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Aloe vera and Probiotics: A New Alternative to Symbiotic Functional Foods

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Authors' contributions

This work was carried out in collaboration between all authors. Author RBCL designed the study. Author BCR wrote the protocol and analyzed the information. Author CHM produced the initial draft. Author SIM anchored the field study and performed preliminary analysis of document while authors CEJC and MSJ managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Providing products that beyond a high nutritional value brings health benefits to consumers is a major challenge to food industry. Functional foods, including prebiotics and probiotic as components, are the protagonists to promote these advantages. *Aloe vera* is a medicinal plant well characterized in terms of its chemical composition and therapeutic properties. Taking into account these characteristics *Aloe vera* represents an excellent natural source of prebiotics, as well as a substrate for lactic acid bacteria fermentation. Thus a symbiotic drink using *Aloe vera* as the main ingredient and lactic acid bacteria as probiotics with significant benefits to human health might represent a promising product to develop.

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1. INTRODUCTION

During the last few decades there has been an increase in the incidence of gastrointestinal disorders with many of them related to pathogenic agents [1,2]. Gastrointestinal disease is considered the third most common cause of death in the world [3]. In this context, the food industry has been facing the challenge to deliver products that will provide health benefits in addition to its basic nutritional value, such as probiotics, prebiotics or functional foods.

According to the World Health Organization probiotics are "live microorganisms" which when administered in adequate amounts promotes a health benefit on the host [4]. Probiotics are bacteria and the successful growth of these organisms depends on indigestible carbohydrates that are available in different plants and fruits. Several mechanisms of probiotic activity have been postulated, such as antimicrobial activity, improvement of the intestinal barrier and immunomodulation [5,6]. Collectively the nutrients that probiotics need for "survival" are called prebiotics, non-living components which provide a health benefit associated with modulation of the gut microbiota [7]. Symbiotic is the term used to describe dietary supplements or foods that contain both prebiotics and probiotics.

Lactic acid bacteria (LAB) are a group of Grampositive, non-sporulating, anaerobic or facultative aerobic cocci or rods, naturally present in raw food materials and in the human gastro-intestinal tract. These bacteria have been proposed as and are used as probiotic strains playing an important role in food production and health maintenance. LAB produces lactic acid as one of the main fermentation products of the metabolism of carbohydrates [8]. Probiotic bacteria have been widely recognized to have health benefits to the consumer such as effects on immunological functions, aiding in digestion, as well as protection against pathogenic bacteria such as Salmonella typhimurium, Helicobacter pylori, and Escherichia coli [9-13]. Despite consumers concerns with chemical preservatives and processed foods, LAB is easily accepted as a natural way to preserve food and promote their health [14].

So-called functional foods have been defined by the Food and Nutrition Board of the National Academy of Sciences as one that encompasses potentially healthful products, including "any modified food or food ingredient that may provide a health benefit beyond that of the traditional nutrients it contains" [15].

Nowadays consumers tend to search for more natural, organic, protein and non-processed foods due to health concerns. Plant-based products become an interesting alternative to include on consumer's diet. Aloe barbadensis Miller (Aloe vera) is a plant native from Africa well known for its considerable medicinal properties [16]. This plant is considered to be the most biologically active of the approximately 420 Aloe species identified and characterized till date. Aloe vera is an outstanding source of natural compounds and contains more than 200 different biologically active substances, including vitamins, minerals, polysaccharides, amino acids, anthraquinones, saponins, phytosterols and salicylic acids, among others [16,17]. Several studies have shown that Aloe vera and its constituents act as antimicrobial agents [18,19]. For this reason, as well as for its prebiotic properties, Aloe vera represents a valuable functional ingredient for the food industry [20].

Interest in *functional foods* has increased *over* the past several years with the market of probiotic dairy foods leading in sales in this food category [21]. On the other hand, few plant-based products with probiotic and probiotics activities have been developed.

This review provides an overview of the development of a probiotic and prebiotic *Aloe vera* enriched drink using a fermentative process with LAB. The current status of this technology, the microorganisms, substrate and the prebiotic – probiotic biotransformation affecting the lactic acid formation are summarized is also discussed.

