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Cactus Mucilages : Nutritional, Health Benefits and Clinical Trials

Mauricio A. Ondarza

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Research Center for Assistanship on Technology and Design for the Jalisco State,Mexico.E-mail : biochem93@hotmail.com

ABSTRACT

For a better understanding of the central function of the intestinal flora, we must know that intestines are constituted naturally by nearly 100 trillions of bacteria, which by the way represents more than 10 times the number of totally cells in our whole body. Those trillions of bacteria are distributed by 500 or 1000 different species that form our intestinal microbiota or flora. Speaking about the fragile equilibrium of our intestinal flora, it is well known that our intestinal flora´s quality is define from the first days of our lives, it is alive and it evolutes according to nutrition, sickness and drugs taken. If you eat a lot of transform ailments, your intestinal bacteria will suffer since those ailments will destroy the healthy microbiota. In view of this exposition to pollutants which affects us more and more every day, nutritionists recommend to seed regularly good bacteria in our intestines through the nourishment of fermented ailments or by taking supplementary probiotics and to ingest prebiotics promotting beneficial effects to this concern, cactus mucilages and more precisely oligosaccharides are a promising ailment that seems to promote either nutritional and health benefits to the human intestinal microbiota.

Key words: Cactus, Mucilages, Oligosaccharides, Intestinal microbiota, Health and nutritional benefits and Synbiotics.

INTRODUCTION

HEALTH ISSUES AND NUTRITION FACTS

There is an elevated awareness in health to increase the consumption of natural products when considering health issues. Epidemiological and clinical studies have consistently shown that high fruit and vegetable consumption is associated with a reduced risk of several chronic diseases such as coronary heart disease, cancer, ageing, atherosclerosis neurodegenerative diseases (such as Parkinson’s and Alzheimer’s disease), and inflammation (Iriti and Faoro, 2006). Although traditionally used as a valuable health supporting nutrient, the vegetative parts of Opuntia spp. plants are scarcely used in modern nutrition and medicine. The Cactaceae family is characterized by its mucilage production. Mucilage is a complex carbohydrate, part of the dietary fibre. Mucilage has excellent prospects as an additive not only for the food industry but also for other industrial uses as well.

CLADODES MUCILAGE PRESENCE

Cladodes are modified stems that replace the photosynthetic function of leaves. The inner part of the cladode is formed by the chlorenchyma, where photosynthesis occurs, and the inside part is formed by a white medullar parenchyma whose main function is water storage. There are mucilaginous cells in both, that store mucilage (Espino-Diaz et al., 2010). Mucilage is distributed in the cladodes and fruits (peel and pulp) of Opuntia spp. Although cactus pear fruits and stems were traditionally utilized for medicinal and cosmetic purposes, as forage, building material, and as a source for natural colours (Stintzing and Carle, 2005) their use is mainly restricted to fresh fruit consumption in their countries of origin but are also exported to the European fresh fruit market (Galati et al., 2005; Guzman-Maldonado et al., 2010). Cactus cladodes and fruits are a known source of a variety of nutritional compounds.

The concentrations of these compounds are dependent on the cultivation site, climate, and respective fruit variety. Generally, cladodes are rich in pectin, mucilage, and minerals, whereas the fruits are good sources of vitamins, amino acids, and betalains (Stintzing and Carle, 2005; Tesoriere et al., 2005). Worth to say, that Opuntia spp. has been extensively studied for their biological effects, such as their therapeutic properties against arthritis and cancer (Lee et al., 2002). Important to consider is the fact that since the shelf life of cactus is short, adequate processing techniques are required to provide highly nutritional products in countries where Opuntia cultivation is not possible.

MUCILAGE INDUSTRIAL APPLICATIONS

Some opportunities for production are: food and beverage industry (for example, various food products and alcoholic and non-alcoholic drinks made from fruit and young cladodes [nopalitos]); livestock feed industry (for example, supplements and feed from cladodes and waste from fruit processing, including peel and seeds); pharmaceutical industry (for example gastric mucosal protectants from mucilage extracts, tablets and capsules of cladode powder and flower extracts); cosmetic industry (for example Creams, shampoos and lotions from cladodes); food supplements industry (for example Fibre and flours from cladodes); natural additives industry (for example Gums from cladodes and colorants from fruit); construction industry (for example Binding compounds from mucilage/cladodes); energy sector (for example Biogas from digestion of cladodes and factory waste streams; alternatively, lignified cladodes burned as fuelwood); agricultural inputs (for example Soils, organic materials and improved drainage from the use of cactus pear plant products); tourism sector (for example artisan crafts made from lignified cladodes); textile industry (for example use of natural colorants, such as carmine from cochineal insects). As we can state, there is a wide range of possibilities for using the different parts of the plant. Various Opuntia species are available with fruit of different colours, and cladodes with many uses, depending on the stage of maturity (either for food or feed).

A component that has to be mention for its physiological importance is mucilage.This compound is found in different proportions in the cladodes and in the peel and pulp of the fruit. Even though cactus mucilage physiological role in the plant and chemistry has been studied in detail, little is known about the molecular and rheological characteristics underlying specialized functional properties as an additive for the food and other industries. These hydrocolloids may be of interest because they can be extracted from mature leaves. This may provide a use for leaves pruned from plants cultivated for fruit production. These hydrocolloids can be used for a wide range of thickening agents for the food and pharmaceutical industries. Viscosity is being studied, with results that may enable them to compete in markets where locust bean gum, guar and other gums are used as thickening agents (Medina-Torres et al., 2000; Goycoolea et al., 2000; Medina-Torres et al., 2003; Sepulveda et al., 2003b). A major review of these compound has been published by Saenz (2004). Mucilage is also reported to have other properties that may make it suitable as a fat replacement in various foods, and also as a flavour binder according to McCarthy. Some have the capacity to form gels. Not so long ago gums and hydrocolloids were not thought to make a valuable contribution to the nutritional value of foods. According to Nelson (2001), adding insoluble fibre to foods is a way of reducing their calorie content. Without detracting from the possibilities described for utilization of Opuntias in the production of food and natural additives and the benefits for integrated use of the plant, many other popular uses have been known for centuries.

HYDROCOLLOIDS (MUCILAGE)

Mucilage or hydrocolloids are products with promising medical applications. They can be extracted from cladodes and the peel of cactus pear fruit. The methods currently used are complex and expensive and yields are low. Nevertheless, emerging industrial interest in using extracts for the treatment of gastric mucosa and other ailments augurs well.

EXTRACTION AND ANALYSIS OF CLADODES POLYSACCHARIDES

A significant amount of scientific investigations have been performed on extraction and analysis of polysaccharides from cladodes (Majdoub et al., 2001), fruit pulp (Matsuhir et al., 2006), and fruit peel/skin (Habibi et al., 2004a, 2004b) of *O. ficus indica*, particularly from mucilage, and their biophysical properties. Such mucilages (extracted by a variety of methods, for example cold water, hot water, ethanol, and acid) contain a complex mixture of glycoproteins and heteropolysaccharides, which have been fractionated and characterised (at least in part). Identified polysaccharides include pectin-type material (galacturonan, some with low methoxyl/high acetyl content), arabinogalactans, rhamnogalactans, arabinoxylans and rhamnogalacturonans (with arabinan, galactan and/or arabinogalactan side-chains).

