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Probiotic Supplements and Food Products: A Comparative Approach

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Abstract

Probiotics have a long overall history of traditional application. Currently they are mainly used as processed foods or nutritional supplements due to customers'awareness about the linkage of diet and health. The live bacteria exist in the probiotic products are mainly lactic acid bacteria, including lactobacilli, bifidobacteriaand Enterococci. Nowadays, the probiotic markets have a considerable markets share either in food or drug industry. However, the impact of ingesting probiotics via food products or drug supplements is not actually the same from consumer point of view as well as from efficacy. In this article, drug supplements and food products containing probiotic microorganisms are considered in a comparative approach from different aspects including functional and efficacy, hedonistic and economical standpoints.

Keywords: Food; Probiotic; Supplement

Introduction

Probiotics are live microorganisms or bacterial cultures able to endure the gastrointestinal tracts condition and be survived to supply healthful effects on the host by balancing the gastrointestinal microbiota [1,2]. Using microorganism as health improver has been increased since the mid-nineteenth century, and probiotics have been well assessed in both clinical and food trials and other prospective studies [3-5]. The main commercial probiotic species used in food and drug technologies are presented in Table 1. The *Lactobacillus* and bifidobacteriaspecies which were inspected more than 150 years ago are the predominately used probiotics up to now [6,7].

A probiotic strain to be used in food matrices and pharmaceutical applications must resist the conditions and interactions when incorporated in foods and drugs and be stable as well during passing throughout the gastrointestinal tracts [15]. It has been revealed that many strains are not as stable as required. This instability could be overcome by different techniques such as adjusting the compositional and process factors during manufacture of food and drug productsin favor of strains used, selecting more tolerant strains and using encapsulation process [1,16].

Commercial probiotics productsfor use of humans are available in two main forms including food products and drug supplements. In supplements, tablets or capsules, very high amounts of viable probiotic cells (at least 10^{10} cfu/mL) are carried through the body, while in food products; the cells are added into carrier foods or applied as starter probiotics in fermented foods. Therefore, a series of complex interactions and interventions is carried out in food matrices that might adversely affect the viability of initially inoculated probiotics in food before consumption.

Several health points have been attributed to probiotics, which increased the commercial attention in development of different applications leading to the rapid augment of this market segment [8]. Of these characteristics, the most agreed-upon are modulation of intestinal microflora, immune response enhancement, improved gastrointestinal health, and protection against infectious illness andinflammatory bowel disease (IBD) [7,9-14,]. Selecting and incorporating a probiotic strain to produce a safe and biological active final product in both food and pharmaceutical formulation contain different steps that are programmed in Figure 1.

Lactobacillus	*pseudocatenulatus*	*Leuconostoc*
acidophilus	*catenulatus*	*mesenteroides*
johnsonii	*bifidus*	*Pediococcus*
plantarum	*infantis*	*acidilactici*
rhamnosus	*longum*	*Enterococcus*
delbruecki	*thermophilus*	*faesium*
reuteri	*adolescentis*	*Lactococcus*
fermentum	*Streptococcus*	*lactis*
Brevis	*intermedius*	*Saccharomyces*
lactis	*salivarius*	*boulardii*
cellobiosus	*cremoris*	*Propionibacterium*
paracasei	*lactis*	*freudenreichii*
helveticus	*Aspergillus*	
Bifidobacterium	*niger*	
lactis	*oryzae*	

Table 1: The main probiotic species applied commercially in food and drug.

