, which result in a change in ingredient sources or variation in the production process. Such changes to complex ingredients can sometimes go undetected, with some probiotic strains have apparently consistent performance; however, the performance of other strains is more obviously affected in a positive or negative way, depending on the nutritional requirements and sensitivities of the probiotic strains being manufactured (Tanguler & Erten, 2008).

3.5 Centrifugation

When the cultures are available, the metabolites are required to segregate from the probiotic strains. A close attention is needed during probiotics production process for confirming the stability of probiotics. Probiotic products start to misplace their freshness during the moment of packaging. Various maneuverers are employed to keep stability of supplements including potency for a long duration storage. There are several processes which are important and affect the viability of probiotic strains' and appropriateness of the application, are refrigeration: probiotic bacteria are taken to severe low temperatures; avoiding hot condition: this step allows the bacteria remove from humidity (a few drying methods); freeze-drying—a more longer,

however gentler process and spray-drying: a shorter process with higher temperatures, however, not too high for the bacteria to live (Nutra Science, 2022).

3.6 Probiotics in Dietary Supplements

Probiotics in the form of freeze-dried powder are commonly used in dietary supplements. For human beings, the most prevalent formats on local stores are capsules, tablets, and powder in stick packaging or sachets, which are typically maintained at room temperature. Beside these, we observed that liquid probiotic formats are available in poultry production. However, dietary supplement items should confirm the probiotic count and clearly mentioned on the label regarding product's shelf life. This ensures that the consumer gets the right amount of probiotics to effect the health claim's targeted structural function or otherwise indicated health benefits. This is crucial to describe each strain's stability, so that the appropriate amount of overage can be added during the preparation of a food additive format to corroborate that each individual strain in a multi-strain formulation has the lowest possible count.

Single strain product quality in a multi-strain formulation is extremely difficult especially when numerous strains from the same species are used. Though theoretical molecular-based strategies have been reviewed, there are currently no widely applicable and effective procedures available (Lai et al., 2017).

3.7 Bottling

The shelf life of dietary supplement forms is often measured in years; therefore, significant precautions should be taken to ensure that the proper probiotic cell count is provided. As the probiotics are living microorganisms, even when freeze-dried, they need proper care and attention than other dietary supplements and food ingredients (Broeckx et al., 2016; Forssten et al., 2011); however, the availability of technical facilities, expertise, and cost of production should be ensured in the format of probiotic supplements. Considering probiotic viability, not all plastic bottles are appropriate, since PET bottles should never be utilized since their structure permits for too much moisture absorption than the high-density polyethylene bottles (Muller et al., 2014).

3.8 The Probiotic and Nutritional Food Markets in Previous Decades

In general, the market demonstrated substantial increase for health-based probiotic products especially among the younger generations. Therefore, probiotics are found to be a part of beverages and functional foods, presented for enhancing gut function, including other benefits such as boosting immunity (Modor Intelligence, 2022).

During the last decade, the public awareness was created due to potentiality and efficaciousness of probiotics, and thus, consumers' trust was developed for something have health benefits, and the people were willing to pay extra money was the primary reasons for the success of probiotics fortified foods in these markets. Until 2011, Japan, United States, and Western Europe were the biggest markets for probiotics in terms of consumption and production. Besides, after 2011, Eastern Europe, Asia Pacific, and Brazil have demonstrated enormous growth in probiotics and are anticipated to remain this production pace over the next 5 years (Lim et al., 2015).

At present time, probiotics documented a very big business, where global functional food market has been approximated yearly USD 50 billion share (Pineiro & Stanton, 2007), including world probiotic market is calculated to USD 15 billion. Nowadays, this market is soaring at a direction of 5% to 30% considering type of product and geographical locations (Bhadoria & Mahapatra, 2011). The marketing company like Frost and Sullivan thinks that very likely to use salutistic marking on the label of the probiotic contained products in accordance to the CE 1924/2006 rules which may further boost the consumers' trust. Sufficient communication in combination with appropriate marketing plan will demonstrate to be competent to this goal. The acceptance among the consumers varied widely across Europe, including Scandinavian countries where the probiotic products were found to be consumed a long traditional way (Bhadoria & Mahapatra, 2011). However, the prevailing consumers' confusion on the different probiotic strains including suspicion about their efficacy cannot be resisted by the salutistic propaganda of the media (Caselli et al., 2013).

In 2011, the global probiotics revenue was earned USD 27.9 billion which was expected to grow with 6.8% per annum. Escalating trend on consumption of fermented dairy products and high concerns on gastrointestinal health are the main contributing factors, and these forces have triggered into high research and development expenses for development of new products over the last three years (Lim et al., 2015).

Probiotic dairy products, particularly probiotic yogurts and milks, have been found the most active segment of the European functional foods market (Catherine et al., 2001). In 1997, these products covered 65% of the European functional foods market with a calculated revenue of USD 889 million which was escalated from 23% of the market with a revenue of USD 320 million at the beginning. However, the market for the functional foods in the United Kingdom, France, Germany, Spain, Belgium, the Netherlands, Denmark, Finland, and Sweden was examined in a recent study conducted by Leatherhead Food RA. According to the findings, the probiotic yogurt market in these nine nations totaled more than 250 million kg in 1997 with France noticed the highest market, with sales of 90 million kg with value of USD 219 million. On the contrary, in Germany, the probiotic yogurt is growing quickly; for instance, during 1996–1997, it increased by 150%, whereas, in the United Kingdom, the market grew by a slow pace of 26% during the same period.

Averagely, the probiotic yogurts accounted for 10% of all yogurts sold in the nine countries studied, with Denmark having the highest consumption (20%) followed by Germany and the United Kingdom (both at 13%), and then France (11%). However, the Netherlands and Belgium (both at 6%) and then Finland and Sweden (both at 5%) (Hilliam, 1998) were documented lower sales.