FRUITS AND CLADODES: FUNCTIONAL PROPERTIES

It is a well accept definition that functional compound are those that help prevent disease. The fruit and cladodes of cactus pear provide interesting sources of functional compounds, including fibre, hydrocolloids (mucilage), pigments (betalains and carotenoids), minerals, (calcium and potassium) and vitamins with antioxidant properties, such as vitamin C. These compounds are valued for their contribution to a healthy diet and also as ingredients for designing new foods (Saenz, 2004). The contents of these compounds differ in fruits and cladodes. For instance, the pulp of the fruit is richer in vitamin C, while cladodes are higher in fibre. Pigments are found mainly in the fruit, and both betalains and carotenoids are present in the peel and pulp of various ecotypes. These compounds can be included in a new range of foods known as functional foods, which are as foods or beverages that provide physiological benefits. They enhance health, help to prevent or treat disease and/or improve physical or mental performance with the addition of one or more functional ingredients or using appropriate biotechnologies (Sloan, 2000). Of the functional compound available, dietary fibre is one of the most widely studied. It has helped to establish nutritional value and the relationships between fibre and health (for example, Cholesterol control and/or prevention of diseases such as diabetes and obesity). Cladodes are an important source of fibre, calcium and mucilage, all of which are valuable in a healthy diet (Saenz et al., 2004).

CLADODES CACTUS BROADEN UTILIZATION

The viscosity of the pulp is influenced by the presence of pectin and mucilage, owing to their capacity to hold and bind water. Both pectin and mucilage are considered hydrocolloids and are valuable components of dietary fibre. Once extracted from the pulp, these compounds can be used as food thickening agents (Saenz et al., 2004a; Sepulveda et al., 2003b). Despite the medicinal and nutritional benefit of cactus, the high mucilage content causes some difficulties for the wide use of cactus, particularly the cladodes. Therefore, a reduction of viscosity has been necessary to broaden the utilization of cactus cladodes. Two enzyme combinations (Rohapect B1L and Fructozym BE) showed the best result for the production of mucilage-free purple pitaya juice comparing with single enzyme use (Herbach et al., 2007). A dose of commercial enzyme, for example Rapidase, which contains pectinases, hemicellulases, and cellulases, has been the accepted method for removing suspended particles (Kashyap et al., 2001). Pectinases such as Rapidase can be added to degrade pectin. For this so, it has been seen that Viscozyme, Rapidase, Pectinex and Cytolase with pectin degrading activities decreased viscosity of the cactus homogenate. These enzymes are responsible for the degradation of the long and complex pectin molecules that occur as structural polysaccharides in the middle lamella and the primary cell walls of young plant cells.

The majority of the galacturonic acid (>90%) in most fruit and vegetable pectins is present as homogalacturonan, which is readily hydrolysed by the Viscozyme enzymes. However, to quantify total galacturonic acid, it is necessary that rhamnogalacturonan I and rhamnogalacturonan II polymers also be hydrolysed. A previous analysis of the neutral sugar content of apple pectin following digestion with Viscozyme showed substantial amounts of rhamnose, indicating that Viscozyme does indeed contain the activity necessary for rhamnogalacturonan hydrolysis (Garna et al., 2004). Cactus hydrolysate, which was acquired by hydrolysis with a Rapidase/Viscozyme mixture, was effective for reducing viscosity, increasing active components, and increasing radical scavenging activity. A study about the use of prickly pear cactus mucilage as an edible coating to extend the shelf life of strawberries revealed that use of mucilage coatings leads to increased strawberry shelf life (Del-Valle et al., 2005). Opuntia genus is widely known for its mucilage production. Mucilage, a complex carbohydrate with a great capacity to absorb water, should be considered a potential source of industrial hydrocolloid. Mucilage contains varying proportions of L-arabinose, D-galactose, L-rhamnose, and D-xylose, as well as galacturonic acid. The mucilage content found in the cactus cladodes is influenced not only by the management of the crop but also on the temperature, irrigation and the rain. In some countries, small farmers use cactus mucilage to purify drinking water. Another traditional use is for improving house paint. Recently, a cactus cladode extract was tested to improve water infiltration in soil (Saenz et al., 2004). The cladodes dehydrated and ground into powder are source of dietary fiber which may be used as natural ingredient in different foods to enhance their beneficial properties. Cactus mucilage can be used as natural thickener. All these components could be used as natural ingredients in foods to enhance their healthy properties. The new functions of some compound open new possibilities for adding value to the cactus pear, a new crop for semiarid regions of the world (Saenz, 2006). Cacti are commonly used for fencing material where there is a lack of either natural resources or financial means to construct a permanent fence.

ANTIULCER EFFECTS IN RATS

It has been shown that juice from whole fruits of Sicilian

O. ficus-indica reduced the carbon tetrachloride-induced liver damage in rats, when orally administered 2 h after the toxic agent (Galati et al., 2005). Preventive effects were also assessed by applying the juice for 9 consecutive days before inducing liver toxicity. Histology evaluation, and measurement of the plasma level of hepatic enzymes provided evidence of the improvement of hepatocytes in rats.

CANCER CHEMOPREVENTION

The suppression of ovarian tumor growth by aqueous extracts from whole fruits of *O. ficus-indica* from Arizona was studied in nude mice, and compared with that of the chemopreventive agent N-(4- hydroxyphenyl) retinamide (4-HPR) (Zou et al., 2005). Immunohistochemistry staining was performed to examine the gene expression. The fruit extracts, injected i.p. (intraperitoneal) one day prior to tumor cells injection, and then during the following 6 weeks, significantly suppressed tumor growth, and modulated expression of tumor-related genes, with effects comparable with those caused by 4-HPR.

CEREBRAL ISCHEMIA

Methanol extracts from whole dried fruits of *O. ficus-indica* from South Korea, preventively administered to gerbils, protected against global ischemic injury surgically induced (Kim et al., 2006). Histological examination showed that the neuronal cell damage in the hippocampal CA1 region, evaluated at 5 days after ischemia, was reduced by more than 30%. These findings may suggest that preventive administration of *O. ficus-indica* extracts may be helpful in alleviating the excitotoxic neuronal damage induced by global ischemia.

ACTIVITY OF FRUIT EXTRACTS IN BIOLOGICAL MODELS

Aqueous extracts from the whole fruit of cactus pear from Arizona were used to treat immortalized ovarian and cervical epithelial cells, as well as ovarian, cervical, and bladder cancer cells (Zou et al., 2005). The treatment of the cells with varied extract amounts, for 1, 3, or 5 days, caused a dose- and time dependent increase in apoptosis and growth inhibition, and affected cell cycle of cancer cells by increasing G1 and decreasing G2 and S phases.

BIOACTIVE COMPONENTS AND FRUIT PROCESSING

Plant cell-wall polysaccharides such as pectins, hemicelluloses, cellulose, and mucilage (unavailable carbohydrate), together with lignin, are recognized as being the most abundant constituents of dietary fiber. Chemical composition, location in the cell wall, and solubility of each of these macromolecules are criteria to classify them as part of soluble or insoluble dietary fiber (Zhao et al., 2007). It is also worth to state that dietary fiber affects both human and animal physiology, and its effects depend on the type, source, and amount of fiber consumed (Weickert and Pfeiffer, 2008). For example, It has been reported that the soluble fibers (including pectins, mucilages, and some kind of hemicelluloses, that is, those loosely bound to cellulose) have hypolipidemic, hypoglycaemic, and hypocholesterolemic properties, that contribute increasing the viscosity of gastric juice in stomach, modifying the absorption of nutrients, and have also been used to treat obesity (Weickert and Pfeiffer, 2008; Saenz, 2006). The biological effects of insoluble fibers (including cellulose and hemicelluloses tightly bound to cellulose in humans have been also documented, these comprise the regulation of intestinal function, bulk movement through the intestines, and its pH (acidity) control and balance. These biological features have all been associated with prevention of gastrointestinal diseases, cancer of colon, and intestinal constipation (Weickert and Pfeiffer, 2008).

