Editorial

Alimentos funcionales y biotecnología

Functional foods and biotechnology

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The modern lifestyle has a strong impact on dietary habits with growing consumption of processed and fast food that has evident adverse effects on health. Food in the western world is associated with pleasure to the extent that the compromise between gratification and health is a dilemma in our society. Health problems associated with dietary habits, such as diabetes, cancer, heart failures, allergies and obesity, equally affect adults and children and have a strong impact on developing countries, where the harmful effects are more evident than in developed countries due to economic limitations (Ezzati *et al*. 2005).

Functional foods have arisen in this context as those that provide health benefits beyond their nutritional function, which is why they are also called health foods. This kind of food has a long tradition in eastern countries where many traditional foods have been recognized as having health benefits. The term "functional food" was coined in Japan in the 1980s, and in 1991, Japan's Ministry of Health, Labor and Wellfare established a set of standards to name a special category of food with health benefits called FOSHU (Foods for Specified Health Uses). This concept refers to food that contains ingredients with health functions for which the declaration of their physiological effects on consumers is authorized. Striving for greater accuracy, food is considered to be functional if beyond its nutritional effect, it promotes one or more physiological functions in the human body, improving the general physical condition and/or reducing the risk of illness. An essential aspect is that the amount and form of consumption must be regular in the diet, which is why functional foods are primarily a food and not a medicine. However, functional foods can contribute to the prevention and treatment of illnesses, in which case, they are called nutraceuticals. It is clear that the trends of our contemporary society and demographic evolution advise the consumption of functional food, which can now be considered to be a sustainable global tendency and not just another passing trend, which is supported by the growing number of them that enter the consumer market every year (Bigliardi and Galati, 2013). The great relevance that functional foods have acquired is clearly established in a recent publication by Boye (2015), which exhaustively explores the topic with special emphasis on technological developments and challenges.

There is a growing awareness among consumers of the importance of diet on the state of health, which is accentuated by the aging population and increased life expectancy; phenomena that are not exclusive to developed countries, but that are also evident in Latin American countries. In turn, this scenario generates a great opportunity and great challenge for the food industry, which is responsible for responding to the growing demand for functional food. The food industry is not considered to be a greatly dynamic sector in research and development, so functional foods represent an important lever for development in the sector. In effect, a significant part of the evolution experienced by the food industry is linked to the development and replacement of products based on health and nutrition considerations and compliance with the provisions that regulate them (Annunziata and Vecchio, 2011).

Functional foods may be natural foods, foods that have had some component added, removed or modified, or those where the bioavailability of one of the components has been modified. A clear example of a functional food is lactose-free milk from which the lactose has been removed through its enzymatic conversion to glucose and galactose. This permits the consumption of milk by people with a lactose intolerance; a phenomenon that affects an important part of the Latin American population. Initially, functional foods primarily referred to enrichment with vitamins and minerals. Later, enrichment with nutrients

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such as soluble fiber, phytosterols and omega-3 fatty acids gained importance (Siró *et al.* 2008), and currently, many products on the market are considered to be functional foods.

A crucial aspect of functional foods is the regulation and declaration of their health effects, which greatly varies from one country to another. In the European Union, the emphasis is on regulations in terms of safety of consumption, while in the United States of America, special importance is given to the declaration of their effects. This is not a trivial problem, because although these foods or their components may alleviate or prevent illnesses, generally, there is not sufficient scientific evidence to identify the effective ingredient and to substantiate its effectiveness and safety of use. As there is no rigorous regulation on functional foods in many countries, it is therefore difficult to establish the scientific validity of the declaration of their health effects (El Sohaimy, 2012).

Consumer acceptance is a key aspect of functional foods, which to their benefit are not generally perceived as a separate category from natural foods. However, their acceptance is not unconditional, and the product's quality and appearance, as well as the clarity of its declaration, are important factors for its acceptance. It has been indicated that level of education, geographical origin and gender are variables regarding perception, and that doctors' and dietitians' attitudes are important (Cha *et al.* 2010).

An important part of health foods currently on the market are linked to the dairy industry, with bakery, children's food, candy and soft drinks also being notable. A large part of functional foods are designed for intestinal health, which is a very important determinant in general health. Therefore, probiotics and prebiotics acquire special importance in functional foods.