The market for functional foods in Europe could ultimately account for 5% of total food expenditure in Europe, which is based on current prices and equivalent to USD 30 billion (Young, 1996). Additionally, diversified soft drinks, the original functional foods are still dominating the Japanese market; dietary fiber and probiotics are the significant functional ingredients in many of these products. The Bikkle which is considered to be the typical functional drink, was introduced in 1993 by Suntory (Osaka, Japan) and contains bifidobacterial cultures, whey minerals, xylooligosaccharides, and dietary fiber. Overwhelmingly, this product achieved sales of 11 billion yen in its first year. However, the fermented milk drink Yakult (Yakult, Japan), which is classified as a functional food in Europe, was not observed as such in Japan as the presence of probiotics in isolation from other functional ingredients does not carry functional food status in Japan (Young, 1996). In addition to functional drinks, functional milk products and products for children are also important, with innovations in a variety of foods and drinks such as ice creams, confectionery, biscuits, snack foods, and calcium-fortified drinks.

There have been several developments in the dairy products category including the development of yogurts supplemented with oligosaccharides and calcium (Young, 1996). It is expected that prebiotics and probiotics will continue to be important for the future growth and expansion of the market for probiotics and functional foods in the United States. Leatherhead Food RA's (1996) report assessed the global market for functional foods at USD 6.6 billion in 1994, with Japan accounting for just under one-half of that among the major functional food ingredients for the projected future in Japan. Estimating the size of the functional foods market in Japan is difficult as there is a lack of a clear boundary between health foods and functional foods; however, the current estimates are in the range of USD 3 to 3.5 billion.

The US functional foods market is comparatively undersized by European standards, with fortified dairy products, particularly, those containing active cultures, obtaining popularity in recent time. In contrast with the situation in Europe, there is lack of notable development of prebiotics in the United States. Vitamin- and mineral-enriched products continue to be incorporated among the more successful functional foods in the United States. Market development has been held back by criticism leveled at companies that have introduced products bearing raucous health claims. However, this is predicted that the US market for functional foods will experience the rapid growth rates compared with other countries in the coming future (Young, 1996).

4 Cost–Benefit Analysis

4.1 Animal Health

Overall production costs may decrease if commercial agriculture's growth performance and feed effectiveness improves. According to Torres-Rodriguez et al. (2007), a cost-effective analysis of the use of probiotic in diet in turkeys revealed that the cost for yielding per kilogram live body weight was lower, even after, including the cost of probiotics, when compared to the same for the control group, and that a small decline in FCR associated with the addition of probiotics would assist in lower production costs (Akhter et al., 2018; Islam et al., 2014).

In case of poultry production paradigm, the main variables of cost items include day old chick cost (DOC), litter cost, vaccination and biosecurity related cost, schedule medication cost, electricity bill cost, cost for purchased probiotic/antibiotic, transportation cost, and other operational cost which are considered to be the primary factors of cost components in chicken production.

In present market, a number of commercial probiotics and prebiotics for poultry production, all of which are typically administered in small doses. However, the cost of probiotics or prebiotics varies depending on the manufacturer and the active components in the final probiotic product (Young, 2008). Besides, in their research, Gutierrez-Fuentes et al. (2013) established the economic effectiveness of employing the probiotic. Their cost-benefit study revealed that body weight gained 100 gm for every dollar for probiotics spend, which was then converted to a cost-benefit ratio of 1: 22.57.

The benefits of all treatment groups overshadowed those of the control groups, and they depicted that using probiotics of any kind is cost-effective and profitable, as well as agreeing with other research statements. Thus, it was evident that that the newly designed probiotics are effective (Ferdous, 2021; Khatun et al., 2017).

4.2 Human Health

Among the side effects of antimicrobial use, the antibiotic-associated diarrhea (AAD) is one of the greatest common. Several meta-analyses confirm that probiotics have pivotal role on the risk, length, and acuteness of AAD (Hempel et al., 2012; Ouwehand et al., 2014). A number of research have made efforts to interpret the economic effect of probiotic use is on AAD-related costs.

The study confirmed in particular hospital, setting an extra annual cost of EUR 77,800 for isolation of the patients with AAD, however, the probiotic use would lessen these specific costs at EUR 63,400. Taken into consideration the extra cost for the probiotic (EUR 4600/annum), the net savings could be EUR 58,800/annum (Dietrich et al., 2014).

The use of oral probiotics as a preventive measures for *Clostridium difficile*-associated diarrhea (CDAD) in adults admitted in hospitals who were having a course of antimicrobials to lessen the CDAD risk and proceeded in a cost-savings

of USD 518/person/treatment. Inferring to a population size >380,000 hospitalized/year, the healthcare system would likely to spend USD 2.2 million for oral probiotics usage; however, this would likely to lessen total cost-savings of USD \$44 million (Leal et al., 2016). Since the CDAD is a sub-class of AAD, *C. difficile* is documented to be accountable for nearly 25% of total AAD cases, and this could be terminated to be acute cases of AAD (Larcombe et al., 2016).

A separate study in human health evaluated the cost-benefit of probiotics usage (*Bifidobacterium bifidum* and *Lactobacillus acidophilus*) in the treatment of hospitalized >100 children with severe diarrhea via both a double-blind randomized and placebo trials. The study confirmed pointedly shorter hospital stay in the probiotics treated group than in the controlled group; however, the median length of diarrhea and direct medical expenses were not significantly changed. Thus, parental income loss, a non-significant low-cost, was seen in the probiotics group. A wider cost-benefit with the probiotic treatment is plausible, however, statistically found to be non-significant due to small sample size. The probiotics application reduced the length of hospitalization in children with diarrhea ailments but the total expenses were not different (Phavichitr et al., 2013).

5 Recent and Future Probiotic Marketing

Compound annual growth rate (CAGR) is a business and investing specific term for the geometric progression ratio that gives a constant rate of return over the time. The CAGR is the yearly average rate of revenue growth over a 2-year period, assuming growth is compounded exponentially. The mathematical progression ratio that gives a constant rate of return over time is referred to as compound annual growth rate in business and investing as per formula given by Fernando (2021).

$$\text{CAGR} = \left(V_{\text{final}} / V_{\text{begin}} \right)^{1/t} - 1 \quad (1)$$

where, CAGR = compound annual growth rate, V_{begin} = beginning value, V_{final} = final value, t = time in years.