OPUNTIA SP. AS A FUNCTIONAL FOOD

Recently, Opuntia cactus has been recognized as a functional food and a source of nutraceuticals (a food or part of a food that provides medical or health benefits, including prevention and/or treatment of a disease); additionally, biological effects of Opuntia spp. pads (mature stems), nopalitos (young, soft, flattened stems known as young cladodes), cactus pear fruits (prickler-pear or tunas) and flowers have been documented (Abd El-Razek et al., 2011; Alimi et al., 2010; Livrea, and Tesoriere, 2006). The chemical components of Opuntia spp. causing such positive effects in human health are only partially known; mucilage, pectins, vitamins, and polyphenols are some of them assumed to provoke these effects. Most of the available literature about polysaccharides from Opuntia cladodes is on mucilages and pectins from few varieties and species (Zhao et al., 2007; Feugang et al., 2010). Until recently, the information on the polysaccharides diversity and dietary fiber composition of nopalitos is still scarce or virtually absent. Nevertheless it has been hypothesized that, regardless of their structural polysaccharide diversity, nopalitos and cactus pear fruits are rich sources of soluble and insoluble dietary fibers. Lopez-Palacios et al. (2012) have demonstrated that, among five Opuntia species within a domestication gradient, nopalitos of both wild species O. *streptacantha* and intermediate domesticated species O. *megacantha* have less mucilages (7.2% DM) than the most domesticated O.

ficus-indica (11.7% DM). Mucilages of O. *ficus-indica* cladodes are complex polymers with highly branched structures containing varying proportions of L-arabinose, D-galactose, L-rhamnose, and D-xylose, as well as galacturonic acid; they have hydrocolloid properties and do not form gels (Matsuhiro et al., 2006; Medina-Torres et al., 2003). However, the mucilages of O. *ficus-indica* show high elastic properties similar to those of synthetic polymers and a high capacity to modify the viscosity of aqueous systems; some of these properties have promoted uses of mucilages in several industrial products. The viscous properties of mucilages are among the most typical characteristics of both nopal pads and nopalitos, and affect the consumer preference. According to Calvo-Arriaga et al. (2010), among the nopalito components, mucilages are functional food substances, but they can be associated with an unpleasant sensation of sliminess. Mucilages are excreted from nopalitos tissue after cutting, cooking, or roasting; the viscosity of these polysaccharides is detected by consumers even during eating raw tissues.

The same authors observed that, even after discarding most of the mucilages present in the broth, as commonly consumers do, mucilage content was similar in cooked nopalitos of O. *ficus-indica* cultivars Copena F1, Copena V, Milpa Alta, and Tobarito, but that viscosity of mucilages of cv. Copena V was significantly higher than of other cultivars. Unpublished results on mucilage rheology permits the assumption that the low flow rates of mucilages of *O. ficus*-indica nopalitos allow these polysaccharides to be easily removed in broth than in wild species; this could help to explain the consumer preference for nopalitos from cultivars than wild.

THERAPEUTIC USES OF OPUNTIA CLADODES, FRUITS AND FLOWERS

Because the oldest Arabic medicine treatises do not mention cactus, it is generally accepted that Spain might have introduced the nopal fig tree in the 15th century from Central America after the conquest of the northwest of Africa. Recent scientific reports have highlighted the presence of natural cactus molecules, which may have high potential interest in human health and medicine (Alimi, 2010; Morales et al., 2012; Valente et al., 2010). In herbal medicine, the extraction of bioactive compounds from permeable solid plant materials using solvents constitutes a key step in the manufacture of phytochemical-rich products.

CACTUS IN NUTRITION AND PREVENTION OF DISEASE

The nutritional value of cactus pear fruit and its benefits have progressively received a scientific basis thanks to numerous experimental models dedicated to the evaluation of cactus compounds to treat different diseases. Therapeutic potential has been suggested for metabolic syndrome (including diabetes type 2 and obesity), non-alcoholic fatty liver disease (NAFLD), rheumatism, cerebral ischemia, cancers, and virological and bacterial infections (Kaur et al., 2012; Lee et al., 2013; Lee, 2012). Interestingly, cactus preparations might exert preventive and therapeutic effects against alcoholism and alcohol addiction (Tomczyk et al., 2012).

CACTUS USE IN TRADITIONAL MEDICINE

In traditional medicine, *O. ficus indica* has been used for the treatment of burns, wounds, edema, hyperlipidemia, obesity and catarrhal gastritis. Alcoholic extracts are indicated for anti-inflammatory, hypoglycemic, and antiviral purposes (Kaur et al., 2012).

IN VITRO STUDIES (ON INTACT CELLS)

Oxidative stress and inflammation are involved in numerous diseases. In human chondrocyte cultures stimulated with IL-1β, lyophilized extracts of *O. ficus-indica* cladodes reduce the production of key molecules usually released upon chronic inflammation such as nitric oxide (NO), glycosaminoglycans, prostaglandin-E2 (PGE-2) and reactive oxygen species (Panico et al., 2007). For this reason, lyophilized extracts of *O. ficus indica* cladodes might have a pharmacological interest in preventing cartilage alterations and in treating joint disease. On the murine microglial cell line (BV-2), a butanol fraction (obtained from 50% ethanol extracts of *O. ficus indica* and hydrolysis products) inhibits the production of NO in LPS-activated BV-2 cells *via* suppression of iNOS protein and mRNA expressions, inhibits the degradation of IκB-α, and displays peroxynitrite scavenging activity (Lee et al., 2006).

PHARMACOLOGICAL POTENTIALITIES OF CACTUS EFFECTS ON NON-ALCOHOLIC FATTY LIVER DISEASE

Non-alcoholic fatty liver disease is a complex pathology involving oxidative stress, inflammation, and cell death. Noteworthy, when obese Zucker (*fa/fa*) rats are fed with a diet containing 4% *O.ficus indica* for 7 weeks, the rats have around 50% lower hepatic triglycerides than the control group along with a reduction of hepatomegaly and biomarkers of hepatocyte injury (alanine and aspartate aminotransferases). A higher concentration of adiponectin and a greater abundance of genes involved in lipid peroxidation, lipids export and production of carnitine palmitoyltransferase-1 and microsomal triglyceride transfer proteins are observed in livers from cactus-treated animals. Furthermore, rats fed with cactus have a lower postprandial serum insulin concentration and a greater phosphorylated protein kinase B (pAkt): Akt ratio in the postprandial state (Moran-Ramos et al., 2012). Altogether, data obtained in obese Zucker (*fa/fa*) rats fed with *O. ficus indica* support that cactus consumption attenuates hepatic steatosis, a pathology currently under the radar screen of the pharmacological industry.

PHARMACOLOGICAL POTENTIALS OF ANTIMICROBIAL ACTIVITIES OF CACTUS

Campylobacter is one of the most common agent causative of food-borne bacterial gastroenteritis in the humans. Epidemiological studies reveal that consumption of poultry products represents an important risk factor of this disease. Noteworthy, the extracts of *O. ficus indica* have marked bactericidal effects on the growth of *Campylobacter jejuni* and *Campylobacter coli*. Moreover, adherence of *Campylobacter* to Vero cells is strongly reduced (Castillo et al., 2011). Antimicrobial activities of methanolic, ethanolic, or aqueous extracts of *O. ficus indica* have also been studied on *Vibrio cholerae*, indicating that the methanolic extract was the most efficient (Sanchez et al., 2010). This extract causes membrane disruption, leading to increased membrane permeability and consequent marked decreases in pH and ATP. Altogether, these data obviously support a pharmacological interest of *O. ficus indica* preventing food contamination by *Campylobacter* and *V. cholerae* and in treating gut tract disorders associated with these microorganisms.