The World Health Organization (WHO) and the Food and Agriculture Organization (FAO) of the United Nations have defined probiotics as "live microorganisms which when administered in adequate amounts confer a health benefit on the host". Many microorganisms are potentially probiotics, but this condition is primarily associated with the *Bifidobacterium* and *Lactobacillus* genera. The requirements for a microorganism to be considered a probiotic are its survival during its passage through the gastrointestinal tract and scientific proof of the health benefits it confers on its host. It must be proven to be non-pathogenic; to be genetically and physiologically stable in its place of action and throughout the whole process of preparation and storage in the food matrix that contains it; and to have a production process that can be carried out on an industrial scale. Different benefits have been declared for probiotics; the majority of them for intestinal health, including relief of lactose intolerance and irritable bowel syndrome, prevention and reduction of diarrhea, reduction of risk of intestinal cancer, reduction of blood cholesterol, stimulation of the immune response and inhibition of pathogens of the gastrointestinal tract (Vasiljevic and Sha, 2008). However, the majority of these studies are considered to be preliminary and therefore, there is still much to learn about probiotic mechanisms of action, which have mainly been proposed based on *in-vitro* studies, which have a debatable predictability of *in-vivo* action. Prebiotics mainly act on the intestine, although beneficial effects on the system as a whole have been observed in some cases (Kellow *et al.* 2014).

Correct dosage and frequency of consumption are perhaps the least clear aspects of using prebiotics. The recommended dosage must be based on efficacy studies in humans, but this depends on many factors with an effect that is difficult to determine or predict. Despite this, as well as insufficient knowledge of mechanisms of action, insufficient documentation of the health effects and limited clarity about regulatory aspects, the probiotic market is experiencing accelerated growth in synchrony with the world trend toward a healthy diet, which is increased by the growing use of probiotics in food for pets and livestock.

The development of probiotics has been strongly driven by progress in biotechnology. New isolated probiotic strains of natural and probiotic niches produced by genetically modified organisms (GMOs) have widened the spectrum of organisms with improved probiotic properties for their incorporation into functional foods. Until now, the use of GMOs has been scarce due to the reservations of consumers, who in principle are open to the use of GMOs for the treatment of severe illnesses, but reluctant toward their use as health promoters (Gupta *et al.* 2014). Like in other situations, these reservations should gradually decrease as the safety of consumption is solidly sustained. On the other hand, progress in knowledge of probiotic mechanisms of action and the dynamics of intestinal populations are strongly linked to techniques developed in biotechnology such as gene amplification through polymerase chain reaction (PCR), denaturing gradient gel electrophoresis (DGGE) and fluorescence *in situ* hybridization (FISH).

Prebiotics have been defined as non-digestible food ingredients that cause specific changes in intestinal microbiota composition and/or activity conferring health and wellbeing on the host (Roberfroid, 2007). The International Life Sciences Institute (ILSI) Europe Prebiotics Task Force has echoed said proposal, defining prebiotic action as the selective stimulation of growth and/or activity of a limited number of microbial species in intestinal microbiota that confer health and wellbeing on the host (Roberfroid *et al.* 2010). The probiotic has an indirect effect as it is not the compound itself, but the effect that it causes on the intestinal microbiota that confers health and wellbeing. Prebiotics stimulate the endogenous microbial population, while probiotics involve the addition of exogenous microbial species. Therefore, it is to be expected that prebiotics are more effective and their action is more predictable than probiotics that with their passing through the gastrointestinal tract and implantation add uncertainty regarding their effectiveness.

Different physiological effects related to health have been associated with prebiotics: improvement and stabilization of intestinal microbiota; improvement of intestinal function; reduction of pathogenic bacteria; reduction of metabolic endotoxins; increased mineral absorption; improvement of the morphology of intestinal mucosa due to the promotion of mucin synthesis; stimulation of antibiotic synthesis; relief of irritable bowel syndrome; control of the sensation of appetite and bodyweight; reduction of the risk of colon cancer and type-2 diabetes; anti-inflammatory effect; and regulation of anxiety and depression (Mcfarlane *et al*. 2008). The accepted criteria for a food ingredient to be considered a prebiotic are resistance to the breakdown of acids and enzymes during its passage through the gastrointestinal tract, fermentability by colonic microbiota, selective stimulation of beneficial colonic bacteria and functional stability in the processing and storage conditions of the food matrix that contains it. Selective fermentation by colonic microbiota is the most rigorous criterion and the most difficult one to conclusively prove (Rastall and Gibson, 2015).