However, the probiotics market witnessed significant growth due to incessant demand for health-based products among the younger generations. Additionally, probiotics are vital part of functional foods and beverages, they are known for improved intestinal function and other health benefits, such as boosting immunity. Of the total retail probiotic food products sales, 71% of market shares is occupied by the probiotic yogurt segment, as stated by the International Probiotics Association (Modor Intelligence, 2022).

The global probiotic markets were estimated to be USD 34.1 billion in 2020 and expected to grow at USD 73.9 billion by 2030, with an 8.6% CAGR. Probiotics are bacteria and yeast-like microorganisms that assist humans and animals maintain a healthy intestinal microbial balance. The probiotics element promotes the body's natural digestive juices and enzymes, ensuring conducive environments for digestion. They can be taken as supplemental or administered orally. Probiotics also

protect healthy microorganisms from potentially dangerous pathogens. In case of human being, probiotics are being used tremendously to diagnose and treat mental illness, as well as digestive and neurological ailments. They also help to strengthen the immune system, protect proteins and lipids from oxidative damage, and reduce pathogen levels in the body. However, a major aspect to influencing the market expansion is due to boost in consumer preference on natural products about preventative healthcare and the efficacy of probiotic microorganisms on health benefits. Demand for probiotics has been risen as a result of growth in the use of functional foods, which, in addition to providing basic nourishment, have the potential to improve health. Thus, market actors have created probiotics products to aid in the treatment of disorders of living hosts. The influence of the rise in health concerns on the probiotics market is mild. Many people, however, are ignorant of the advantages of probiotics. In developing nations such as India and China, the supplement business is rapidly expanding due to health-related concerns. To address the needs of the industry and remain competitive in the market, the companies today have their own research and development facilities. Huge investments in research and development institutes are projected to increase probiotic product quality in the future. The probiotics market is likely to be driven by growth in the food and beverage industry as a result of higher consumer expenditure and positive government backing. Probiotics market growth is likely to be powered by an increase in demand for nutritional supplements among health-conscious consumers. Market expansion is expected to be hampered by a lack of proper regulations in the industry. Furthermore, because probiotics are highly sensitive organisms that can be readily weakened by a range of environmental factors, it requires safe storage facilities.

The growing recognition of the health benefits of probiotics, along with the aging population, is predicted to present a major growth opportunity. The market is predicted to rise as the number of workers has increased, as well as consumer expenditure on healthy food products. The market has experienced an increase in demand for goods that boost immunological health as the impact of COVID-19, which is expected to boom the probiotics market. Therefore, the major products formulation are taking place in order to meet the increased demand of both in animals and humans. Human consumers prefer probiotic dairy products such as yoghurt, ice cream, and cheese to absorb beneficial bacteria in addition to existing medical health supplements.

5.1 Probiotics Market by Ingredients

The market can be classified by ingredient, function, application, end user, and geography, according to probiotics market analysis. Bacteria and yeast are the two types of ingredients that are being used in probiotics. Considering these ingredients of the end product, the yeast segment is anticipated to grow at highest CAGR of 8.9% during the forecast period (2020–2030) (Fig. 1). However, due to an increase in demand for bacteria-derived probiotics food products, the bacteria category had the greatest probiotics market share by ingredient in 2020.

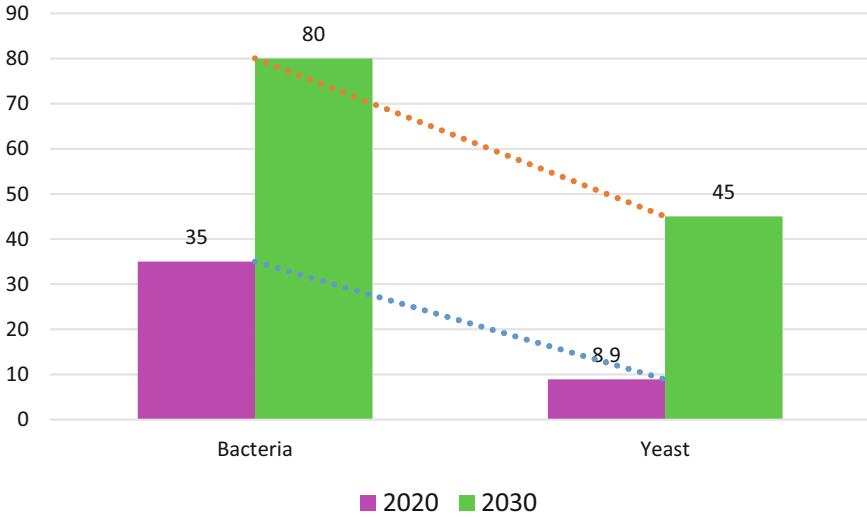


Fig. 1 Probiotic market by ingredients. The yeast segment is anticipated to grow at highest CAGR of 8.9% during the forecast period (adapted from Jaya & Roshan, 2021)

5.2 Probiotics Market by Purpose of Use

The probiotics industry is divided into three categories based on function: daily, preventative healthcare, and therapeutic healthcare. Among the three categories (regular, preventive, and therapeutic healthcare), interestingly, preventative healthcare segment is anticipated to grow at highest CAGR of 9.4% during the forecast period (Fig. 2).

However, the utilization of *Streptococcus* probiotics strains and other new species and/or strains in strengthening animal feeds are the major current market's

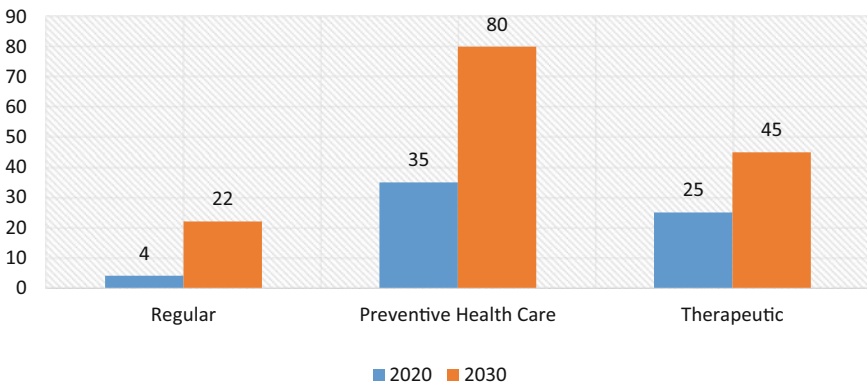


Fig. 2 Probiotic market by functions (adapted from Jaya & Roshan, 2021)

breakthroughs. Also, probiotics are increasingly being introduced in supplement formulations to treat inflammatory skin infections, viz., atopic dermatitis and eczema. All of these reasons are expected to contribute to the probiotics market's development.