2. PROBIOTIC MICROORGANISMS AND THEIR EFFECT ON THE HOST

This definition was later extended to include other health benefits such as their ability to modulate the immune system, as well as by their specification of mechanisms, site of action, delivery format, or host [22]. Probiotics attracted great interest in the last decades for their health promoting effects. The term "probiotic" was first used in 1965 by Lilly and Stillwell, describing them as substances secreted by one organism which stimulate the growth of another [23]. Afterwards, it was popularized by R. Fuller [24] being defined as a live microbial feed supplement which beneficially affects the host by improving its intestinal microbial balance.

Probiotics are bacteria that interfere and kill pathogens but different mechanisms are employed by these agents in preventing infection and disease from host to host. For example, researchers evaluated the potential antiviral activity of probiotic LAB employing animal and human intestinal and macrophage cell line models of non tumor origin [25]. Several probiotic strains were found to exhibit moderate to complete monolayer protection against rotavirus or transmissible gastroenteritis virus disruption. However, the highest protective effects were recorded with Lactobacillus rhamnosus GG and Lactobacillus Casei shirota strains against both rotavirus and transmissible gastroenteritis virus. Antiviral activities were also attributed to the following probiotic strains: Enterococcus faecium PCK38, Lactobacillus fermentum ACA-DC179, Lactobacillus pentosus PCA227 and Lactobacillus plantarum PCA236 and PCS22 [25]. This study demonstrated that probiotic bacteria can activate macrophages to release reactive oxygen species that inhibits cytokines which controls viral infections and helps to protect the host from those infections.

and Another very interesting successful application of probiotics has been explored in apiculture (beekeeping). Evans and Lopez have investigated the effect of probiotic bacteria to induce immune system activation in the honey bee (Appis mellifera L.) toward Paenbacillus larvaelarvae. а Gram-positive bacterium responsible for the widespread Honey Bee disease known as American foulbrood [26]. These researchers demonstrated that probiotics enhanced immune responses in the bee by stimulating the production of antimicrobial peptides to protect against Paenibacillus infections.

Probiotics have also been used to control pathogenic agents that affect theshrimp aqua farming industry in New Caledonia. Farmed shrimp production has been affected by two bacterial diseases: Winter Syndrome caused by *Vibrio peneicida* and Summer Syndrome caused by *Vibrio nigripulchritudo*. The probiotic *Bacillus* strains have been used with success in lowering the abundance of the pathogenic vibrios by

colonizing the shrimp intestinal tract and displacing vibrios in the gut [27].

Overall, probiotic agents block sites pathogenic agents need for adherence to surfaces and simultaneously activates innate and adaptive components of the immune system.

Probiotics are limited to products that 1) contain live microorganisms, 2) have the ability to improve the health and well-being of humans or animals (including growth promotion of animals), and 3) can affect all host mucosal surfaces, including the mouth and gastrointestinal tract, the upper respiratory tract, or the urogenital tract [28].

3. LACTIC ACID BACTERIA AS PROBIOTIC AGENTS

Lactic acid bacteria are industrially important organisms recognized for their fermentative ability, as well as their health and nutritional benefits [29]. Some species of LAB are components of the normal human intestinal microflora and play an important role in the normal function of digestive tract, as well as in the prevention of intestinal disorders. These bacteria have been widely used as starter cultures for fermentation in the dairy products. like cheese, yoghurts, fermented milk products. as well as in meat, beverages and other food industries [30,31]. Due to their antimicrobial potential these food-grade bacteria are also used as biopreservatives improving the safety, shelflife, nutritional value, flavour and quality of products [32]. The heterogeneous group of LAB used for food fermentations includes, according to morphology, the rod-shaped bacteria genus Lactobacillus, and coccisuch like as Streptococcus, Lactococcus, Pediococcus and Leuconostocs (Table 1). Several studies report the probiotic effect of LAB [33]. Some species involved are Lactobacillus acidophilus, L. casei, L. johnsonii, L. fermentum, L. rhamnosus, L. plantarum, L. reuteri, L. salivarius, L. paracasei, L. delbrueckii subsp. bulgaricus, Saccharomyces boulardii. Streptococcus thermophilus, Bifidobacterium lactis, B. longum and B. breve.

