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Chapter

Probiotics and Other Bioactive Compounds with Proven Effect against Obesity and Hypertension: Food Design Opportunities from Lulo Fruit (*Solanum quitoense*)

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Abstract

This book chapter aims to identify those bioactive compounds that are the most effective in obesity and hypertension prevention and/or treatment, these being the two main disorders associated with metabolic syndrome. Focusing on probiotics and phytochemicals, the document will provide evidences from both in vitro and in vivo studies as well as information about the action mechanisms and how they are affected by the interaction with other food ingredients, the food matrix in which they are placed, etc. Given its high antioxidant capacity, in part due to its spermidine content, lulo fruit has generated considerable interest among health researchers. This, together with its exotic organoleptic properties, offers interesting growth opportunities for the design of new food products from lulo fruit. This book chapter will also discuss some of them.

Keywords: probiotics, phytochemicals, metabolic syndrome, spermidine, lulo

1. Foods, technology, and metabolic syndrome

Overweight and obesity are defined as "abnormal or excessive fat accumulation that may impair health" [1]. Since 1975, obesity has almost tripled worldwide so that in 2016, 39% of the adult population and 18% of children and adolescents were overweight. Very often, a high body mass index (BMI $\geq$ 25–30) is associated with other metabolic abnormalities, such as high blood pressure (hypertension), high blood sugar (hyperglycemia), high serum triglycerides, and low serum high-density lipoprotein (HDL) [2]. The occurrence of at least three of these interconnected physiological, biochemical, clinical, and metabolic factors that directly increase the risk of atherosclerotic cardiovascular disease, cancer, and type 2 diabetes is known as metabolic syndrome [3]. The International Diabetes Federation estimates that one-quarter of the world's adult population suffers from this syndrome, with little

difference between developed and developing countries. Main factors contributing to it include, beyond the genetic susceptibility, the increased consumption of calorie-dense food and the scarce physical activity. Given that metabolic syndrome can occur in several forms, according to the combination of the different components, it is apparently difficult to treat it pharmacologically, being lifestyle change the most effective preventive approach. However, the fact that a low-grade chronic inflammatory state accompanies the metabolic syndrome in any of its forms suggests that anti-inflammatory therapies could have a place in its prevention and treatment [4].

Inflammation is a response of the body's immune system to harmful stimuli. In the case of metabolic syndrome, inflammation takes place in response to imbalance of blood glucose and insulin levels or insulin resistance, which leads to unhealthy high concentration of unused sugar in the bloodstream that is sent to the liver, muscle, or pancreas [5, 6]. Once there, the sugar is converted into fat, thus leading to progressive adipocyte enlargement. Hypertrophy reduces blood supply to adipocytes and causes hypoxia. Subsequent necrosis and macrophage infiltration into adipose tissue lead to overproduction of reactive oxygen species (ROS), low-density lipoproteins (LDLs), inflammatory cytokines (tumor necrosis factor-alpha, interleukin-6, adiponectin, etc.), and C-reactive protein (CRP). High-fat diets, frequently consumed by obese individuals, aggravate this problem both directly, when the fat is rich in saturated fatty acids, and indirectly, through effects on the microbiota and intestinal permeability [5]. The normal blood plasma concentration of CRP varies between 0.08 and 0.3 mg/dL in healthy adults and reaches values between 2 and 10 mg/dL in individuals suffering from metabolic syndrome. High levels of the inflammatory marker CRP in blood are associated with increased odds of having plaque in the carotid arteries and, therefore, with increased risk of myocardial infarction and stroke [7].

In addition to CRP, some dietary food components involved as intermediates in various metabolic pathways appear altered in population with metabolic syndrome, making possible its use as biomarkers. Polyunsaturated fatty acids (PUFA), specifically eicosapentaenoic acid (20:5 n-3; EPA) and docosahexaenoic acid (22:6 n-3; DHA), are inversely related to metabolic syndrome in adults [8]; several studies have stablished an association between this syndrome and selenium blood concentration [9] or serum levels of vitamin B12 [10]; Urrunaga-Pastor et al. [11] also found an association between vitamin D deficiency and hyperinsulinemia; adults with metabolic syndrome also have suboptimal concentrations of several antioxidants (retinyl esters, vitamin C, and all carotenoid concentrations, except lycopene), partly due to the lower intake of fruit and vegetables by these individuals [12]. These results reinforce the relationship between diet and the incidence of metabolic syndrome.