There are many substances that may be considered to be prebiotics, however, the majority of them are non-digestible oligosaccharides (NDOs). Their prebiotic effects are mainly related to stimulation of the production of short-chain fatty acids (SCFAs), which reduce pathogenic microbiota and selectively stimulate the population of probiotic bacteria (mainly Bifidobacteria and also Lactobacilli) by reducing the intestinal pH. However, there are specific effects associated with these SCFAs, such as the effect of the propionate on the reduction of cholesterol synthesis and excretion of adipose tissue, which has been associated with depressing appetite and obesity, and the effect of butyrate considered to be a regulator of intestinal homeostasis. Out of the NDOs, those strictly considered to be prebiotics based on sound scientific evidence are fructans: inulin and fructooligosaccharides (FOS), and galactans: galacto-oligosaccharides (GOS) and lactulose. Other NDO candidates that satisfy some but not all of the criteria to be considered prebiotics are isomaltooligosaccharides (IMOS), xylooligosaccharides (XOS), soy oligosaccharides (SOS) and gluco-oligosaccharides (GlOS). Although it is probably not the most effective prebiotic, inulin is the one most used in the creation of functional foods, additionally providing textural and rheological properties to the food matrix that contains it (Karimi *et al*. 2015).

The contribution of biotechnology to the production of prebiotics is notable. Apart from inulin, a fructose polymer produced by the extraction of natural products (mainly chicory), other prebiotics are produced by bioprocesses with the intervention of microorganisms or enzymes specifically conditioned for the efficient synthesis of NDOs. FOS are NDOs comprised of fructose units (usually between 2 and 6) joined at a glucose terminal. They are obtained by controlled enzymatic hydrolysis of inulin or by synthesis from sucrose through soluble or immobilized glucosyl transferase enzymes, or cells rich in said activity (Dominguez *et al*. 2014). GOS are NDOs comprised of fructose units (usually between 2 and 5) joined at a glucose terminal. They are obtained by transgalactosylation of lactose through β-galactosidases in a kinetically controlled reaction in which the lactose acts as a donor and receptor of the galactosyl groups. The process is particularly attractive as it uses lactose as the only substrate, which can be obtained at very low prices as a byproduct of cheese-making and it is a low cost enzyme wildly used by the food industry in the hydrolysis of lactose in milk and dairy products. In this case, β-galactosidase is not used in its potential of hydrolysis (rupture of the β-1.4 link of lactose), but in its potential of synthesis (formation of β-1.4 type links or similar). This requires depression of the system's water activity, which is achieved by working with very elevated concentrations of lactose (Vera *et al*. 2012). GOS have a special application as a functional component in dairy products. They are notably used in special milk products for unweaned babies with formulas based on cow's milk, where they represent a special component as immunostimulants, because human milk has an elevated GOS content and they fulfill said essential role, while cow's milk has a very low GOS content. With dairy foods being the main products for their functioning through the addition of prebiotics, GOS are particularly attractive from an industrial perspective, as the whole process is exclusively for the same kind of industry. Additionally, GOS are very stable NDOs thermally and regarding pH, which ensures their integrity during processing of the food and consumption to its place of action in the colon.

Functional foods now represent a solidly established trend toward a healthy diet in response to erroneous dietary habits encouraged by contemporary modern living. Consumption of functional foods is no longer just a sophistication of the most developed countries. On the contrary, the trend for their consumption in Latin American countries has experienced a notable increase, which with the contribution of biotechnology should result in better quality products at a lower cost, contributing to social integration with respect to diet. There are many options for research and development in the area, which must be adopted by our researchers as a very favorable model to provide significant added value to the raw materials that are so abundant Latin America.

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