Low pH, gastric enzymes and bile salts are some of the gastrointestinal tract barriers that probiotic bacteria need to resist after being ingested [35,36]. Lactic acid bacteria are known for being acidophilic, which means they are tolerant to low pH values [37]. Menconi and others [38] studied the physiological properties of two strains of lactic acid bacteria (LAB 18 and 48) present in a commercial probiotic culture. They concluded that both strains had tolerance to pH 3.0 and a high bile salt concentration (0.6%). These are important characteristics of lactic acid bacteria that should be evaluated when selecting strains to be used as probiotics. Antimicrobial activity of these effective isolates may contribute to efficacy, possibly by direct antimicrobial activity in vivo. These are important characteristics to be evaluated in lactic acid bacteria when selecting strains to be used as probiotics. Table 2 shows pH and temperature tolerances of some LAB.

Another important characteristic that differentiate LAB is their metabolic pathway of carbohydrates fermentation under standard conditions (excess sugar, growth factors like amino acids, vitamins and nucleic acid precursors, and limited oxygen availability). LAB can be divided into two groups: homofermentative and heterofermentative bacteria. Homofermentative LAB convert sugars almost quantitatively to lactic acid, and heterofermentative LAB produce in addition to acid considerable lactic amounts of ethanol/acetic acid, and carbon-dioxide (CO2). In practical terms, a test for gas production from glucose fermentation allows to distinguish the two groups [41]. The main feature of the metabolism of LAB is the degradation of different carbohydrates and related compounds to acid lactic. This process is coupled with energy (adenosine-tri-phosphate = ATP) production.

Fermented foods and beverages	Lactic acid bacteria*
Dairy products	L. lactis subsp. lactis, L. lactis subsp. cremoris
- Hard cheeses without eyes	
- Cheeses with small eyes	L. lactis subsp. lactis, L. lactis subsp. lactis var.
	diacetylactis, L. lactis subsp. cremoris, Leuc.
	menesteroides subsp. cremoris
 Swiss-and Italian-type cheeses 	Lb. delbrueckiisubsp.lactis, Lb. helveticus, Lb. casei,
	Lb. delbrueckiisubsp.bulgaricus, S. thermophilus
 Butter and buttermilk 	L. lactis subsp. lactis, L. lactis subsp. lactis var.
	diacetylactis, L. lactis subsp. cremoris, Leuc.
	menesteroides subsp. cremoris
- Yoghurt	Lb. delbrueckiisubsp.bulgaricus, S. thermophilus
 Fermented, probiotic milk 	Lb. casei, Lb. acidophilus, Lb. rhamnosus, Lb.
	johnsonii, B. lactis, B. bifidum, B. breve
- Kefir	Lb. kefir, Lb. kefiranofacies, Lb. brevis
Fermented meats	Lb. sakei, Lb. curvatus
 Fermented sausage (Europe) 	
 Fermented sausage (USA) 	P. acidilactici, P. pentosaceus
Fermented vegetables	Leuc. mesenteroides, Lb. plantarum, P.
- Sauerkraut	acidilacticiLeuc. mesenteroides, P. cerevisiae, Lb.
	brevis
- Pickles	Lb. plantarum, Leuc. mesenteroides, Lb. pentosus, Lb.
	plantarum
 Fermented olives 	P. acidilactici, P. pentosaceus, Lb. plantarum
 Fermented vegetables 	Lb. fermentum
Fermented cereals	Lb. sanfransiscensis, Lb. farciminis, Lb. fermentum, Lb.
- Sourdough	brevis, Lb. plantarum, Lb. amylovorus, Lb. reuteri, Lb.
	pontis, Lb. panis, Lb. alimentarius, W. cibaria
Fermented fish products	Lb. alimentarius, C. piscicola

Table 1. LAB associated with fermented foods and beverages [34]

*B.=Bifidobacterium, C.=Carnobacterium, L.=Lactococcus, Lb.=Lactobacillus, Leuc.=Leuconostoc, O.=Oenococcus, P.=Pediococcus, S.=Streptococcus, T.=Tetragenococcus, W.=Weissella

Table 2. Tolerance conditions of LAB

Bacteria	рН	Temperature	References
Lactobacillus casei	2.5	15 - 45℃	[39]
Pediococcus acidilactici	6.5	50℃	[40]
Lactococcus lactis	9.2	40 ℃	[40]
Enterococcus casseliflavus	9.6	10 ° C	[40]