Evidence from prospective observational in vitro and in vivo studies (preclinical and clinical trials) has converged to support the importance of individual nutrient or food intake and dietary patterns in the prevention and management of obesity and metabolic syndrome. In vitro studies seek to determine the biochemical mechanisms at the cellular level as physiological ones, which are involved in the proper functioning both at the transcriptional and protein expression in the pancreas, skeletal muscle, liver, and adipose tissue. In vivo studies allow establishing a cause-effect relationship in experimental animals (preclinical trials) or in humans (clinical trials). While in vitro or animal in vivo studies are standardized and there are countless works done, even today a standard profile for clinical trials in humans with metabolic syndrome has not yet been established. Clinical trials about therapeutic efficacy for metabolic syndrome are scarce and concentrated in the last 8 years in high-income countries (USA, Italy, and Spain). Interventions that affect three or more factors and evaluate various outcome variables are reduced, highlighting the lifestyle factors (diet and physical activity) as the most important

in this multifactorial syndrome [13]. Specifically, a low intake of saturated and total fat; reduced consumption of sodium, simple sugars, and high glycemic index foods; and increased intake of fruits, vegetables, legumes, and whole grains are suggested to be the most effective actions in reducing the incidence of obesity and cardiovascular disease. However, the urban lifestyle leads us to mainly consume foods in processed form, which reinforces the decisive role that the food industry plays in the promotion of healthy diets. In fact, in recent years the supply of functional foods with a reduced content of fat, sugar or salt, as well as that of functional foods formulated with phytosterols or polyunsaturated fatty acids has increased considerably. In order to achieve this, not only traditional techniques of food formulation and blending or cultivation and breeding are involved but also more recent ones, such as microencapsulation, vacuum impregnation, or coating with edible films [14]. Moreover, the increasing knowledge about the negative impact that processing and cooking techniques have on the concentration and functionality of the active compounds naturally present in foods has encouraged the use of alternative techniques, such as the application of high-pressure homogenization replacing the pasteurization or freeze-drying instead of hot air drying.

Later in this book chapter, the most relevant bioactive compounds with proven effect against any disorder associated with the metabolic syndrome are listed. Focusing on probiotic microorganisms and phytochemical compounds, evidences obtained from in vitro, in vivo, or clinical studies in the last 10 years have been compiled. Finally, new functional foods made from lulo fruit are suggested as being suitable for metabolic syndrome prevention and/or amelioration.

2. Food components against metabolic syndrome

Main food components considered in the literature as having potential ameliorating effect on any disorder associated with metabolic syndrome may be included in one of the following groups:

- *Fiber*, both soluble (e.g., pectins, beta-glucans, naturally occurring gums, inulin, psyllium) and insoluble (e.g., cellulose, hemicellulose, lignin), is reported to have laxative properties and to mitigate both hypercholesterolemia and hyperglycemia [15]. When fermented by probiotic bacteria, *prebiotic fiber* (fiber that resists digestion in the stomach and the small intestine and reaches the colon intact) breaks down into short-chain fatty acids (butyrate, acetate, and propionate), which are reported to enhance glucose and fat metabolism [16].

- *Monounsaturated fats, polyunsaturated fats (both omega-3 and omega-6), plant sterols, and essential fatty acids* instead of saturated fats and trans-fatty acids are proved to be effective in decreasing total cholesterol and increasing the blood level of high-density lipoproteins (HDLs) [17].