PHARMACOLOGICAL POTENTIALS IN TARGETING ALCOHOLISM WITH CACTUS EXTRACTS

Several studies have evaluated the benefits of *O. ficus indica* against symptoms of alcohol hangover in humans. The cause of severity of the alcohol hangover can be, at least in part, inflammation and disruption of lipid metabolism homeostasis. In the rat, the effect of mucilage obtained from cladodes on the healing of ethanol-induced gastritis seems correlated with a (re)stabilization of plasma membranes in damaged gastric mucosa. Molecular interactions between mucilage monosaccharides and membrane phospholipids (mainly phosphatidylcholine and phosphatidylethanolamine) may represent the molecular basis for changes in the functions of membrane-attached proteins observed during the healing process consecutive to chronic gastric mucosal damages (Vazquez-Ramirez et al., 2006).

CLADODES MEDICAL APPLICATIONS

Besides being a traditional source of vegetable, cladodes also have medical applications. The *O. ficus-indica* var. *saboten* is used for wounds, burns, edema, dyspepsia, and as a neuroprotective, cytoprotective, antispasmodic, and chemopreventive in traditional medicine (Galati et al., 2007; Baldassano et al., 2010; Brahmi et al., 2011). The extracts of fruits have shown to have antioxidant (Zourgui et al., 2009; Alimi et al., 2011), and anti-inflammatory activities. Clinical studies have shown the effect of nopal on type 2 diabetic patients (Najm et al., 2010; Yang et al., 2008; Zhao et al., 2011; Andrade-Cetto and Wiedenfeld, 2011), suggesting that the the anti-hyperglycemic effect may be due to its fiber and pectin content, which may decrease carbohydrate absorption (Shane-McWhorter, 2005). On the other hand, it was confirmed that the plant and filter plant extracts from *O. streptacantha* produce the anti-hyperglycemic effect on streptozotocin (STZ)-diabetic rats, and some other bioactive compounds more than fiber and mucilage are responsible of this beneficial activity (Andrade-Cetto and Wiedenfeld, 2011). Also it was demonstrated that the petroleum ether extract from the edible part of *O. Milpa Alta* showed remarkable decrease of blood glucose levels, which may be a potential natural hypoglycaemic functional ingredient (Luo et al., 2010).

In other studies, Godard et al. (2010) have shown that the commercial preparation made from cladode extracts and fruit skins of *O. ficus-indica* (OpunDiaTM), was useful to decrease blood glucose. Other species such as *O. streptacantha* cladodes have been used as anti-diabetic foods (Becerra-Jimenez and Andrade-Cetto, 2012). Theories such as the stimulation in the insulin secretion observed in *O. ficus-indica* (Butterweck et al., 2011) should also applied to *O. streptacantha*; but further studies should be done toward the understanding of the molecular mechanisms of *Opuntia* extracts towards its anti-diabetic effects. Also, it was observed that *Opuntia* extracts have anti-tumoral (Zou et al., 2005*)* and hepatoprotective effects in mice. Park et al. (2010) reported that the β-sitosterol acts as an active anti-inflammatory principle from the stem extract. The n-butanolic extracts of *O. ficus-indica* has beneficial effects on memory performance in mice (Kim et al., 2010). By the other hand, the hexane, ethyl acetate, and water partitioned extracts from *O. humifusa*, were tested on proliferation, G1 arrest and apoptosis in U87MG human glioblastoma cells (Hahm et al., 2010). In addition, *O. ficus-indica* fruits extracts were able to increase apoptosis, and to inhibit the ovarian cancer and vesicle, cervical and immortal epithelial cell growth. The inhibition has been shown to be dose-time dependent (Butterweck et al., 2011).

WOUND HEALING EFFECTS OF OPUNTIA´S MUCILAGE

Studies on cactus mucilage are of interest since this polysaccharide complex plays a significant role in plant physiology, allowing the plant to retain water and live in extreme conditions. In fact, mucilage has been defined as a complex polysaccharide that has important humidity retaining and water binding capacities (Saenz et al., 2004). Mucilage has also been reported to have attractive wound healing activity (Carvalho et al., 2014). When soaked in water, O. *ficus-indica* flowers swell up to form a mucilaginous mass. Despite the relatively large flow of data on this on the wound healing effects, this property still remains unexplored for Opuntia flowers. Wound healing is a dynamic process that involves a complex sequence of cellular and biochemical events generally organized in three major steps, namely tissue inflammation, proliferation, and remodeling. The wound healing effect of O. *ficus-indica* flower treatments was evidenced by the early formation (particularly on days 3 and 5 of post-wounding) of a provisional matrix (scabs) used to protect the surface from infections and irritations. The provisional matrix is then followed by the earlier formation of a granulation tissue in the groups treated with the flower preparations, thus accelerating the wound healing process.

The topical application of both Opuntia flower extracts, as well as the reference drug, increased the percentage of wound contraction, inhibited infections, and accelerated re-epithelialization. The results also showed the presence of well-structured epidermal layer, which was close to normal skin. This indicated that the reepithelialization process in the wounds treated with the mucilage extract preparation was in a more advanced stage, which was further confirmed by the good reorganization of the derma layers with vascular neoformations. Overall, the results from the chromatic study during the 13 days of experiment showed that the topical application of O. *ficus-indica* flower preparations exhibited marked wound healing effects. The healing effect of glycerol was improved after the addition of the methanol extract, and the mucilage extract induced the best results, characterized by the faster wound contraction and advanced phase of re-epithelialization. In fact, the mucilage extract had the ability to retain water while maintaining high humidity at the interface of the wound. The literature indicates that a well-hydrated wound epithelializes faster than a dry one, which could have also affected the wound healing process. Thus, the mucilaginous extract from O. *ficus-indica* flowers could be considered a promising candidate for future application as a wound healing agent. These results are in agreement with the findings previously reported by Trombetta et al. (2006) who demonstrated that cladode polysaccharides, which are the main constituents of mucilage, could be useful for wound healing.

The antioxidant activity detected for the mucilage and methanol extracts from O. *ficus-indica* flowers could be attributed to their phenolic composition, previously demonstrated in the literature (Ammar et al., 2015), which might be active as electron donors and, hence, inhibit free radical reactions. Moreover, the literature indicated that monosaccharide composition could contribute to the scavenging ability of plant extracts. The DPPH radicals scavenging activity of mucilage could be related to its monosaccharide composition and related hydrogen donating ability. In fact, Lo et al. (2011), have previously reported on a significant relationship between monosaccharide composition, mainly arabinose, mannose and glucose, and scavenging capacity (Lo et al.,2011). Antimicrobial agents also provide a better and rapid healing by forming a barrier against microbial contamination. In fact, the injured skin remains vulnerable to invasive microbial infections of all kinds, which can lead to wound inflammation and fluid exudation, thus interfering with the healing process. The results from antibacterial activity assays indicated a remarkable activity against Gram-positive bacteria, the pathogens that are usually involved in skin infections. It can, therefore, be concluded that the antibacterial activity of the tested extracts could contribute to the creation of a suitable environment for wound healing by preventing and managing wound infections. Interestingly, the extracts under investigation showed higher levels of antibacterial activity compared to aqueous and ethanolic extracts of hibiscus (Hibiscus *rosa-sinensis* L.) and Cassia (*Senna bicapsularis* L.) that are known for their medicinal values (Mak et al., 2013). Although the exact mechanisms and modes of action of the O. *ficus-indica* flower extracts described in this latter work have not yet been fully determined, their wound healing effects could presumably be attributed to their bioactive molecules and their associated antimicrobial and antioxidant activities. Taken together, these properties provide further evidence in support for the useful pharmacological effects of Opuntia flowers in wound healing. The Opuntia cactus genus is widely known for its ability to produce and store mucilage. Most of the studies so far performed on the chemical composition of the mucilage extracted from Opuntia cactus have focused on extracts from cladodes, peels, and pulps (Matsuhiro et al., 2006). To the best of our knowledge, no study has up to the present date investigated the compositions and potential effects of the mucilage extracted from Opuntia flowers.