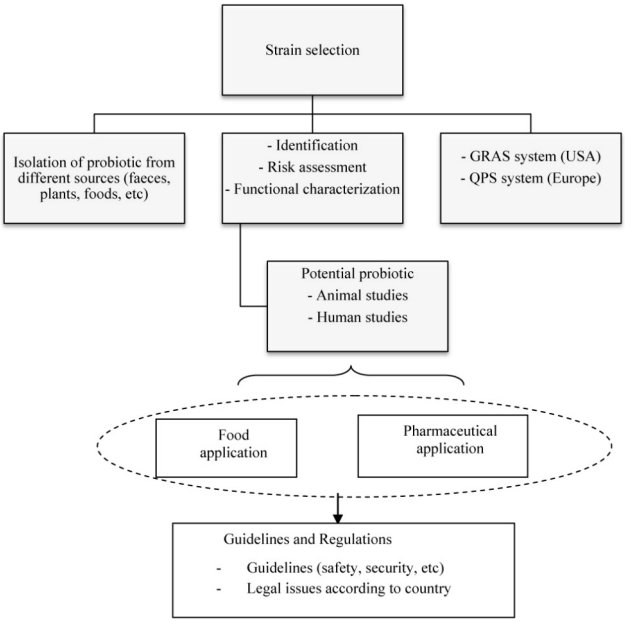

Figure 1: The sequential steps from probiotic selection to their application in final products.

Therefore, the matrix and process engineering in food probiotic production are nowadays an advanced and developed science and technology [17-19]. However, although production and maintenance of probiotic food products are considerably more difficult than the drug ones, the consumers are expected and enjoy inherently ingesting medicinal additives via food stuffs rather than the drugs. Having mentioned approach, this article reviews the functionality of probiotic food products in front of drug supplements in different aspects such as efficacy and effectiveness, hedonism, price and trade.

Probiotic Products

Oral consumption of probiotics could be occurred via drug products, namely supplements, and food products. They have their own characteristics and functions which are discussed below and are shown concisely in Table 2.

Probiotic dietary supplements

A dietary supplement (also might be called 'food supplement') is an orally administered substance designed to deliver a certain dietary ingredient, to complement the diet [20-22]. In other words, they are not substantially applied to treat or cure a specific human disease. They are usually packaged in different forms of capsules, tablets, powders (in sachets), or liquids in measured doses [23,24]. In order to produce a beneficial supplement, probiotic must be able to toleratethe severe conditions of gastrointestinal tract and arrive viable to the site of action [25-27]. This fact must be considered during supplement formulation, production and storage.

The manufacturing process of a dietary supplement is similar to medicines however the severe courses of action used in medicinal products are not necessary to pursue. Probiotic formulations comprise selecting microorganisms able to subsist throughout the technological process and remain viable subsequently with unaffected properties for long periods of storage [28,29]. The active element of aprobiotic supplement is the resistant probiotic microorganism(s) in a highly enough amount to guarantee precise dosing and good stability [30].

Stage	Parameter	Basis of effect
Cultures selection	Strain	Variation in the nature and quantity of genetically- determined cell components
Fermentation	Above optimal growth condition	Strains structure determined by fermentation condition in a way that mentioned parameters are able to enhance
	Sub- optimal growth temperature	exopolysaccharides production by some species and also change their lipid composition of cell membranes
	Sub-optimal pH	
	Presence of oxygen	
Concentration	Pumping during ultrafiltration	
	Pressure during centrifugation	The damages induced during ultrafiltration and centrifugation is able to decrease the ability of probiotic bacteria to resist the stress.
Stabilization	Freezing or drying	Freezing and drying condition damage the cell wall, membranes and intracellular components of probiotic bacteria. Consequently those exposed to freeze-dried condition are more prone to be damaged during food/drug or GIT stress.
Encapsulation	-	Free cells are exposed to stressful condition more rapidly compared to encapsulated ones.
Shipping	Temperature	Increasing the temperature enhance the cells damage.

Table 2: Parameters determined the ability of commercial probiotic cultures to survive stress conditions in food/drug preparation or in the gastrointestinal tract (GIT).

Lyophilizates of microorganisms are usually used to produce probiotic dosage forms. Lyophilization is a process widely used to preserve biological samples. However, the severe environmental conditions that the cells experienced during freeze-drying may damage their structure and physiology following by decrease in viability. To reduce these adverse effects, shielding agents are usually added to the samples before freezing or freeze-drying [29].