- *Vitamin E and C* consumption is associated to a reduction of vascular risk by decreasing oxidative stress (lipid peroxidation) and proinflammatory cytokines [17]. Improved vitamin C status is hypothesized to alleviate endotoxemia and its consequent proinflammatory responses that are suggested to initiate insulin resistance and related metabolic disorders; on the contrary, inadequate vitamin C status contributes to small intestinal bacterial overgrowth, transcytosis of enteric bacteria, and an elevation of circulating lipopolysaccharide, which elicits a low-grade inflammatory response [18]. As for *vitamin D*, it reduces the intestinal absorption of fat by increasing that of calcium [17].

- *Bioactive peptides*, having a size range of 2–50 amino acids, have potential to regulate blood pressure and glycemia, reduce cholesterol level and body mass, and scavenge free radicals [19]. Lactotripeptides isoleucine-proline-proline and valine-proline-proline, whose concentrations increase during the ripening process of cheese, are particularly considered as strong antihypertensive agents [20]. In the case of obesity, foods that contain bioactive peptides provide a satiating effect and lead to appetite suppression.

- *Minerals'* (selenium, magnesium, and zinc) ability to decline metabolic syndrome is related with their antioxidant properties and their participation in insulin synthesis and regulation [20]. Moreover, calcium intake (1200 mg/day) has been demonstrated to increase fat mass loss in overweight and obese adults [21]. Mechanisms to explain this effect include that during low calcium intake, more calcium enters adipose tissues cells and subsequently stimulates the expression of lipogenic genes in parallel with suppressing lipolysis [22]. Also, calcium increases fecal fat loss by binding to fat in the lumen and forming non-absorbed complexes [23]. This ability of calcium to decrease lipogenesis may be enhanced due to a synergistic effect with other components in dairy products (vitamin D and angiotensin-converting enzyme inhibitors) [21].

- *Essential amino acids*, mainly histidine and glycine, are associated with a decrease in insulin resistance and blood pressure, respectively, although conclusive evidence is lacking and additional studies are needed [17].

- *Phytochemicals*, mainly polyphenols (phenolic acids, curcuminoids, stilbenes, lignans, flavonoids, flavonols, flavones, anthocyanins, etc.) but also other bioactive components present in small quantities in fruits and vegetables (triterpenes, carotenoids, etc.), have demonstrated anti-inflammatory, anti-oxidative, antiadiposity, and cardioprotective functions in a huge amount of studies [24–28]. Some phytochemicals, among which are caffeine, ephedrine, capsaicin, and salicylic acid, also act as thermogenic compounds that produce heat from lipids and fats, thus burning extra calories and preventing the accumulation of fat in body tissues [20].

- *Probiotics* are microorganisms that improve the availability and digestibility of nutrients while maintaining the balance of intestinal microflora in the gut [20]. Mainly belonging to the *Lactobacillus* and *Bifidobacterium* genera, probiotics emerge as prospective biotherapies in the management of metabolic disorders including obesity and diabetes by counteracting the adverse effects of a high-fat diet [29].

2.1 Phytochemicals

Phytochemicals are naturally occurring plant chemicals that, beyond providing plants with color, odor, and flavor, can influence chemical processes within human bodies in a beneficial way. Main phytochemicals under research include carotenoids (β-carotene, lycopene, lutein, zeaxanthin) and polyphenols, which include phenolic acids, flavonoids, and stilbenes/lignans [30]. Flavonoids can be further divided into groups based on their similar chemical structure, such as anthocyanins, flavones, flavanones, isoflavones, flavonols, and flavanols. Flavanols further are classified as catechins, epicatechins, and proanthocyanidins.

Phytochemical compounds have gained popularity in recent years due to their broadly documented effect in cancer prevention among other biological effects,

such as the prevention and treatment of obesity, cholesterol, and diabetes [31]. Mechanisms employed by phytochemicals in ameliorating metabolic syndrome risk factors are diverse and dependent on their particular chemical structure. Whereas catechins mainly induce fat oxidation and improve endothelial function, cyanidins and theaflavins inhibit enzymes involved in the synthesis of fatty acids and triglycerides. Other phytochemicals, such as gallic acid, quercetin, and capsaicin, reduce preadipocyte proliferation by induction of cell apoptosis, while low-molecular proanthocyanidins have the ability to inhibit the activity of specific angiotensin-converting enzyme. Having a similar chemical structure, isoflavones can also influence the activity of human estrogens.