According to the probiotics market projection, the preventative healthcare category lead the industry in terms of market share. This can be related to the rise in health concerns, which has prompted market participants to engage in research and development and offer new and innovative probiotics products. The dietary supplements category is expected to take the lead with the greatest market share over the projection period, based on application. This is due to the fact that some dietary supplement manufacturers concentrate on including a specific type of dietary fiber that contains probiotics and prebiotics (synbiotic). Diarrhea, indigestion, dermatitis, yeast infections, and other health complications, all are now attempt to treat with these substances (Jaya & Roshan, 2021).

5.3 Probiotic Market by Application

Food and beverage, dietary supplement, and animal feed are the three categories according to application. The dietary segment is expected to grow the highest CAGR (9.2%) during the anticipated period (Fig. 3).

During the projection period, the dietary supplement segment is predicted to increase 9.2% of compound annual growth rate. In 2020, the human group led the market by end user. This is owing to a rise in health concerns and understanding about the need of keeping the gut healthy, which has increased consumer demand for probiotics. The market is likely to be dominated by Asia-Pacific. Due to an increase in demand for food and health products that contain probiotics, Japan is the biggest consumer for probiotics in Asia-Pacific. Probiotics are live bacteria that, when taken in adequate amounts, give health advantages to humans. Probiotics for humans are

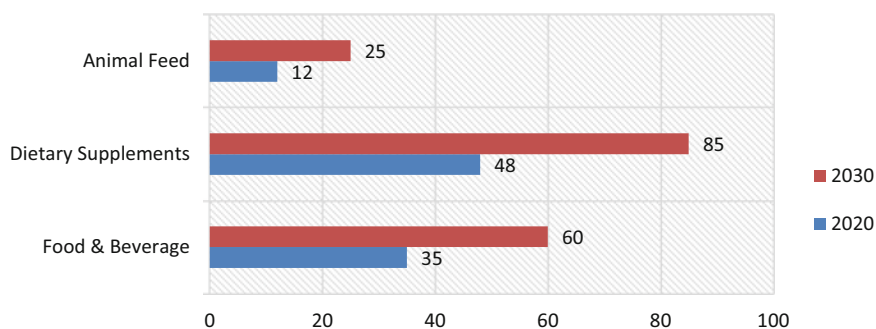


Fig. 3 Probiotic market by applications. The dietary segment expected to grow the highest CAGR (9.2%) during the anticipated period (adapted from Jaya & Roshan, 2021)

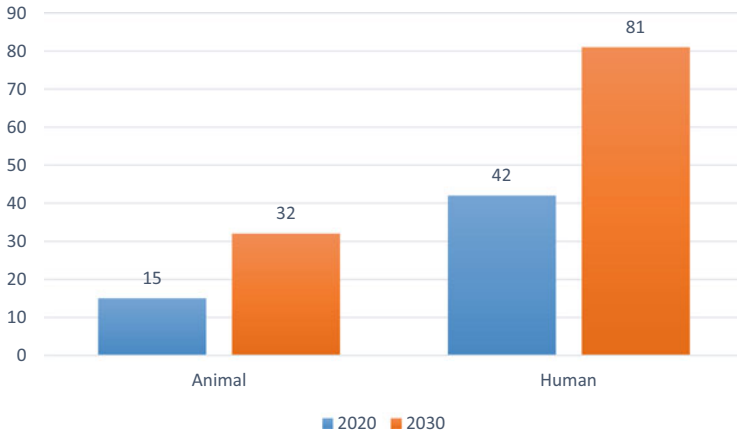


Fig. 4 Probiotic market by end users. The animal segment is expected to grow at highest CAGR (9.1%) during the forecast period (adapted from Jaya & Roshan, 2021)

used to address intestinal issues. Antibiotic-induced diarrhea and spasms are also treated with them.

5.4 Probiotic Market by End User

It is divided into human and animal categories based on the end user. During the projection period, the animal segment is predicted to increase 9.1% of compound annual growth rate (Fig. 4).

Around the world, BioGaia AB, Danone, Chr. Hansen Holding A/S, Yakult Honsha Co. Ltd., Probi AB, Lifeway Foods, Inc., Nestle S.A., Ganeden, Inc., E. I. du Pont de Nemours and Company, and Protexin are leading most probiotics companies. The most common growth strategy employed by market participants is product introduction, which is followed by partnership and agreement, expansion, and acquisition. To broaden their product offers, several companies have developed unique goods. Product launches are used by a variety of companies to broaden their market reach and service international clients (Jaya & Roshan, 2021).

5.5 Probiotics Market by Regions

The probiotics market is divided into four regions: North America, Europe, Asia-Pacific, and Latin America and the Caribbean (LAMEA). Asia-Pacific countries currently leads the market, with a compound annual growth rate (CAGR) of 9.0% predicted over the projection period, followed by North America, Europe, and Latin America (Jaya & Roshan, 2021).

6 Future Trend of Prebiotics and Probiotics

In coming days, prebiotics will expected to be identified from novel sources (Fig. 5) considering sustainability, price, and its judicial use (Mano et al., 2018). Yearly, 1.3 billion tons of food waste produced per year in the food chain demonstrated a good and viable source of natural bioactive substances.

Important prebiotics are produced from fruits, grains, and vegetable processing, for example, pectin from orange peel (Gómez et al., 2014) and arabinoxylans from distillery and brewing waste (Monteagudo-Mera et al., 2018). Application of sonication future prebiotic compounds may also be chemically or structurally altered using high pressure, enzyme, acid, and oxidation treatments for functionality modification. Finally, unique mixtures of prebiotics in improved mixtures could offer the capability to produce novel profiles of benefits (Lam & Cheung, 2019).