The endurance of probiotics in oral solid dosage forms, such as tablets, pellets, and capsules, have also been inspected in order to formulate a stable oral dosage forms. A strong negative correlation between bacterial viability and compression force was observed; revealing that probiotic survival decreased via increasing the tablet compaction forces [31].

Probiotic food products

Functional foods, which are given additional function, are paying growing attention nowadays due to people's awareness about the importance of food in human health [32-34]. Functional foods containing probiotics as biologically active ingredients create metabolic and physiological health effects more than their nutritional characteristics [35]. Despite of some scientific proofs state the creating of health benefits due to some microbial strains consumption, no clear suggestions indicate the effective dose for these strains. It has been accepted that higher numbers of viable bacteria are required to create probiotic foods efficiency. Different food matrices have the potential to be used as probiotic delivery systems which are discussed in the next:

Dairy products

Dairy products are the main group of foodstuffs able to transfer and deliver probiotic bacteria [36]. Today, the consumption of probiotic dairy products have been recommended considering their effectiveness on human health like reducing the lactose fanaticism, increasing the absorption of mineral and the efficacy against *Helicobacter pylori* infection, improvement and prevention of diarrhea and constipation [37,38]. Currently, different kinds of probiotic dairy products are produced and consumed all over the world including pasteurized milk, ice cream, fermented milks, cheese and baby milk powders. Milk and dairy products acquire some nutritional properties like the high lactose content which permit the growth and the existence of probiotic bacteria [17]. Some dairy products likefermented milks and cheesesare also preferred to be a vehicle for probiotic regarding their pH, buffering capacity, and fat content which create an additional protection for probiotics passing gastrointestinal tract and improve their maintenance [39-42].

Probiotic microorganisms are added to fermented milks by different methods including: addition as non-starter culture with the main aim of delivering through gastrointestinal tract, and addition as starter culture. Considering both the complex relationships between probiotic microorganisms and milk components and the inadequacy of probiotic to ferment milk lonely, in latter method, probiotics are mainly added to milk with assistant lactic starter cultures (mainly, traditional yogurt bacteria) [43,44]. However, the most accepted probiotic dairy products have been fermented ones like yogurts and other fermented milks, in which the oxygen exposing may decrease their functionality. Considering the fact that a great numbers of probiotic bacteria grow in anaerobic condition, keeping them maintained during refrigerator storage constitute a technological challenge. A potential alternative to enhance the survival of probiotic bacteria is using glucose oxidase enzyme [45]. The existence and viability of probiotic may also be influenced by processing condition and product environment.

Nondairy products

However dairy products are still the favored product to be used to incorporate probiotic bacteria, their high lactose and cholesterol content, their necessity to be stored at refrigerator temperature, the consumers demand for vegetarian based probiotic bacteria and even new taste and flavor are the motivation factors to produce nondairy products [46,47]. Accordingly, different types of probiotic contained non-dairy products have been produced during past two decades including juices and nondairy beverages, vegetable, cereal based products, chocolate based products, processed meats and etc. [32,33,48,49]. Production of a new non-dairy probiotic product should accomplish the consumer's demand for the products which are pleasant and healthy. So the development process of a new non-dairy probiotic product would be challenging either scientific or applied research [50,51]. In fact to design a new food, it is necessary to optimize the best formulation.

Regulatory Administration and Legislation of Probiotic Products

Considering the high growth rate of probiotic markets, the coordination of national and international regulations and rules are going to be extremely important to assess the efficacy and safety of probiotic bacteria. Considering that the risk of marketing false and ineffective probiotic products with untrue claims are always existed, it is necessary that these products be standardized and carried out essential requirements before being marketed. The regulatory necessities of probiotic products differed greatly among different countries regarding their anticipated use, whether as a food/food ingredient, a dietary supplement, and/or a drug [52,53]. In most countries, if a probiotic is going to be used as a drug, it must undertake the regulatory process of a drug same as other new therapeutic agent. In fact the probiotic drug safety and efficacy must be assessed and approved before marketing. In the case of probiotic dietary supplement, it is recognized as foods, and it isn't necessary to be evaluated or approval before being marketed. However, it is necessary that the regulatory standards on these probiotic bacteria be harmonized at the international level to guarantee their safety and efficacy to be effectively used in different countries around the world.