From several sugars occurring in foods, hexose is most often the substrate for lactic acid bacteria. The two major pathways of hexose fermentation by LAB differ in the way in which the C6 skeleton is split and this yields different sets of end-products. The homofermentative LAB theoretically produce two molecules of lactic acid from one molecule of glucose using the Embden-Meyerhof pathway (glycolysis) [41]. Other sugars such as mannose, galactose and fructose are also fermented by many LAB. These sugars enter the major pathways of glycolysis after isomeration and/or phosphorylation. In further of the fermentation process steps the phosphorylated hexose is split by the enzyme aldose into triosephosphates and then through oxidation and dephosphorylation to pyruvic acid. The final reaction of the fermentation process is the reduction of pyruvic acid to lactic acid. Homofermentative LAB include Lactococcus spp. that are widely used in dairy starter culture applications where the rapid development of lactic acid and reduced pH is desirable. Other homofermentative LAB include yogurt strains consisting of rods (Lactobacillus delbruckii subspecies bulgaricus, Lb. acidophilus) and (Streptococcus salivarius cocci subsp. thermophilus) and thermophilic strains that might be used in cheese (Lb. helveticus) [42,43]. Other homofermentative cocci that might be found in milk and dairy products, but are rarely used as starter cultures include other Streptococcus spp... Enterococcus, Pediococcus and Aerococcus.

With the exception of certain fermented milk products, heterofermentative LAB are rarely used as dairy starter cultures, but they are commonly found in milk and dairy products. At significant numbers these LAB can cause defects related to their acid and CO₂ production, such as slits in hard cheeses or bloated packaging in other dairy products [44]. Heterofermentative LAB include Leuconostoc spp. (Gram-positive cocci) and Gram-positive rods such as Lactobacillus brevis, Lb. fermentum, and Lb. reuteri. Pentoses are sugars readily fermented by heterofermentative LAB. In the cell these sugars are converted to ribulose-5-phosphate or xilulose-5-phosphate by epimerases or isomerases, and then enter the pentose-phosphate pathway [45]. Then the resultant xylulose-5-phosphate is split by the phosphoketolase enzyme to yield а triosephosphate that is converted to lactic acid, and acetyl phosphate that is a precursor of either ethanol or acetic acid depending on the oxidation-reduction potential of the system.

In addition to the main two metabolic pathways of LAB connected to fermentation of carbohydrates, LAB nitrogen metabolism is related to hydrolysis and synthesis of proteins. These processes play a significant role in cheese production [46].

Plant-derived LABs are usually found in fermenting fruits, vegetables or traditional foods and pickles in Asia. Plant-derived LABs were first investigated in Japan [47]. These studies focused on the isolation of acid and bile tolerant LAB, and it was found that plant-derived LAB are much more resistant to artificial gastric juices and bile than animal-derived LAB.

4. PREBIOTICS AND THEIR STRUCTURE

There is a great interest in the use of prebiotics as functional food ingredients since they promote the growth of the beneficial/probiotic microorganisms Bifidobacteria and Lactobacillae present in the gastro-intestinal tract, thereby improving consumer's health. Among prebiotics, dietary fibers, i.e. oligosaccharides, are the most represented components [48]. These nondigestible complex carbohydrates are naturally present in plant sources like chicory, onion, garlic, asparagus, artichoke, bananas, and many others [49]. Prebiotics can also be produced by microorganisms and their enzymes through the fermentation processes. The classification of prebiotic as food or a food ingredient requires a scientific demonstration that it:

- resists gastric acidity, hydrolysis by mammalian enzymes and gastrointestinal absorption;
- is fermented by intestinal microflora;
- selectively stimulates the growth and/or activity of intestinal bacteria associated with health and well-being [7].

Prebiotics fermentation in the gut generates short-chain fatty acids and, in particular, acetic acid, propionic acid, and butyric acid which provide energy to microbiota as well as to epithelial cells [50]. The most common prebiotics include galacto-oligosaccharides (GOS), fructo-oligosaccharides (FOS), xylo-oligosaccharides, soybean-oligosaccharides, inulin, lactulose, lactosucrose, among others; nevertheless, the best-known and studied are inulin, GOS and FOS from plants are the best-known sources of prebiotics [51,52].