For some bioactive components, several in vitro and in vivo (either animals or humans) studies have been performed; however, as evidenced in **Tables 1**–**3**, results differ among them. While in vitro or animal studies usually yield positive results, clinical human studies are still inconclusive. The lack of standardization or aspects related to the dose or duration of supplementation may be the cause of these results. Moreover, studies both in vitro and with animals (**Tables 1** and **2**) have been carried out with synthetic components (only spermidine was obtained directly from lulo fruit), while in vivo studies with humans have been carried out mainly with extracts including the bioactive compounds (**Table 3**).

Phytochemical(s)	Methodology	Beneficial effect(s)	Reference
Synthesis naringenin	3T3-L1 cell line and *Pemphigus vulgaris*-treated HaCaT cell line. Naringenin was added to the cell growing media in a dose of 25 μg/mL, and effect was measured after 24, 48, 72, 96, or 120 hours	Anti-adipogenic, antioxidant, anti-inflammatory, and antiapoptosis effects	[32, 33]
Pentacyclic triterpenes (oleanolic acid, 18β-glycyrrhetinic acid, ursolic acid, celastrol, maslinic acid, ilexgenin A)	3 T3-L1 cell line or 10 T1/2 cells and primary fat SVF cells or HepG2 cells Doses and times were not specified	Decreased obesity-induced inflammation, stimulated lipolysis, and decreased adipocyte differentiation	[26]
Synthesis carvacrol	Cyclooxygenase-2 assay IC50 = 0.8 μM	Anti-inflammatory potential	[34]
Spermidine (from ethanolic lulo pulp extract)	In vitro measurement of angiotensin-converting enzyme inhibition IC50 = 1.8 ppm	Hypertension control	[35]
Flavonoids (naringenin, rutin, hesperidin, resveratrol, naringin, and quercetin)	3 T3-L1 cell line IC50 = 40.4 μM for quercetin IC50 ≥ 500 μM for naringenin, rutin, hesperidin, resveratrol, and naringin	Quercetin efficiently inhibited cell population growth and increased induction of apoptosis	[36]
Resveratrol	Maturing preadipocytes and adipocytes. Dose not specified	Decreased adipogenesis, increased lipolysis, induced apoptosis, and reduced lipogenesis and proliferation, thereby contributing to reduce lipid accumulation. Reduced inflammatory response and improved insulin sensitivity	[37]

Phytochemical(s)	Methodology	Beneficial effect(s)	Reference
Ajoene	Mature 3T3-L1 adipocytes Ajoene at 200 μM decreased cell viability in 50% after 24 hours of treatment	Influenced the regulation of fat cell number	[38]
Green tea catechins	3 T3-L1 cells Epigallocatechin or epigallocatechin gallate was added to the cell growing media in a dose from 1, 10, 50, 100, 200, and 200 μM for some hours until some days (8–16 days)	Increased apoptosis and decreased preadipocyte proliferation	[27]

Table 1.
Fruits, vegetables (or extracts), and phytochemicals endorsed by recent in vitro studies.