Probiotic bacteria are regulated by food and dietarysupplements in most countries because they are mainly taken orally as foods. Dietary supplements differed from drugs mainly considering their claims. Drugs are usually claimed to be effective in thetreatment, alleviation or cure of a disease, while foods, feed additives and dietarysupplements are considered as their general health claims [54,55].

Probiotics have been used by European Union (EU) customers by considering the fact no specific health claims on probiotic food labels is allowed by the agency responsible for evaluating the health claim proof in the EU, the European Food Safety Authority (EFSA). The European Commission also point out that the term 'probiotic' has a health claim in itself, consequently it should not be used for products with the lack of accepted health claims [52,53,56,57].

It must be considered that the valuable effect of probiotic microorganisms emerge when they arrive viable and in high enough counts after ongoing the GIT severe condition. In order to achieve the beneficial effects of probiotics in consumed food supplements/

processed foods, the minimum number of viable cells (cfu/g) must be consumed in products. Regarding to the International Dairy Federation (IDF) suggestion, this index is ≥ 10^7 cfu/g up to the time of its minimum durability [58]. Forbifidobacteria, viable count of ≥ 10^6 cfu/g has been approved in some countries such as Argentina, Prague and Brazil. This standard has been agreed >10^7 cfu/g in Japan [59]. In addition to the viability of probiotics in the product, the amount of product consumed is also determinable in its functionality and efficacy. Overall, considering bothmentioned, the recommendeddaily intake (DI) of each probiotic strain is estimated about 10^9 viable cells per day [1].

Suitable labeling and health claims are also the main requirement to provide a well-versed choice for the consumers [60,61]. Therefore, the subsequent information must be exhibited on the label:

a. Genus, species and strain which should pursue the standard international categorization;

b. Minimum viable numbers of each probiotic strain at the end of shelf life;

c. The serving size that delivers the effective dose of probiotic bacteria related to the health claim;

d. Appropriate storage conditions including the suitable temperature to be kept;

e. The recommended condition to be used.

Selecting Suitable Probiotic Cultures for Food Supplements or Processed Foods

Carrying foods are effective when the beneficial bacteria are added in a sufficient amounts and the conditions are set in a way to maintain their viability [62]. Different parameters affect the survivability of probiotic bacteria and their protection against challenges associated with food and supplement production and the gastrointestinal tract condition. These factors are summarized in Table 2.

The main aspect in formulation of a stable probiotic product is strain selection. Lactic cultures are well recognized for variability of their talents (even within a given species) to grow on food matrices as well as subsist heating, freezing, or storage in acid environments [63]. However, probiotic cultures intended for addition to foods were formerly chosen on the basis of their technological properties [64] the established health effects is the main factor must be considered nowadays. Selecting an appropriate condition during fermentation is a critical parameter that must be considered to prevent lethal or sub-lethal hurt to cells and also higher biomass yield [65]. Processing parameters change is able to affect the cell wall and/or the membrane positively or negatively. For example, fermentation temperature alters the composition of bacterial membranes [66]. It is also of great importance that survivability of the cultures to subsequent severe conditions will be increased using limited controlled stresses [67]. As an example, the exposure of *Lactobacillus delbrueckii* ssp. *Bulgaricus* cells to a heat pre-treatment at 50°C or to a hyper-osmotic pre-treatment will increase their viability to a lethal temperature challenge (65°C) [68]. Respecting to these two hypotheses it is obvious that biomass production parameters will alter the resulting probiotic cells and their viability.

Comparison of Probiotic Delivery Supplement and Probiotic Food Products

Probiotic supplements and food products can be compared from different points of view including efficacy, hedonism and sensory function, and economical aspect (price and marketing). These characteristics are compared below between the two products:

Efficacy

As mentioned previously the extent of health benefits related to probiotic products is determined by their abilities to deliver an efficient viable culture at their site of action. This viability will change during processing and storage exposing different conditions which are separately discussed in the next.