Common name	Scientific name	Compound	References
Sabila	Aloe vera	Fructans	[54]
Agave	Agavesalmiana	Fructooligosacharides	[55]
Agave	Agave fourcroydes	Fructans	[56]
Agave	Agave angustifolia	Fructans	[57]

Table 3. Plants with prebiotic potential grown in Mexico

extensive literature search developed Α by Dwivedi and others [53] revealed the presence of prebiotic carbohydrates in a considerable number of food crops, with vegetable and root and tuber crops being the predominant sources including garlic (Allium sativum L.), Jerusalem artichoke (Helianthus tuberosus L.), leek (A. ampeloprasum L.), okra (Abelmoschus esculentus L. Moench), onion (Allium cepa L.) and shallot (A. cepa L. var. aggregatum) among vegetables; dragon fruit (Hylocereus species), jack fruit (Artocarpus heterophyllus Lam), nectarine (Prunus persica L. Batsch), and palm fruit (Borassus flabellifer L.) among fruits; chicory (Chicorium intybus L.) and vacon [Smallanthus sonchifoliu (Poepping and Endlicher) H. Robinson] among root crops: or the tuber crops dahliya (Dahlia species) and gembili (Dioscorea esculenta (Lour.) Burk.) as major sources of FOS. Table 3 presents some plants with prebiotic activity that are of great relevance in Mexico, such as Aloe vera (known as Sabila) and Agave.

FOS are polysaccharides also known as fructans of inulin. FOS are linear polymers of D-fructose linked by links glycosidic β (2 \rightarrow 1), some with a terminal glucose, and occur in many higher plants as reserve carbohydrates. On the other hand, GOS are polymers of galactose and have been recognized as safe by the American Food and Drug Administration (GRAS- FDA) since they are components of human milk, and the traditional yogurt that is produced by resident intestinal bacteria that producing β-galactosidase from the ingested lactose [58]. They are produced commercially from lactose using activity galactosiltransferase of β-galactosidase, which is the main enzyme in the hydrolysis of lactose in high concentrations of the latter [59].

5. *Aloe vera* AND ITS PREBIOTIC CHARACTERISTICS

Aloe barbadensis Miller (Aloe vera) has a long history of use as a topical and oral therapeutic. It is an acaulescent, perennial plant, and belongs to Xanthorrhoeaceae family. Aloe vera is a native plant of the Mediterranean region but it can be found all over the world [60]. The Aloe vera leaf (Fig. 1) can be divided into two main fractions: which the green skin, is in 1.8dihydroxyanthraguinone derivatives and their glycosides, and the colour less pulp that it is richer in complex carbohydrates [54]. Aloe vera has a thick epidermis (skin) covered with a cuticle surrounding the mesophyll, which can be differentiated into chlorenchyma cells and thinner walled cells forming the parenchyma (fillet) [54,61]. Mucilaginous jelly like parenchyma is referred to as Aloe vera pulp or gel. This gel has a large content of water (95-99%), and contains proteins, lipids, amino acids, vitamins, enzymes, inorganic compounds, and small organic compounds in addition to the different carbohydrates [61.62]. Chemical components of Aloe vera are shown in Table 4. Acemannan (acetylated gluconmanan), also known as carrysin, is probably the best known among the polysaccharides found in Aloe vera gel [54,63].

Aloe vera is a source of essential micronutrients and active phytochemicals such as ascorbic acid, tocopherols and phenolic compounds which are able to reduce the free radicals that cause reactions of oxidation associated with cardiovascular diseases, carcinogenesis and aging [64-66]. Many biological activities, including antimicrobial, laxative. protection against radiation, antioxidant, antiinflammatory, anti-tumour, anti-diabetic, antiwell hypoglycaemic. allergic. as as gastroprotective, immunomodulatory and woundhealing effects, have been attributed to this [67-70]. Some plantgel studies have demonstrated that the biological activities of Aloe vera may be related to a synergistic action of several compounds rather than to a single chemical substance [54,71].