Phytochemical(s)	Methodology	Beneficial effect(s)	Reference
Naringenin	Rats and mice 10 mg/kg•day by oral gavage for 4 weeks; 0.1% in an experimental diet for 6 months; 1% and 3% in a high-fat diet for 4 and 30 weeks, respectively	Antioxidant, antihyperlipidemic, anti-obesity, antihyperglycemic, anti-diabetic, anti-inflammatory, antihypertensive, and cardioprotective activities	[39]
Synthesis apigenin	Mice 50 mg/kg•day by oral gavage for 4 weeks	Attenuated insulin resistance, dyslipidemia and liver injury, and mitigated oxidative stress	[40]
Pentacyclic triterpenes: oleanolic acid, 18β-glycyrrhetinic acid, ursolic acid, α, β-amyrin, carbenoxolone, asiatic acid, corosolic acid, bardoxolone methyl, lupeol, ilexgenin A	Rats and mice Oleanolic acid (25 mg/kg•day, once daily, 10 weeks) to fructose-fed rats; ursolic acid-treated fat-fed mice at a dose of 50 or 200 mg/kg of body weight (orally for 8 weeks); lupeol at 0.67 g/kg, given orally for 7 weeks	Decreased fatty acid synthesis, triglyceride synthesis and plasma triglycerides, leptin and free fatty acids, and also triglyceride content in skeletal muscle Reduced fatty liver, adipocyte size, hepatic steatosis, insulin resistance, inflammation, oxidative stress, body weight, atherosclerosis, and hypertension Decreased cholesterol synthesis, total cholesterol, VLDL and LDL-cholesterol, cholesterol in liver and in adipose tissue	[26]
Synthesis carvacrol	Mice Carvacrol was added to the diet in a 0.1% (w/w) (equivalent to 100 mg/kg body weight) for 10 weeks	Prevented obesity by decreasing body weight gain, visceral fat-pad weights, and plasma lipid levels; also inhibited visceral adipogenesis and attenuated the production of pro-inflammatory cytokines in visceral adipose tissues	[41]
Oryzanol and ferulic acid	Mice High-fat diet supplemented with 0.5% (w/w) oryzanol or 0.5% (w/w) ferulic acid for 7 weeks	Decreased in body weight, improved blood glucose metabolism, may be beneficial for the treatment of diabetic hyperglycemia	[42]

Phytochemical(s)	Methodology	Beneficial effect(s)	Reference
Curcuminoids	Rats Rats were fed with high-fat diets with curcuminoid supplement at concentrations of 30, 60, and 90 mg per kilogram of body weight every day for 12 weeks	Decreased plasma free fatty acid levels and improves cardiac autonomic nervous system activity in obesity Contributed to lower body fat and body weight gain Improved obesity-associated inflammation and associated metabolic disorders such as insulin resistance, hyperglycemia, hyperlipidemia, and hypercholesterolemia	[43]
Quercetin	Rats and mice Rats and mice fed with a Western diet containing 0.05% quercetin for 20 weeks	Decreased body weight, visceral fat, blood glucose, free cholesterol, total antioxidant status, lipid accumulation, and systolic blood pressure	[24]
Green tea catechins	Rats and mice Different dose-time treatment: from 0.5–4% of different catechins for 6–22 weeks	Decreased body weight, total lipids, cholesterol, and triglycerides in liver and plasma. Also improved glucose homeostasis: increased glucose tolerance and decreased serum glucose, insulin resistance, and homeostasis model assessment of insulin resistance	[27]

Table 2.
Fruits, vegetables (or extracts), and phytochemicals endorsed by recent in vivo (preclinical trials) studies.

Phytochemical(s)	Methodology	Beneficial effect(s)	Reference
Resveratrol	A randomized, double-blind, placebo-controlled clinical trial was carried out in 24 patients with diagnosis of metabolic syndrome 12 patients received trans-resveratrol (500 mg) three times per day before meals for 90 days	Decreased weight, body mass index, fat mass, waist circumference, and total insulin secretion	[44]
Artichoke leaf extracts rich in flavonoids and caffeoylquinic acid derivatives	Double-blind placebo-controlled randomized clinical trial was carried out in 80 patients with a diagnosis of metabolic syndrome 80 patients with metabolic syndrome received 1800 mg of artichoke leaf extract as four tablets per day for 12 weeks	Decreased ox-LDL and triglyceride levels	[45]
Oligonol extract	Randomized double-blind, placebo-controlled study with 18 subjects. All subjects took two capsules of Oligonol (50 mg/capsule) twice a day for 10 weeks.	Decreased body weight, abdominal circumference, and visceral fat volume	[46]
Pomegranate juice	A randomized, double-blind, placebo-controlled clinical trial was carried out in 20 obese [body mass index (BMI) 30.0–39.9] adults 10 patients received 120 mL of pomegranate juice or placebo while in a fasted state before breakfast every day for 1 month	Did not modify insulin secretion and sensitivity in patients with obesity; however, the natural evolution to increased weight and adiposity was halted	[47]