Factors influencing the probiotic delivery by food supplements

Food supplements are naturally rescued in caplets or capsules which their ability to deliver probiotics is mainly set at the production level. The main factors, influence the viability of probiotics during storage, are namely temperature, oxygen and relative humidity [62]. Generally, cultures must be kept refrigerated even if they are dried. It is observed that increasing the cultures temperature from 4 to 25°C during traditional freeze-drying courses results in a ten-fold stability reduction [69]. Some commercial products are able to be kept at room temperature over a few months without losses in their viability greater than 1 log [69]. It should be noted that to achieve such products the manufacturing setting must be highly specific and controlled [70]. Another problem is the diversity of death rate among different strains during storage. Therefore, the 'total' population in the product is proper the strain ratios might change during storage [71].

Moisture is the second restriction must be considered. Generally, dried cultures must have a water activity (a_w) around 0.1, and aw increasing above 0.3 decreased their viability [72]. It is obvious that the moisture in the air increase the a_w of the culture powder during storage. In order to prevent the cultures contact with water during storage, two actions are done by companies: 1) packing in water-resistant bottles or films; and 2) adding small moisture binding agent in bottles. These strategies are valid until the packaging is opened. So, the stability of the culture depends on the water absorbance of the product, especially when its packaging is repetitively opened.

Oxygen is another harmful factor to the viability of probiotics during storage. In order to overcome the detrimental effects of oxygen and increase the stability of product, companies usually add antioxidants in the drying medium. It is also some oxygen binder agents which their protection effects decreased when the product is opened.

Factors influencing the probiotic delivery by processed foods

Yogurtsare the first foods with probiotic bacteria, and fermented milks are the most important food vehicle for the delivery of probiotics even now [46]. However, other foods have now emerged which transfer probiotic bacteria like chocolate, cheese, sausage and cereal products. An assembly of food products suppresses lactic cultures and is subject to be fortified by probiotic bacteria [65]. There are three critical stages which may affect the viability of probiotic bacteria in processed foods, namely: a) the state of starter cultures addition to food matrix; b) processing condition; and c) storage condition.

Probiotic cultures are usually added to food matrixes in the state of frozen or dried. However, it seems easy, it will lose probiotics viability if done improperly. Certainly, the condition of thawing or hydrating influence the colony-forming units (cfu) counts. With respect to frozen cultures, thawing temperature is a critical parameter that must be considered, but different factors are important in the state of dried cultures like the composition of rehydration media, rehydration time and temperature and etc. Regarding to this fact, inoculation with frozen cultures seems much easier with lower mistakes [62].

Food processing includes different technological steps like addition of starter cultures to food matrix, blending, pumping, pasteurization and freezing which may be damaging for the viability of probiotic bacteria. In order to avoid viability losses during food processing, the two main approaches have been confirmed explicitly as following:

a. Adjusting the food matrix for example by pH adjustment (neutral pH is preferred), adding antioxidants, adding growth factors (prebiotics, plant or yeast extracts), selecting non-toxic ingredients (flavors, preservatives), and selecting adjusted and adapted starter cultures, applying inoculation rate, enzymes.

b. Adapting the process via for instance decreasing the storage temperatures, using vacuum or nitrogen flushing system in packaging.

While it appears easy to adapt media and processing setting it is not. Processed foods storage condition will influence the viability of probiotic bacteria as mentioned for food supplements. It warrants to be mentioned that storage not only influences the viability of cells but also the viable cells talent to endure the severe condition of the gastrointestinal tracts subsequently.

Hedonism and sensory function

Sensory analysis developed in the mid-19th century and gain greater importance at the end of the 1960s [45]. From a sensory evaluation viewpoint, reliability and validity are the two important issues which are basic to develop a convincing program and given that feasible approval within the context of a company's business and brand approach.