Current advancement in microbiome science is permitting new horizons of enquiry for probiotics and prebiotics. New genres, mode of action, and practices presently under review have the importance to adjust the scientific knowledge including healthcare and nutritional applications of these inventions. The extension of related domains of microbiome-targeted findings and an emerging landscape for execution across policy, regulatory, prescriber, and consumer-levels signify an epoch of meaningful change (Cunningham et al., 2021).

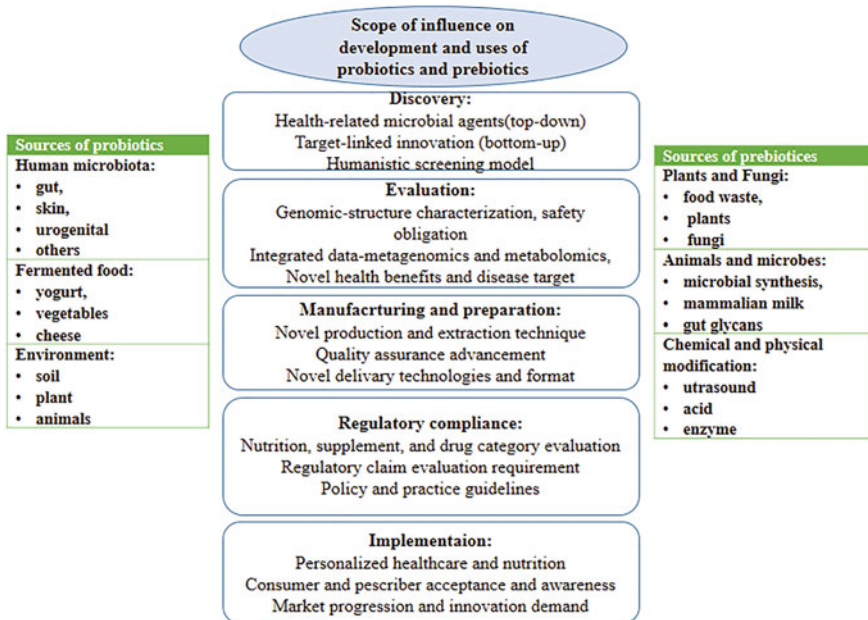


Fig. 5 Development and application of future of probiotics and prebiotics. The snapshot displays present and evolving effects on probiotics and prebiotics along with new sources, novel discovery and assessment techniques, manufacturing and formulation advances, regulatory issues, including effect on execution in nutrition and healthcare (adapted from Cunningham et al., 2021)

7 Conclusion

In view of multifaceted health-promotion effects connected with the use of probiotics in humans and animals, these organisms are currently occupied by many industries in producing probiotic-origin food and animal-feed, pharmaceutical products, dietary supplements including natural therapeutic agents. Successfully conveying probiotic benefits to the consumers and qualitative business with probiotics must be ensured. Precautions to be taken to select the most suitable species and/or strains, cultivation conditions, and product manufacture. The probiotic commercialization will run concurrently with media engagement which vary greatly according to cost and other considerations. The required doses of the species and/or strains towards the end of shelf life, as well as incorporating them in consumer goods, are often ignored challenges in the manufacturing of probiotics. To assure the supply of high-quality prebiotic-probiotic-containing products to customers, legislation and regulation should be developed around the world. Furthermore, manufacturers of probiotic-containing goods should have responsibility for delivering scientifically and legally accurate information to consumers. Inclusion of probiotics into a product is predominately investigated thorough sensory and physicochemical characteristics, however, to assess whole metabolite profile using metabolomics can give deep-insights into many substances of appropriateness to odor and food value. The future probiotic microbes will significantly lead for making money and food microbiology based entrepreneurship will arise dramatically around the earth.

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References

- Akhter, A. H. M. T., Islam, S. S., Sufian, M. A., Hossain, M., Rahman, S. M. M., Kabir, S. M. L., Uddin, M. G., & Hossain, M. M. (2018). Implementation of code of practices (CoP) in selected poultry farms in Bangladesh. *Asian-Australasian Journal of Food Safety and Security*, 2, 45–55.
- Arif, M., Akteruzzaman, M., Tuhin-Al-Ferdous, Islam, S. S., Das, B. C., Siddique, M. P., & Kabir, S. M. L. (2021). Dietary supplementation of *Bacillus*-based probiotics on the growth performance, gut morphology, intestinal microbiota and immune response in low biosecurity broiler chickens. *Veterinary and Animal Science*, 14, 100216.
- Bengmark, S. (1998). Ecological control of the gastrointestinal tract. The role of probiotic flora. *Gut*, 42, 2–7.
- Bhadoria, P., & Mahapatra, S. (2011). Prospects, technological aspects and limitations of probiotics—a worldwide review. *European Journal of Nutrition & Food Safety*, 2011, 23–42.
- Broeckx, G., Vandenhuevel, D., Claes, I. J., Lebeer, S., & Kiekens, F. (2016). Drying techniques of probiotic bacteria as an important step towards the development of novel pharmabiotics. *International Journal of Pharmacology*, 505, 303–318.
- Canganella, F., Gasbarri, M., Massa, S., & Trovatielli, L. D. (1996). A microbiological investigation on probiotic preparations used for animal feeding. *Microbiological Research*, 151, 167–175.