METABOLIC SYNDROME

Metabolic syndrome describes the increasing incidence of type 2 diabetes in association with obesity, hyperinsulinemia associated with disorders of metabolism of carbohydrates and lipids. Diabetes mellitus represents one of the biggest problems in public health. An alternative for its control is found in medicinal plants. Plants in the genus *Opuntia* are the most clinically and experimentally studied and traditional preparations from those species have been evaluated in temporarily hyperglycemic rabbits, in alloxan-diabetic rabbits, type II diabetic patients and normal volunteers (Luo et al., 2010; Zhao et al., 2011; Hahm et al., 2011; Becerra-Jimenez and Andrade-Cetto, 2012). Recently, Lopez-Romero et al. (2014) reported that consumption of *O. ficus-indica* could reduce postprandial blood glucose, serum insulin, and plasma glucose-dependent insulinotropic peptide peaks, as well as increase antioxidant activity in healthy people and patients with type 2 diabetes. Two different studies were performed. In study 1, the glycemic index, insulinemic index, glucose-dependent insulinotropic peptide index, and glucagon-like peptide 1 index were calculated for seven healthy participants who consumed 50 g of available carbohydrates from glucose or dehydrated *O.ficus-indica*.

In study 2, 14 patients with type 2 diabetes consumed *O. ficus-indica* in a high-carbohydrate breakfast or high-soy-protein breakfast with or without 300 g of steamed nopal. The glycemic index of nopal was 32.5 ± 4, its insulinemic index was 36.1 ± 6, the glucose dependent insulinotropic peptide index was 6.5 ± 3.0, and the glucagón like peptide 1 index was 25.9 ± 18. Patients with type 2 diabetes who consumed the high-carbohydrate breakfast + *O. ficus-indica* showed a significantly lower area under the curve for glucose than those who consumed the high-carbohydrate breakfast only. Patients who consumed *O. ficus-indica* with their high-carbohydrate breakfast also showed a lower incremental area under the curve for insulin, while those patients with type 2 diabetes who consumed the high-soy-protein breakfast avoided postprandial blood glucose peaks. Consumption of the high-soy-protein breakfast + *O. ficus-indica* significantly reduced the postprandial peaks of glucose-dependent insulinotropic peptide concentration at 30 and 45 min and increased antioxidant activity after 2 h, measured by the 2,2-diphenyl-1-picrilhidracyl method (Lopez-Romero et al., 2014).

A clinical trial evaluated the acute and chronic effects of cactus in obese, pre-diabetic men and women and found acute blood glucose lowering effects and the long-term safety of the cactus, supporting its traditional use for blood glucose management (Godard et al., 2010). On the other hand, it was evaluated the effect of *O. ficus-indica* cladode and fruitskin extract on blood glucose and plasma insulin increments due to high-dose carbohydrate ingestion, before and after exercise. It was also found *O. ficus-indica* cladode and fruit-skin extract increased plasma insulin and thereby facilitated the disposal of an oral glucose load from the circulation. This reduction in blood glucose was more explicit after exercise than in a basal state (Van Proeyen et al., 2012).

A randomized, double blind, placebo-controlled trial with 30 males and 93 females suffering from overweight and obesity was conducted to research the efficacy of Litramine IQP-G-002AS, a dietary fiber derived from *O. ficus-indica*, in reducing body weight. The subjects consumed either 3 g/day of Litramine IQP-G-002AS or placebo tablets for 12 weeks. Results showed a statistically significant increase in total weight loss (2.4 kg more) among the Litramine IQPG-002AS group when compared to the placebo group (3.8 kg (SD 1.8 kg) versus 1.4 kg (SD 2.6 kg); $P<0.001$). Furthermore, subjects treated with Litramine IQP-G-002AS also showed a significantly increased reduction in body fat composition (0.7% (SD 1.7%) versus +0.1% (SD 2.5%) ; difference 0.8%; $P<0.031$) and waist circumference (3.9 cm (SD 2.7 cm) versus 2.2 cm (SD 2.9 cm) ; difference 1.7 cm; $P<0.001$) when compared to the placebo group (Grube et al., 2013). More recently, it was reported that supplementation with methanolic extract from *O. joconostle* seeds that are rich in antioxidant compounds was effective in reducing cholesterol and LDL-C in hypercholesterolemic mice (Osorio-Esquivel et al., 2011); authors suggest that this methanolic extract has potential to be included in short-term hypercholesterolemia treatment regimens because it exhibited hypolipidemic activity with no apparent toxic manifestations.

ANTI-ATHEROGENIC EFFECTS

The administration of *O. ficus-indica* glycoprotein decreased NO amounts in hyperlipidemic mice, probably *via* its antioxidant effects and by reducing lipid peroxidation (Oh and Lim, 2006). It has also been found that *O. ficus-indica* var. saboten significant decreased of plasma lipid levels in Triton WR-1339-treated mice such as total cholesterol (TC), triglyceride (TG), and low-density lipoprotein (LDL) (Zhao et al., 2012). Therefore, clinical and experimental studies suggest that *O. ficus-indica* possesses potential hypoglycemic, hypolipidemic and hypocholesterolemic effects, and has the potential for being used in the treatment of metabolic syndrome.

NEURONAL DISEASE

Previous reports have shown that methanol extract of the fruits of *O. ficus-indica* var. *saboten* inhibit free radical induced neuronal injury in mouse cortical cultures. It was also reported that, in addition to the fruit extract, the methanol extract of the stems also inhibited the oxidative injury induced by H_2O_2 or xanthine (X)/ xanthine oxidase (XO) in rat cortical cell cultures. Reports also revealed that the expression levels of brain-derived neurotrophic factor (BDNF), phosphorylated cAMP response element bindingprotein (pCREB), and phosphorylated extracellular signal-regulated kinase (pERK) 1/2 were significantly increased in hippocampal tissue after 7 days of *O. ficus-indica* var. *saboten* administration. These results suggested that the subchronic administration of *O. ficus-indica* var. *saboten* enhances long-term memory, and that this effect is partially mediated by extracellular signal regulated kinase, cAMP-response element-binding protein, and brain-derived neurotrophic factor (ERK-CREB-BDNF) signaling and the survival of immature neurons (Kim et al., 2010).

OTHER DISEASES AND PHARMACOLOGICAL EFFECTS

Other reports suggest that *O. ficus-indica* has a pharmacological effect in a variety of diseases. The improvement of bone mineral density and calciuria to prevent osteoporosis was reported by Aguilera-Barreiro et al. (2013). For this, a longitudinal, quasi-experimental, blinded and randomized 2-years temporary study was carried out with 181 women. The consumption of dehydrated *O. ficus-indica* after six months reportedly improved calciuria levels and turned them back to normal, remaining constant for the rest of the treatment. Bone mineral density increased in the total hip and lumbar region in those groups who consumed 600 g of dehydrated *O. ficus-indica*. The authors have suggested that the high amount of calcium in dehydrated *O. ficus-indica* could be acting as a supplementary resource.

TOXICOLOGY OF *O. FICUS INDICA*

Orally, *O. ficus-indica* is usually well tolerated. However, it has been reported that it may cause mild diarrhea, nausea, increased stool volume, increased stool frequency, abdominal fullness, and headache and low colonic obstruction (Gagnier et al., 2006). Although the public and some health care professionals believe that herbal medicines are relatively safe because they are “natural”, there are remarkably little data to support this assumption. However, side effects may also occur due to contaminants in herbal products, as heavy metals, including lead, mercury, or arsenic, and other undeclared pharmaceuticals, purposefully and illegally added to the herbs to produce a desired effect (Gagnier et al., 2006). In addition, there exist other factors that might also affect the content of active constituents in the herbal product (as microorganisms, microbial toxins, and genetic factors). Although plant remedies contain chemical compounds that are considered potentially toxic and they are cited in the Hazardous Substances Data Bank (National Library of Medicine, Bethesda, Maryland), it is worthwhile to launch more investigations to evaluate the risks and benefits of using *O. ficus-indica.* Preclinical and clinical information indicates that *O. ficus-indica* is efficacious for certain chronic diseases, although there is a dearth in the field of pharmacodynamics and pharmacokinetics or safety aspects of the genus *Opuntia*. There have been very few studies pertaining to the molecular aspects of genus *Opuntia*, which is clearly evident by the sequence of information available in the public domains. Even though genus *Opuntia* is rich in healing properties, due to the lacunae in many aspects, there is an urgent requirement for further investigations to delineate its precise mechanisms and possible therapeutic values, particularly in the field of chronic diseases.