Vega and others [72] state that the nutritional and functional properties of *Aloe vera* are attributed to minerals, hydrosoluble vitamins and glucomannan. Taking into account the chemical composition and structure of *Aloe vera*, this plant represents an important and natural source of prebiotis. Cuvas-Limón et al.; ARRB, 9(2): 1-11, 2016; Article no.ARRB.22622



Fig. 1. Micrographs of Aloe vera (Barbadensis Miller) leaf and pulp. Magnification: 10x and 100x

Group	Compound
Antraquinones	Aloetic acid, cinamic acid, barbaloın, crisofanic acid, emodin, aloe emodin,
	cinnamic acid ester, aloin, isobarbaloın, anthracene.
Vitamins	Folic acid, vitamin B1, vitamin C, vitamin B32, vitamin E, vitamin B,
	betacarotene.
Minerals	Calcium, magnesium, potasioum, zinc, sodium, copper, Iron, manganese,
	phosphorus, chromiun.
Carbohydrates	Celulose, galactose, glucose, xilose, manose, arabinose, aldopentose,
•	glucomanose, fructuose, acemanan, pectic sustance sustance, L-ramnose.
Enzims	Amilase, cyclooxydase, carboxypeptidase, lipase, bradikinase, catalase,
	oxidase, alkaline phosphatase, xyclooxygenase, superoxide dismutase.
Lipids and organic	Steroids, salicylic acid, potassium sorbate, triglycerides, lignin, uric acid,
compounds	saponins, gibereline, triterpenos.
Aminocids	Alanin, spartic acid, arginin, glutamic acid, glycin, histidine, isoleucine,
	lysine, methionine, phenylalanine, proline, tyrosine, threonine, valine.

Table 4. Chemical components of the Aloe vera plant (Barbadensis Miller)

6. Aloe vera AS A SUBSTRATE FOR LACTIC ACID BACTERIA FERMEN-TATION

Despite of numerous biological activities of *Aloe vera*, particularly antimicrobial and antioxidant activities, the leaf gel is prone to oxidation, which leads to fermentation. According to Estaban-Carrasco and others [73] this phenomenon might be explained to the degradation of phenolic compounds in *Aloe vera* that can be related to a defense mechanism of the plant. Thus, the oxidation of phenolic compounds results in bacterial growth.

There have been very few studies conducted on *Aloe vera* fermentation. Kim and co-workers [74] have developed a preliminary investigation of *Aloe vera* pulp fermentation and found the presence of lactic acid bacteria (LAB). Based on these findings they hypothesized that LAB can produce compounds with antimicrobial activities in the pulp of *Aloe vera* and that these bacteria could proliferate after plant's antimicrobial compounds deteriorate. These researchers isolated five novel *Lactobacillus brevis* strains from naturally fermented *Aloe vera* pulp and evaluated their probiotic properties, i.e., antimicrobial activity and tolerance to acid and bile salt. These strains showed high tolerance to

acid, surviving in pH2.5 for up to 4 hours, and were resistant to 5% bile salts at 37℃ for 18 hours. Due to its tolerance to acid and bile salts, one strain passed through the gastric barrier and colonised the intestine after oral administration. All five strains were able to inhibit the growth of several harmful enteropathogens (C. jejuni and C. perfringens, S. aureus, Salmonella, E. coli) without restraining most of normal commensals bacteria in the gut. Researchers named these LAB as POAL (Probiotics Originating from Aloe Leaf) strains. Additionally, each strain exhibited discriminative resistance to anample range of antibiotics (tetracycline, norfloxacin, sulfatrimethoxazole, colistin, and the common Gram-negative antibiotics). The L. brevis POAL strains also expressed high levels of the glutamate decarboxylase (GAD) gene which produces a beneficial neurotransmitter, yaminobutyric acid. These results suggest that the novel L. brevis strains can be considered as potential food additives and resources for pharmaceutical research. Overall this study also showed that probiotic bacteria may enhance the therapeutic value of *Aloe vera* products and that these bacteria strains may be useful resources the development of antibiotics for and antimicrobial substances.

Finally, considering the chemical and therapeutic characteristics of *Aloe vera* and the development of LAB as a starter culture using this plant as substrate for their fermentation, it might be possible to obtain a symbiotic drink with prebiotics and probiotics that will beneficiate human health.

7. CONCLUDING REMARKS

Functional foods development using plantderived ingredients have great potential to expand due to the increased consumer desire to improve health through food. The purpose of a symbiotic drink using *Aloe vera* as a substrate for LBA fermentation is to increase the number of probiotic bacteria that become established in the digestive tract and provides health benefits. More research is needed in order to confirm whether a symbiotic product using *Aloe vera* as a substrate for LAB fermentation might have a greater effect on consumer's health than individual prebiotic and probiotic products.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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