- Caselli, M., Cassol, F., Calò, G., Holton, J., Zuliani, G., & Gasbarrini, A. (2013). Actual concept of “probiotics”: Is it more functional to science or business? *World Journal of Gastroenterology*, *19*, 1527–1540.
- Catherine, S., Gillian, G., Hillary, M., Kevin, C., Gerald, F., Brendan, L. P., & Paul, R. R. (2001). Market potential for probiotics. *The American Journal of Clinical Nutrition*, *73*, 47–83.
- Champagne, C. P., Ross, R. P., Saarela, M., Hansen, K. F., & Charalampopoulos, D. (2011). Recommendations for the viability assessment of probiotics as concentrated cultures and in food matrices. *International Journal of Food Microbiology*, *149*, 185–193.
- Chandel, D., Sharma, M., Chawla, V., Sachdeva, N., & Shukla, G. (2019). Isolation, characterization and identification of antigenotoxic and anticancerous indigenous probiotics and their prophylactic potential in experimental colon carcinogenesis. *Scientific Reports*, *9*, 1–12.
- Crittenden, R. (2009). Incorporating probiotics into foods. In Y. K. Lee & S. Salminen (Eds.), *Handbook of probiotics and prebiotics* (2nd ed., pp. 58–70). Wiley.
- Cuevas-González, P., Liceaga, A., & Aguilar-Toalá, J. (2020). Postbiotics and paraprobiotics: From concepts to applications. *Food Research International*, *136*, 109502.
- Cunningham, M., Azcarate-Peril, M. A., Barnard, A., Benoit, V., Grimaldi, R., Guyonnet, D., Holscher, H. D., Hunter, K., Manurung, S., & Obis, D. (2021). Shaping the future of probiotics and prebiotics. *Trends in Microbiology*, *29*, 667–685.
- Dietrich, C. G., Kottmann, T., & Alavi, M. (2014). Commercially available probiotic drinks containing *Lactobacillus casei* DN-114001 reduce antibiotic-associated diarrhea. *World Journal of Gastroenterology*, *20*, 15837–15844.
- Drago, L., Gismondo, M. R., Lombardi, A., De Haën, C., & Gozzini, L. (1997). Inhibition of in vitro growth of enteropathogens by new *Lactobacillus* isolates of human intestinal origin. *FEMS Microbiology Letters*, *153*(2), 455–463.
- Edens, F. W., Parkhurst, C. R., Casas, I. A., & Dobrogosz, W. J. (1997). Principles of ex ovo competitive exclusion and in ovo administration of *Lactobacillus reuteri*. *Poultry Science*, *76*, 179–196.
- Ferdous, T. A. (2021). Isolation, identification and molecular detection of selected probiotic bacteria from broiler chickens and their evaluation for the development of potential probiotic. PhD Dissertation, Department of Microbiology and Hygiene, Bangladesh Agricultural University, Mymensingh, Bangladesh.
- Fernando, J. (2021). Compound annual growth rate (CAGR). *Investopedia Viitattu*, *22*, 2021.
- Forssten, S. D., Sindelar, C. W., & Ouweland, A. C. (2011). Probiotics from an industrial perspective. *Anaerobe*, *17*, 410–413.
- Fuller, R. (1986). Probiotics. *Society for Applied Bacteriology Symposium Series*, *15*, 1–7.
- Gao, J., Li, X., Zhang, G., Sadiq, F. A., Simal-Gandara, J., Xiao, J., & Sang, Y. (2021). Probiotics in the dairy industry—Advances and opportunities. *Comprehensive Reviews in Food Science and Food Safety*, *20*, 3937–3982.
- Gardiner, G., Stanton, C., Lynch, P. B., Collins, J. K., Fitzgerald, G., & Ross, R. P. (1999). Evaluation of cheddar cheese as a food carrier for delivery of a probiotic strain to the gastrointestinal tract. *Journal of Dairy Science*, *82*, 1379–1387.
- Gómez, B., Gullon, B., Remoroza, C., Schols, H. A., Parajo, J. C., & Alonso, J. L. (2014). Purification, characterization, and prebiotic properties of pectic oligosaccharides from orange peel wastes. *Journal of Agricultural and Food Chemistry*, *62*, 9769–9782.
- González, J., Lezcano, F., & Castañeda, S. (1993). Feeding systems for fattening pigs based on diets with final molasses and concentrates with bagasse pith Saccharina. *Cuban Journal of Agricultural Science*, *27*(2), 177–181.
- Górska, A., Przystupski, D., Niemczura, M. J., & Kulbacka, J. (2019). Probiotic bacteria: A promising tool in cancer prevention and therapy. *Current Microbiology*, *76*, 939–949.
- Gutierrez-Fuentes, C. G., Zuñiga-Orozco, L. A., Vicente, J. L., Hernandez-Velasco, X., Menconi, A., Kuttappan, V., Kallapura, G., Latorre, J., Layton, S., Hargis, B. M., & Téllez, G. (2013). Effect of a lactic acid bacteria based probiotic, Floramax-B11®, on performance, bone qualities, and morphometric analysis of broiler chickens: An economic analysis. *Biological System: Open Access*, *12*, 322–327.