NEW DEMAND FOR INDUSTRIAL PRODUCTS SUCH AS OLIGOSACCHARIDES

Oligosaccharides represent the products that food industry is looking to produce easily and which provide health benefits to consumers. There is an increasing demand for these products with a growing interest in research and to identify alternative ingredients that may lead to enhanced health (Boler and Fahley, 2012). Oligosaccharides are low-molecular weight carbohydrates with a low degree of polymerization that resist digestion and absorption by mammalian enzymes and also are named “nondigestible oligosaccharides” (NDO). These NDO have been classified as prebiotics, defined as “nondigestible food ingredients that affects the host beneficially and selectively and stimulating both the growth and activity of one or a limited number of bacteria in the colon and thus improving host health” (Gibson et al., 2004). Some health benefits of prebiotics ingestion are reduction of inflammatory bowel disease (Borruel, 2007), increase of absorption of a variety of minerals (Griffin and Abrams, 2008) and regulation of triacylglycerol and cholesterol metabolism (Beylot et al., 2008), beside colorectal cancer prevention (Asad et al., 2008). Only three NDO can be classified as prebiotics : fructans, galactooligosaccharides and lactulose. Dietary fiber is defined as “primarily derived from plant material and is composed of complex, non-starch carbohydrates and lignin that are not digestible within the small intestine because mammals do not produce enzymes capable of hydrolyzing them into their constituent monomers” (Turner and Lupton, 2011).

The main types include nonstarch polysaccharides, cellulose, hemicellulose, pectin, resistant starch and other NDO associated with dietary fiber polysaccharides, especially lignin. The effect of dietary fibers differs in their physicochemical characteristics on transit through various segments of the GI tract and fermentation in the large intestine and is well documented in the scientific literature such as reduction effects on fasting glucose, triglycerides and cholesterol serum concentrations (Paturi et al., 2012). Rats may provide a useful model to examine interacting variables of importance to human health, since the caecum is the most active fermentation locus and rat colon can be functionally equated with human distal colon (Monro et al., 2012). In this view, agroindustrial co-products as apple marc flour or cactus pear peel flour can be employed as an alternative fiber and other fermentable sugars by intestinal bacteria. The composition of these flours will affect their physiological performance. By the other hand, it is worth to remember that Dietary fiber that escapes digestion in the small intestine enters in the large intestine where it is utilized as a fermentable substrate by the microbiota, principally Bifidobacteria and lactobacilli. Bifidobacteria possesses the characteristics to treat infections as diarrhea, improve lactose digestion and protect against infection (Li et al., 2014). The accepted mechanism by which Bifidobacterium spp. is thought to be inhibited is related to the higher production of acetic and lactic acids during fermentation. Increasing acid production resulted in lower pH which prevents enteric colonization of potentially pathogenic microorganisms and growth of putrefactive bacteria (Paturi et al., 2012). Cactus pear peel flour has shown to enhance the growth of beneficial microorganisms as lactic acid bacteria and Bifidobacteria, although allowed the growth of Bacteroides and Enterobacterias as well. Apple marc allowed a better growth of lactic acid bacteria and reduced the growth of Enterobacterias and Bacteroides. Non digestible sugars or combination of different dietary fibers have been noted to increase Bifidobacteria and lactobacilli populations in rats (Dongowski et al., 2005; Rodriguez-Cabezas et al., 2010). Inulin on the other side, has been reported as a highly fermentable fiber (Franck and Bosscher, 2009). Highly fermentable dietary fibers are characterized by being readily fermented by enteric bacteria, producing short-chain fatty acids especially butyrate, which are the end products of fermentation of polysaccharides by the colonic flora and that are used as an energy source by intestinal epithelial cells.

The SCFA (short chain fatty acids) are known to influence several functions on the colon, for example ionic transport, colonic motility and mucosalcell proliferation, the caecum is a major site of SCFA production in rats. Butyric acid is of particular importance in human physiology due to its role as an energy source for colonic epithelium.There are two categories of faecal samples based on their polysaccharide content. The relative resistance of cellulose to fermentation and its consequent survival in the faeces contrast with the susceptibility to fermentation of the remaining fibers (inulin) and the resulting lower polysaccharide content in faeces from rats fed with these dietary fibers (Paturi et al., 2012). For the nondigestible polysaccharides in faecal samples, higher content of insoluble or partially insoluble fibers (lignin, hemicellulose and cellulose) content in cactus pear peel flour and apple marc flour increased the amount of non-digestible polysaccharides.

MUCILAGE AS A DIETARY FIBER

Mucilage and pectin are considered soluble dietary fibers and exert physiological effects like hypocholesterolemic and hypoglycemic in humans during short-term trials. Mucilage obtained from nopal (*O. ficus-indica*) was reported as a therapeutic agent against topical inflammation, skin ulcerations, gastritis, and also showed anti-ulcer activity. Other benefits that have been attributed to the ingestion of mucilage and pectin are interactions with drugs and intestinal ion homeostasis (Stintzing et al., 2005). As other dietary fibers, pectin reaches the large intestine intact where it is extensively fermented by the gut microflora, creating a prebiotic effect. *In vitro* fermentations of other plant polysaccharides such as xyloglucan showed that some intestinal bacteria that did not grow on the polysaccharide were capable of completely fermenting the oligosaccharides. This difference in fermentation patterns among some polysaccharides and oligosaccharides has also been reported for dextran, oligodextrans and various glucose oligosaccharides with different degrees of polymerization (Rycroft et al., 2001). Mucilages from nopal are complex polysaccharides with extremely branched structures.

The suggested primary structure describes the molecule as a linear repeating core chain of 1,4-β-D-galacturonic acid, and α-1,2-L-rhamnose with trisaccharide side chain of β-1,6-D-glucose attached to O- 4-L-rhamnose residues (Matsuhiro et al., 2006). In nopal the water-soluble polysaccharide fraction with thickening properties represents less than 10% of the water-soluble material. The nopal pectin composition varies depending on the source and conditions of extraction, location, and other environmental factors. The main component in pectin is a backbone chain structure of α-(1→4)-linked D-galacturonic acid units interrupted by the insertion of (1→2) linked Lrhamnopyranosyl residues in adjacent or alternate positions. The linear segments consisting predominantly of galacturonan are called homogalacturonans. The nopal pectin sugar composition extracted by alkaline process is uronic acid 56.3%, rhamnose 0.5%, arabinose 5.6%, galactose 6.5%, and xylose 0.9% while in acid process the sugar composition is uronic acid 64.0%, arabinose 6.0%, galactose 22.0%, glucose 2.6%, and xylose 2.1%. Other characteristic from nopal pectin is the low-methoxyl degree (<50). Nowadays, we might relate this effect with the soluble fiber composition (mucilage and pectin) and its content (1 to 2% wet weight) in prickly pear cactus stems (Stintzing et al., 2005). Therefore, it is likely that mucilage (MO) and pectic-derived (PO) oligosaccharides have a prebiotic effect. In terms of the rapidly growing bio-functional food industry, the use of cactus steam PO and MO as prebiotics has not yet been investigated.