Generally, as a clear principle, people prefer to consume food rather than medicine and drug, because of hedonism from its sensory properties. This hint has been the philosophy of the birth of 'functional foods'. However, foods are preferable to drug provided that they do not possess off-flavor, off-texture and off-appeal after adding functional ingredients to food bases (such as probiotics).

Since sensory characteristics are based on consumers' preference and acceptance, it is required to assess the sensory effect of probiotics in food. The efficiency of probiotic foods must be as same as the performance of conventional foods [73]. Most of the studies concerning this issue conclude probiotic bacterial content less than 10% of total microbial content is not able to affect sensory characteristic of final product [74,75]. Some studies revealed the opportunity of probiotic foods to provide similar, or even improved performance compared to conventional ones like functional yogurt with *L. reuteri* RC-14 and *L. rhamnosus* GR-1 added [45]. The ability of probiotic cultures to decrease pentanal and n-hexanal amounts responsible for beany taste of soya improved its flavor in the case of soy-based probiotic foods [31]. Generally components produced during metabolism of probiotic cultures may have negatively effects on aroma and taste of the food product which create off-flavor. For example, the acetic acid which produced by *Bifidobacterium* spp. can create a vinegary flavor in the product. Masking is a technique that has been done by adding new substances to reduce the off flavors produced by probiotic cultures. It has been revealed that tropical fruit juices addition, mainly pineapple and mango positively change the aroma and flavor of the processed food to prevent the recognition of off-flavors produced by probiotic by the consumers [73]. It is worthy to mention that increasing the frequency of exposure to a food stimulus make the food stimuli have been better liked. So, repeated exposing and increased awareness to sensory off-flavors is able to change consumer outlook positively to increase their eagerness to use processed foods. Non-sensory techniques are able to increase the sensory quality of products like ensuring consumers by health advantage information related to probiotic cultures. It has been identified that health information is a great motivation to consume probiotic food products. Finally, microcapsules of probiotics may help prevent the off flavor of cultures [73].

Economicand trade aspect

Many factors including economical should be considered to designs a new product. Increasing in global health knowledge and their affinity to take supplements and processed food products is anticipated with the rise in global probiotics market [76]. According to recorded data, about 10% of global functional food market is occupied by probiotic industry which more than 84% of the probiotic market is processed foods following dietary supplements which represented 10 billion Euros in 2008 [76,77]. It is also documented that the overall probiotic supplement market alone was worth about $1.5 billion in 2008 [78]. Recent data reveal that products containing probiotic bacteria have a growth rate approximately 25% in North America and Eastern Europe, while the highest annually growth rates recorded for Asia and Western Europe are between 5 and 8% [78].

Conclusions

The importance of probiotic consumption to increase the quality of life is clearly illustrated by the scientific literature, and the numbers of food products or drug supplements which can be functioned by probiotics are growing. Different parameters including the probiotic viability in the product until the time of consumption as well as during delivery throughout the gastrointestinal tract (efficiency), sensory characteristic of product, the natural positive imagination of consumers for foods versus drugs, economical point of view and even the shelf life of products are important factors that determine the customer's consumption pattern. Drugs are able to transfer high numbers of viable probiotics into GIT without considerable loss during the storage. In contrast, the viable number of probiotics in food products especially fermented types can considerably decrease, but foods provide their matrix protection on probiotics during the delivery in GIT, particularly in dense ones such as cheeses. Foods have the advantages of being consumed for hedonism than supplements, the element that is crucially important for human kind. Food products have very high potential of variation and development compared to drug supplements and adding probiotics to them leads to considerable product and market development. Generally, designing the probiotic food formulation is more-to-much complex than drugs considering the stability of probiotics during the process and storage as well as achieving appropriate sensory characteristics, because probiotics mightnegatively change the sensory characteristics of foods. Also, probiotic foods can have more difficulties from regulatory administration and legislation standpoint compared to supplements.

Overall, for general usage, probiotic foods with high viability standards are superior to supplements, but for specific therapeutic applications, the latter is more efficient and therefore, preferred.

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