Phytochemical(s)	Methodology	Beneficial effect(s)	Reference
Cocoa extract	Double-blind, randomized, placebo-controlled parallel nutritional intervention with 50 obese volunteers [30.59(2.33) kg/m^2]. Meals supplemented with 1.4 g/day cocoa extract for 4 weeks	A marginal decrease (P = 0.072) in oxidized bases was observed, which attributed to weight loss	[48]
Green tea catechins	Various randomized, double-blind, placebo-controlled clinical trials. Some studies with different dose-time treatment: from 38 to 600 mg/day of different catechins for 6–24 weeks	Not all studies have found positive results for obesity-related measures. Green tea administration has also shown no influence on body weight, body mass index, fat mass, and waist and hip circumference	[27]
Black seeds and turmeric	Double-blind randomized controlled trial Black seeds (1.5 g/day), turmeric (2.4 g/day), its combination (900 mg black seeds and 1.5 g turmeric/day) for 8 weeks	Improved blood pressure, waist circumference, hip circumference, body mass index, LDL-cholesterol, HDL-cholesterol, and triglyceride content	[49]

Table 3.
Fruits, vegetables (or extracts), and phytochemicals endorsed by recent in vivo (clinical trials) studies.

In vitro studies achieve 50% of cell population growth inhibition with active compound amount of ppm, and, in some cases (some flavonoids, ajoene, catechins), a dose-time-dependent effect is detected. These dose-time-dependent effects, together with the multivariate effects observed in most cases, are largely due to the antioxidant properties of the phytochemicals considered. Flavonoids tested on cell population growth were well correlated with their antioxidant activity [36].

The doses used in the preclinical studies were much higher than those used in the clinical trials, and the limitations in the ingested doses may be the cause of the ineffective results. Kobori et al. [24] concluded that in vitro anti-aggregatory effects of flavonoids are caused by concentrations that cannot be attained in vivo by dietary consumption.

In most preclinical studies, imbalances are induced in mice with a high fructose diet, and the effect that the active component has on these induced disorders is determined. Also in the clinical studies performed with positive results, the component of interest was provided as part of a low-fat diet to patients with physiological alterations associated with metabolic syndrome. In these conditions the results show a palliative effect but in no case a preventive effect. Thus, quercetin supplementation did not affect the antioxidant status under healthy, normal conditions [24].

Sometimes solubility and bioavailability are a major limitation factor. As an example, pentacyclic triterpenes such as ursolic acid are poorly bioavailable because of poor aqueous solubility and permeability through biological membranes [26]. These limit their biological effects. Some strategies have increased bioavailability. For example, on comparing the oral bioavailability of ursolic acid microcrystals and nanocrystals to its coarse suspension in rats, ursolic acid microcrystals and nanocrystals exhibited 1.40- and 2.56-fold enhancement, respectively. Also, a new

product from polyphenols of lychee has been developed. Oligonol, a unique low-molecular-weight polyphenol, was developed to enhance absorption of polyphenols from the intestines. It contains 15.7% polyphenol monomer ((+)-catechin, (−)-epicatechin, etc.) and 13.3% polyphenol dimer (procyanidin B2, etc.), while lychee fruit-derived polyphenol contains 6.4% polyphenol monomer and 9.9% polyphenol dimer [46].

Concluding from above, translational studies from animal observations to human clinical trials and ultimately community interventions are needed to further confirm the effects of phytochemicals and foods rich in these bioactive compounds. The technological development should be aimed at the implementation of strategies that increase the bioavailability of active components with proven activity and that allow to provide the adequate doses avoiding toxicity problems.

2.2 Probiotics

Probiotics are defined as live microorganisms which, when administered in adequate amounts, confer a health benefit on the host [50]. Evidence from the latest studies in which probiotic efficiency in metabolic disorder management is assessed by both in vitro and in animal or human subjects is compiled in **Tables 4** and **5**.