The overall beneficial effects produced by MO have shown to be higher than those induced by PO. Administration of MO and PO to the cultures have also shown to beneficially influenced the fermentation patterns of the colon microbiota reflected as higher SCFA production and remarkable higher propionate and butyrate levels. This can be considered as positive beneficial effects on human health since propionate is largely metabolized in the liver, it is gluconeogenic, and can inhibit de novo lipogenesis (Macfarlane et al., 2008). Butyrate is the major energy source for the colonocytes and it has been implicated in the prevention of colitis and colorectal cancer. Both butyrate and propionate stimulate apoptosis of colorectal carcinoma and gastrointestinal tract cells (Maciorkowska et al., 2010). Moreover, microbial propionate also contributes to decrease plasma cholesterol levels by inhibiting the synthesis of hepatic cholesterol (Bischoff and Schluck, 2010). This shift on SCFA leading to higher propionate and butyrate production was previously noted during supplementation with fructooligosaccharides to rats and with different oligosaccharides on both *in vitro* (Torres et al., 2010) and *in vivo* systems. Nevertheless, higher propionate and butyrate production levels were not accompanied to an increased growth for bifidobacteria or lactobacilli in the same proportion, as these bacteria primarily produce acetic acid and 2- hydroxypropanoic acid (lactate). The increased SCFA production can be explained by the additional bifidobacterial biomass, created by the prebiotic effect from nopal-derived oligosaccharides. Additionally, other microbial groups from the colon microflora might alternatively ferment carbon sources from the medium to produce SCFA. Other microbial groups have been implicated in the conversion of lactate or acetic acid into butyrate as found by Louis et al. (2007). Belenguer et al. (2006) have described that butyrate-producing species such as Anaerostipes caccae and Eubacterium halli can be cross-fed with lactate produced by Bifidobacterium adolescentis grown in the presence of fructo-oligosaccharides, while a non lactate utilizing, butyrate-forming Roseburia sp. could assimilate products of the oligosaccharide hydrolysis performed by Bifidobacterium.

In regard to the effects on the microbial community, bifidobacteria have a competitive advantage over other intestinal microorganisms in a mixed culture environment, due to their β-fructofuranosidase and similar enzymes, allowing them to break down and utilize inulin-type fructans and other oligosaccharides. Besides their nutritional advantage, bifidobacteria have been suggested to inhibit excessive growth of pathogenic bacteria, modulate the immune system, suppress the activities of rotaviruses, and restore microbial integrity in the gut microbiota after antibiotic therapy (Kolida and Gibson, 2007). Plate count analysis revealed that the addition of MO primarily increased lactobacillus, whereas PO resulted in an increase of the bifidobacteria population. Both bacterial groups are part of the lactate-producing bacteria that can produce an acidic environment leading to detrimental conditions for opportunistic pathogens. The pathogen inhibitory effects from lactic acid bacteria can explain the unchanged concentrations of enterococci, enterobacteria, staphylococci, and clostridia during both the MO treatment and the post-tretment. This result is supported by other findings showing a negative influence of MO on the growth of Clostridium *difficile in vitro* (Zanoni et al., 2008). Several authors have reported a significant increase in bifidobacteria and a concomitant decrease in Enterococcus spp. upon fructooligosaccharides supplementation in humans (Beards et al., 2010) and rats (Licht et al., 2006). Since long chain oligosaccharides are typically digested slowly in comparison to the shorter ones, a relatively long supplementation period is required for long chain oligosaccharides to exert a prebiotic effect *in vitro* and *in vivo*. It was observed that a combination of shortchain and long-chain oligosaccharides is physiologically more active than the individual fractions (Louis et al., 2007). However, complaints of flatulence, abdominal pain, and bloating have been reported in human feeding studies involving prebiotics (Macfarlane et al., 2008). Evidence suggests that a rational dose of up to 20 g/day can produce gas distension (Kolida and Gibson, 2007).

The *in vitro* system of these studies, showed that MO and PO from nopal act as prebiotics which implies specific changes in the composition and/or metabolism of the colon microbiota, which could provide benefits on host's health. According to the definition, functional food offers health benefits and reduces the risk of chronic diseases beyond the widely accepted nutritional effects. Among the functional components, probiotics, prebiotics, omega-3-polyunsaturated fatty acids, antioxidative molecules, vitamins and minerals are commonly used (Grajek et al., 2005). As a consequence of increasing demand, probiotics and prebiotics currently have strategic importance in the market of functional food. Probiotics are defined as 'live microbial food supplements, which benefit the health of the consumers by maintaining or improving their intestinal microbial balance. Because of their health benefits, selected strains belonging to *Lactobacillus*, *Bifidobacterium*, and *Streptococcus thermophilus* have been included as probiotics in yoghurt and fermented milks during the past two decades (Guarner et al., 2005; Casiraghi et al., 2007; Fabian, 2007; Guyonnet et al., 2007). Growing scientific evidence supports the concept that the maintenance of healthy gut microbiota may provide protection against gastrointestinal disorders including gastrointestinal infection, inflammatory bowel disease (IBD) and even cancer. The physiological effects attributable to probiotic bacteria may be strain dependent and include the reduction of gut pH and growth inhibition of human pathogens, vitamin and amino acid production (Pompei et al., 2007), reduction of cholesterol level in the blood, anticarcinogenic activity, stimulation of immune functions, reduction of the conversion of primary bile salts to secondary bile salts and the improvement of calcium absorption. An essential feature in the choice of a probiotic micro-organism is its ability to reach, survive and persist in the environment in which it is intended to act. Resistance to human gastric transit has been demonstrated *in vivo* for probiotic lactic acid bacteria and bifidobacteria and constitutes an important *in vitro* selection criterion for probiotic micro-organisms. Thus, probiotic micro-organisms should be tolerant to acid and bile salts.

In the colon, probiotic bacteria and the saccharolytic microbiota utilize the carbohydrates that resist hydrolysis by human digestive enzymes and are not absorbed on transit through the small intestine. Prebiotics are nondigestible food ingredients, which beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of probiotic bacteria in the colon, thus improving host health. These complex carbohydrates are not digested in the small intestine and a number of investigations have shown that they stimulate, preferentially, the growth of bifidobacteria and lactic acid bacteria (Rossi et al., 2005; Brunser et al*.,* 2006). To date, probiotics and prebiotics are predominantly used in food, and their application in medicine is on the rise (Furrie et al., 2005; Pool-Zobel, 2005). The consumption of a probiotic in combination with a suitable prebiotic (synbiotic) can result in synergistic effects, by improving the growth of the strain in the colon and by increasing autochthonous bifidobacteria levels.

SYNBIOTICS ARE PRODUCTS THAT EXPLOIT THE SYNERGY BETWEEN PROBIOTICS AND PREBIOTICS

The simultaneous administration of a preferred indigestible carbon source advantages the growth and the metabolic activity of administered probiotic bacteria in the intestine. In the perspective to supply *L. plantarum* LP 1, *S. thermophilus* Z 57 and *B. lactis* B 933 in an effective synbiotic, their carbohydrate preferences were investigated. All the strains were not able to ferment, or fermented to a limited extent, inulin, AG, dextran, guar gum (PHGG) and resistant starch (RS 1). XOS and some glucose-based indigestible carbohydrates, such as isomalto-oligosaccharides, polydextrose and resistant starch (RS 2) were utilized only by *L. plantarum* LP 1 and *B. lactis* B 933. GOS and fructo-oligosaccharides (FOS 1 and FOS 2) were successfully utilized by all the strains, yielding high biomass concentration, and may represent the appropriate prebiotic ingredients in a synbiotic that contains the three antioxidant strains. The capability of bifidobacteria, lactobacilli and *S. thermophilus* to ferment FOS and GOS has been widely described by Rossi et al. (2005) Saulnier et al. (2007). Actually, FOS are extensively used as prebiotic ingredients for dietary or pharmaceutical applications, while GOS have been increasingly introduced as prebiotics in the last few decades (Fanaro et al*.,* 2005; Macfarlane et al*.,* 2006; Roberfroid, 2007). The addition of FOS and GOS mixtures to infant formulas stimulated the growth of bifidobacteria and metabolic activity in the colon, thus reproducing the bifido-dominant microbiota of breast-fed infants (Knol et al., 2005; Rinne et al., 2005).