- He, L., Yang, H., Tang, J., Liu, Z., Chen, Y., Lu, B., He, H., Tang, S., Sun, Y., & Liu, F. (2019). Intestinal probiotics *E. coli* Nissle 1917 as a targeted vehicle for delivery of p53 and Tum-5 to solid tumors for cancer therapy. *Journal of Biological Engineering*, *13*, 1–13.
- Healthline (2022). *What are the most common types of probiotics?* <https://www.healthline.com/health/types-of-probiotics#common-probiotics>
- Hebert, E. M., Raya, R. R., & de Giori, G. S. (2004). Nutritional requirements of *Lactobacillus delbrueckii* subsp. *lactis* in a chemically defined medium. *Current Microbiology*, *49*, 341–345.
- Hempel, S., Newberry, S. J., Maher, A. R., Wang, Z., Miles, J. N., Shanman, R., Johnsen, B., & Shekelle, P. G. (2012). Probiotics for the prevention and treatment of antibiotic-associated diarrhea: A systematic review and meta-analysis. *JAMA*, *307*, 1959–1969.
- Hill, C., Guarner, F., Reid, G., Gibson, G. R., Merenstein, D. J., Pot, B., Morelli, L., Canani, R. B., Flint, H. J., & Salminen, S. (2014). Expert consensus document: The international scientific association for probiotics and prebiotics consensus statement on the scope and appropriate use of the term probiotic. *Nature Reviews. Gastroenterology & Hepatology*, *11*, 506–514.
- Hilliam, M. (1998). Functional foods in Europe. *The World of Ingredients*, *1998*, 45–71.
- Hudault, S., Lievin, V., Bernet-Camard, M. F., & Servin, A. L. (1997). Antagonistic activity exerted *in vitro* and *in vivo* by *Lactobacillus casei* (strain GG) against *Salmonella typhimurium* C5 infection. *Applied and Environmental Microbiology*, *63*, 513–528.
- Islam, M. A., Kabir, S. M. L., Rahman, M. B., Das, S. K., Hossain, K. M. M., Mustafa, M. M. H., & Poonsuk, K. (2014). The viability of dietary probiotics (Bactosac[®]) influencing growth parameters, cellular alteration in intestinal wall and immune response of broilers. *Current Research Journal of Biological Sciences*, *6*, 128–133.
- Jaya, B., & Roshan, D. (2021). Probiotics market by ingredient (bacteria and yeast), function (regular, preventative healthcare, and therapeutic), application (food and beverage, dietary supplements, and animal feed), and end user (human and animal): Global opportunity analysis and industry forecast 2021–2030. *Allied Market Research*, *2021*, 302.
- Kabir, S. M. L. (2009). The role of probiotics in the poultry industry. *International Journal of Molecular Sciences*, *10*, 3531–3546.
- Kamruzzaman, S. M., Kabir, S. M. L., Rahman, M. M., Islam, M. W., & Reza, M. A. (2005). Effect of probiotics and antibiotic supplementation on body weight and haemato-biochemical parameters in broilers. *Bangladesh Journal of Veterinary Medicine*, *3*, 100–104.
- Khatun, M. T., Kabir, S. M. L., Islam, M. S., Tuhin-Al-Ferdous, M. M. I., Rahman, M. M., Mustafa, M. M. H., Latif, M. A., Thitisak, P., & Poonsuk, K. (2017). Effects of dietary inclusion of a commercially available probiotic on growth performance, cecal microbiota and small intestinal morphology in broiler chickens. *International Journal of Livestock Production*, *8*, 33–39.
- Kurt, F., Barbara, F., Chris, H., Connie, W., Rune, R. L., & Arthur, C. O. (2019). The production and delivery of probiotics: A review of a practical approach. *Microorganisms*, *7*, 1–16.
- Lai, C. H., Wu, S. R., Pang, J. C., Ramireddy, L., Chiang, Y. C., Lin, C. K., & Tsen, H. Y. (2017). Designing primers and evaluation of the efficiency of propidium monoazide-Quantitative polymerase chain reaction for counting the viable cells of *Lactobacillus gasseri* and *Lact. salivarius*. *Journal of Food and Drug Analysis*, *25*, 533–542.
- Lam, K.-L., & Cheung, P. C.-K. (2019). Carbohydrate-based prebiotics in targeted modulation of gut microbiome. *Journal of Agricultural and Food Chemistry*, *67*, 12335–12340.
- Larcombe, S., Hutton, M. L., & Lyras, D. (2016). Involvement of bacteria other than *Clostridium difficile* in antibiotic-associated diarrhoea. *Trends in Microbiology*, *24*, 463–476.
- Leal, J. R., Heitman, S. J., Conly, J. M., Henderson, E. A., & Manns, B. J. (2016). Cost-effectiveness analysis of the use of probiotics for the prevention of *Clostridium difficile*-associated diarrhea in a provincial healthcare system. *Infection Control and Hospital Epidemiology*, *37*, 1079–1086.
- Lee, C. S., & Kim, S. H. (2020). Anti-inflammatory and anti-osteoporotic potential of *Lactobacillus plantarum* A41 and *L. fermentum* SRK414 as probiotics. *Probiotics and Antimicrobial Proteins*, *12*, 623–634.

- Lee, J.-H., & O'Sullivan, D. J. (2010). Genomic insights into bifidobacteria. *Microbiology and Molecular Biology Reviews*, 74, 378–416.
- Lilly, D. M., & Stillwell, R. H. (1965). Probiotics: Growth-promoting factors produced by microorganisms. *Science*, 147, 747–748.
- Lim, K., Jeong, J., Oh, S., Moon, Y.-I., & Koh, J. (2015). Current market trends and perspectives of probiotics. *Current Topics in Lactic Acid Bacteria and Probiotics*, 3, 46–53.
- Mackowiak, P. (2013). Recycling metchnikoff: Probiotics, the intestinal microbiome and the quest for long life. *Frontiers in Public Health*, 1, 52.
- Mano, M. C. R., Neri-Numa, I. A., da Silva, J. B., Paulino, B. N., Pessoa, M. G., & Pastore, G. M. (2018). Oligosaccharide biotechnology: An approach of prebiotic revolution on the industry. *Applied Microbiology and Biotechnology*, 102, 17–37.
- Marco, M. L., Sanders, M. E., Gänzle, M., Arrieta, M. C., Cotter, P. D., De Vuyst, L., Hill, C., Holzapfel, W., Lebeer, S., & Merenstein, D. (2021). The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on fermented foods. *Nature Reviews. Gastroenterology & Hepatology*, 18, 196–208.
- Marotta, A., Sarno, E., Del Casale, A., Pane, M., Mogna, L., Amoruso, A., Felis, G. E., & Fiorio, M. (2019). Effects of probiotics on cognitive reactivity, mood, and sleep quality. *Frontiers in Psychiatry*, 10, 164.
- Marteau, P., & Rambaud, J. C. (1993). Potential of using lactic acid bacteria for therapy and immunomodulation in man. *FEMS Microbiology Reviews*, 12, 207–220.
- Mendoza, L. (2019). Potential effect of probiotics in the treatment of breast cancer. *Oncology Reviews*, 13, 422.
- Mishra, V., Shah, C., Mokashe, N., Chavan, R., Yadav, H., & Prajapati, J. (2015). Probiotics as potential antioxidants: A systematic review. *Journal of Agricultural and Food Chemistry*, 63, 3615–3626.
- Modor Intelligence. (2022). *Global probiotics market (2022-27). Industry reports*. Consulting, Intelligence Center.
- Monteagudo-Mera, A., Chatzifragkou, A., Kosik, O., Gibson, G., Lovegrove, A., Shewry, P. R., & Charalampopoulos, D. (2018). Evaluation of the prebiotic potential of arabinoxylans extracted from wheat distillers' dried grains with solubles (DDGS) and in-process samples. *Applied Microbiology and Biotechnology*, 102, 7577–7587.
- Muller, C., Mazel, V., Dausset, C., Busignies, V., Bornes, S., Nivoliez, A., & Tchoreloff, P. (2014). Study of the *Lactobacillus rhamnosus* Lcr35(R) properties after compression and proposition of a model to predict tablet stability. *European Journal of Pharmacology*, 88, 787–794.
- Neu, H. C. (1994). The crisis in antibiotic resistance. *Science*, 257, 1064–1073.
- Nutra Science. (2022). *Five essential steps of the probiotic manufacturing process explained*. Retrieved from <https://www.nutrasciencelabs.com/blog/5-essential-steps-of-the-probiotic-manufacturing-process?msclkid=c99546afba0911ecaedd78429d74a3fd>
- Ouwehand, A. C., DongLian, C., Weijian, X., Stewart, M., Ni, J., Stewart, T., & Miller, L. E. (2014). Probiotics reduce symptoms of antibiotic use in a hospital setting: A randomized dose response study. *Vaccine*, 32, 458–463.
- Phavichitr, N., Puwdee, P., & Tantibhaedhyankul, R. (2013). Cost-benefit analysis of the probiotic treatment of children hospitalized for acute diarrhea in Bangkok, Thailand. *The Southeast Asian Journal of Tropical Medicine and Public Health*, 44, 1065–1071.
- Pineiro, M., & Stanton, C. (2007). Probiotic bacteria: Legislative framework—requirements to evidence basis. *The Journal of Nutrition*, 137, 850–853.
- Plaza-Díaz, J., Ruiz-Ojeda, F. J., Vilchez-Padial, L. M., & Gil, A. (2017). Evidence of the anti-inflammatory effects of probiotics and synbiotics in intestinal chronic diseases. *Nutrients*, 9, 555.
- Posocco, B., Buzzo, M., Follegot, A., Giodini, L., Sorio, R., Marangon, E., & Toffoli, G. (2018). A new high-performance liquid chromatography-tandem mass spectrometry method for the determination of paclitaxel and 6 α -hydroxy-paclitaxel in human plasma: Development, validation and application in a clinical pharmacokinetic study. *PLoS One*, 13, e0193500.