PREBIOTICS AND PROBIOTICS

Probiotics are specific live microorganisms which, when ingested in sufficient amounts, can promote health in the host (Food and Agriculture Organisation of the United Nations). In order to qualify as probiotic, microorganisms must fulfill a number of criteria (Borchers et al., 2009). They should be strictly specified at the genus, species, and strain levels, and specific strains should be registered and disposed in an international culture collection. Thus, generalizations concerning the efficacy of a whole species or even genus might be misleading. Probiotics should be extremely safe; their safety is supported by the fact that many strains are of human origin and have a long history of safe use. Many probiotics and their applications have been granted GRAS (generally regarded as safe) status. Although this classification should not be generalized, it does not warrant permanent surveillance for potential risks, such as invasiveness and potential for transfer of antibiotic resistance to other microorganisms (Whelan et al., 2010; Liong, 2008). Because the effects of probiotic microorganisms are generally dependent on their viability, their stability during processing and storage, as well as their ability to survive intestinal transit through the stomach and proximal small bowel to finally adhere to mucosa and colonize the intestine, should be demonstrated (Borchers et al., 2009).

The final, but perhaps one of the most important, criteria for specific microorganism to be qualified as probiotic is a scientifically proven effect on the promotion of health or prevention and treatment of a specific disease (Borchers et al., 2009). Prebiotics are non-digestible food ingredients that selectively stimulate favorable bacterial growth and/or promote activity of a limited number of health-promoting bacteria, hence benefiting the host (Thomas and Greer, 2010; Quigley, 2012). However, prebiotics can also be applied to enhance the survival and action of ingested probiotic bacteria. When probiotics and prebiotics are combined in one product to achieve synergistic effects they are usually called synbiotics. The vast majority of prebiotic substances are carbohydrates that are indigestible for human digestive enzymes but can be fermented by beneficial bacterial genera in the colon and serve as a substrate for their metabolism. Some of them can be found in natural foods, such as human milk oligosaccharides in mother's milk, while others are added to food. Good examples of prebiotics are fructo-oligosaccharides (FOS), inulin, galacto-oligosaccharides (GOS), soybean oligosaccharides, and complex polysaccharides that constitute dietary fiber (Thomas and Greer, 2010). Probiotics or prebiotics may achieve their therapeutic effect in IBD through many different mechanisms. They influence the composition of intestinal microbiota and alter the metabolic properties of the microbiome (Mack, 2011). By increasing the production of short-chain fatty acids, they may lower the pH of the colonic environment and thus inhibit the growth of potentially pathogenic microorganisms. Butyrate plays a trophic role as a nutrient for colonocytes and enhances repair of injured gut epithelium in IBD. Moreover, evidence shows that butyrate acts directly as an anti-inflammatory agent by inactivating the intracellular transcriptional factor NFκB pathway, consequently attenuating synthesis of inflammatory cytokines (Kanauchi et al., 2005).

A large number of probiotic strains are able to produce antibacterial substances, such as hydrogen peroxide, hydrogen sulfide, lactic acid, and specific bacteriocins (Kotzampassi and Giamarellos-Bourboulis, 2010), as well as displace deleterious microbes from the luminal-mucosal interface by competing for binding sites on the epithelial cell surface or mucus layer (Collado et al., 2007; Veerappan, 2012). Probiotics communicate with epithelial cells and different sets of cells implicated in both innate and acquired immune response via pattern-recognition receptors (Stephani et al., 2011). They can enhance gut barrier function and reduce intestinal permeability for intestinal microorganisms and other antigens (Garcia Vilela et al., 2008). For example, several strains of *Lactobacilli* can up-regulate MUC3 gene expression, resulting in increased mucus production by intestinal goblet cells (Caballero-Franco, 2007). Several probiotic strains can induce the production and secretion of different anti-microbial peptides by epithelial cells, such as defensins, lysozyme, lactoferrin, or phospholipase, and directly decrease permeability of the epithelial layer by enhancing tight junctions and reducing epithelial cell apoptosis (Veerappan et al., 2012; Karczewski et al., 2010; Ukena et al., 2007). Each probiotic strain may have distinct immunoregulatory properties, thus probiotics can indirectly or directly modulate intestinal immune response.

In very simplified terms, probiotics can be classified into two groups with regards to their influence on the immune system : one exhibiting immunostimulating activities and the other anti-inflammatory properties (Macho Fernandez et al., 2011). Numerous studies have revealed the mechanisms by which probiotics down-regulate the inflammatory immune response, including those with proven clinical efficacy in the therapy of IBD. Some probiotic strains may induce maturation of intestinal dendritic cells, an important part of antigen presenting and immune regulation, and extend their survival (Prisciandaro et al., 2009). Several probiotics act through strengthening the regulatory T cell (Treg) response. Tregs are antigen-specific T cells which prevent autoimmunity and preserve tolerance towards harmless antigens, including intestinal commensal microbiota (Collado et al., 2007). They can control excessive NFκB pathway activation, decrease production of pro-inflammatory cytokines (for example, TNFα, INFγ, and IL-8), and induce the production and secretion of anti-inflammatory cytokines such as IL-10 and TGFβ (Stephani et al., 2011; Macho Fernandez et al., 2011; O'Mahony et al., 2008). It is possible that there are further mechanisms of probiotic action that have not yet been demonstrated. Regarding the fact that pathogenesis of each type of IBD differs and that mechanisms of action of probiotics are strain-specific and very different, we might expect that different probiotics would be effective for each type and phase of the disease.

Over the last two decades, several interventional clinical studies comparing the efficacy of probiotic therapy against placebo or standard therapy with drugs have been published. The use of different study designs (for example, concomitant use of other forms of therapy) and various probiotic strains and doses, with only a few studies resembling one another in such a manner to be able to uniformly compare the results, makes it very difficult to derive any firm conclusions.

Conclusions

Polysaccharides capable of forming gels in water are common throughout the plant kingdom. Some of them, such as the pectins in higher plants, carrageenans and agarose in algae, algal and bacterial alginates and xanthan, have been investigated in great detail. A relatively good understanding, of their biochemistry and biophysical properties has already been achieved. An important point in the choice of the cactus mucilage as a coating is its low cost. The cactus needs to be pruned; therefore, the cactus stems are a waste product capable of several applications, such as afore mentioned. Cactus mucilages obtain either from the stem, the cladodes or the fruit, act as Prebiotics which are non-digestible food ingredients that selectively stimulate favorable bacterial growth and/or promote activity of a limited number of health-promoting bacteria, hence benefiting the host. However, prebiotics can also be applied to enhance the survival and action of ingested probiotic bacteria. When probiotics and prebiotics are combined in one product to achieve synergistic effects they are usually called synbiotics. The vast majority of prebiotic substances are carbohydrates that are indigestible for human digestive enzymes but can be fermented by beneficial bacterial genera in the colon and serve as a substrate for their metabolism. Some of them can be found in natural foods, such as human milk oligosaccharides in mother's milk, while others are added to food. Probiotics or prebiotics help to the maintenance of healthy gut microbiota that provide protection against gastrointestinal disorders including gastrointestinal infection, IBD and even cancer. They influence the composition of intestinal microbiota and alter the metabolic properties of the microbiome. Finally, further *in vivo* studies must be held in order to assure the benefits of an ingestion of cactus mucilages on the intestinal microbiota of human beings and the health and nutritional properties.

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