- Rai, A. K., Sanjukta, S., & Jeyaram, K. (2017). Production of angiotensin I converting enzyme inhibitory (ACE-I) peptides during milk fermentation and their role in reducing hypertension. *Critical Reviews in Food Science and Nutrition*, 57, 2789–2800.
- Ray, B. C., Chowdhury, S. D., & Khatun, A. (2019). Productive performance and cost effectiveness of broiler using three different probiotics in the diet. *Bangladesh Journal of Animal Science*, 48, 85–91.
- Reid, G., Bruce, A. W., & Smeianov, V. (1998). The role of lactobacilli in preventing urogenital and intestinal infections. *International Dairy Journal*, 8, 555–562.
- Reid, G., Bruce, A. W., & Taylor, M. (1995). Instillation of *Lactobacillus* and stimulation of indigenous organisms to prevent recurrence of urinary tract infections. *Microecology*, 23, 32–45.
- Reid, G., Lam, D., Bruce, A. W., van der Mei, H. C., & Busscher, H. J. (1994). Adhesion of lactobacilli to urinary catheters and diapers: Effect of surface properties. *Journal of Biomedical Materials Research*, 28, 731–734.
- Sieuwerths, S., Molenaar, D., van Hijum, S. A., Beerthuyzen, M., Stevens, M. J., Janssen, P. W., Ingham, C. J., de Bok, F. A., de Vos, W. M., & van Hylckama, V. J. E. (2010). Mixed-culture trans criptome analysis reveals the molecular basis of mixed-culture growth in *Streptococcus thermophilus* and *Lactobacillus bulgaricus*. *Applied and Environmental Microbiology*, 76, 7775–7784.
- Siragusa, S., De Angelis, M., Calasso, M., Campanella, D., Minervini, F., Di Cagno, R., & Gobbetti, M. (2014). Fermentation and proteome profiles of *Lactobacillus plantarum* strains during growth under food-like conditions. *Journal of Proteomics*, 96, 366–380.
- Smokvina, T., Wels, M., Polka, J., Chervaux, C., Brisse, S., Boekhorst, J., van Hylckama, V. J. E., & Siezen, R. J. (2013). *Lactobacillus paracasei* comparative genomics: Towards species pan-genome definition and exploitation of diversity. *PLoS ONE*, 8, 8731.
- Tangler, H., & Erten, H. (2008). Utilisation of spent brewer's yeast for yeast extract production by autolysis: The effect of temperature. *Food and Bioproducts Processing*, 86, 317–321.
- Torres-Rodriguez, A., Donoghue, A., Donoghue, D., Barton, J., Tellez, G., & Hargis, B. (2007). Performance and condemnation rate analysis of commercial turkey flocks treated with a *Lactobacillus* spp.-based probiotic. *Poultry Science*, 86, 444–446.
- Underdahl, N. R., Torres-Medina, A., & Doster, A. R. (1982). Effect of *Streptococcus faecium* C-68 in control of *Escherichia coli*-induced diarrhea in gnotobiotic pigs. *Journal of Veterinary Research*, 43, 2227–2232.
- Wang, J., Bai, X., Peng, C., Yu, Z., Li, B., Zhang, W., Sun, Z., & Zhang, H. (2020). Fermented milk containing *Lactobacillus casei* Zhang and *Bifidobacterium animalis* ssp. *lactis* V9 alleviated constipation symptoms through regulation of intestinal microbiota, inflammation, and metabolic pathways. *Journal of Dairy Science*, 103, 11025–11038.
- Wang, L., Shang, Q., Guo, W., Wu, X., Wu, L., Wu, L., & Chen, T. (2020). Evaluation of the hypoglycemic effect of probiotics via directly consuming glucose in intestines of STZ-induced diabetic mice and glucose water-induced diabetic mice. *Journal of Functional Foods*, 64, 103614.
- WHO. (2021). *Antimicrobial resistance: Key facts*. World Health Organization.
- Young, J. (1996). *Functional foods: Strategies for successful product development*. FT management report (pp. 1–13). Pearson Professional Publishers.
- Young, T. M. (2008). *Beta glucan better immunity*. Retrieved from <http://youngagain.com/store/cart.php>