Regarding the strains employed in the management of several inflammatory diseases, they usually belong to the *Lactobacillus* and *Bifidobacterium* genera, although *Pediococcus pentosaceus* LP28, *Bacteroides uniformis* CECT 7771, and *Akkermansia muciniphila* have also been proved to have anti-obesity effects [65]. In general, doses

Probiotic organism	Methodology	Beneficial effect(s)	Reference
Lactobacillus plantarum Ln4 isolated from napa cabbage kimchi	3T3-L1 adipocytes	Inhibited adipogenesis and stimulated glucose uptake	[51]
	Mice fed on a standard diet or a high-fat diet (5–7 mice per group) supplemented or not with 5×10^8 CFU/day for 5 weeks	Reduced diet-induced weight gain, lipid accumulation, and insulin resistance	
Lactobacillus reuteri 263 patented strain	10 rats fed on a normal diet and 30 rats fed on a high-energy diet supplemented or not with 2.1×10^9 CFU/rat/day or 1.05×10^{10} CFU/rat/day for 8 weeks	Reduced obesity by decreasing pro-inflammation factors and increasing antioxidant enzymes in the serum	[52]
Green tea (rich in epigallocatechin gallate) and *Houttuynia cordata* leaf (rich in chlorogenic acid) extract fermented with *Lactobacillus paracasei* subsp. *paracasei* NTU 101 originally isolated from infant	3T3-L1 pre-adipocyte model	Fermented tea powder promoted lipase activity in adipocytes, which thereby improves the lipolytic effect	[53]
	Rats fed for 8 weeks on a normal diet or a high-fat diet supplemented or not with: • Unfermented tea powder • (12.5 mg EGCG/day) Fermented tea powder • (12.5–25 mg EGCG/day plus $3.75–7 \times 10^{10}$ CFU/day) NTU 101 powder • (7.5×10^{10} CFU/day) • EGCG powder (25 mg/day)	NTU 101-fermented tea had a more significant effect on the reduction of body weight gain and body fat content than the unfermented tea	

Probiotic organism	Methodology	Beneficial effect(s)	Reference
Lactobacillus fermentum strain 4B1 isolated from fermented rice and shrimp compared to a commonly prescribed weight loss drug	35 obese induced mice. Daily dose: none, 12 mg/kg orlistat (Xenical®) or 2.5×10^{10} CFU/kg for 21 days	Prevented obesity in lean hosts and reduced body weight gain and adipose tissue weight in mice receiving the high-fat diet	[54]
Heat-killed and live *Lactobacillus reuteri* GMNL-263	Rats fed for 12 weeks on a normal diet or a high-fat diet supplemented or not with 2×10^9 cells/day for 12 weeks	Both heat-killed and live cells prevented obesity, insulin resistance, and hepatosteatosis in high-fat diet rats by suppressing the inflammatory response and the expressions of specific cytokines	[55]
Live or pasteurized *Akkermansia muciniphila*	Obese and diabetic diet-induced mice	Pasteurization-enhanced bacterium capacity to reduce fat mass development, insulin resistance, and dyslipidemia induced by a high-fat diet	[56]
Bifidobacterium pseudocatenulatum SPM 1204, *Bifidobacterium longum* SPM 1205, and *Bifidobacterium longum* SPM 1207	36 rats fed for 5 weeks on a normal diet or a high-fat diet supplemented or not with 10^8–10^9 CFU(1:1:1)/day	Reduced body weight and fat gain, as well as total cholesterol, HDL-cholesterol, and LDL-cholesterol levels in serum blood and harmful enzyme activity	[57]
Lactobacillus reuteri ATCC PTA 4659, *Lactobacillus reuteri* DSM 17938, and *Lactobacillus reuteri* L6798	40 mice fed on a high-fat diet for 12 weeks supplemented or not with 10^9 CFU/day of a specific strain	Strain ATCC prevented obesity, lowered blood insulin level, and affected liver steatosis in hypercholesterolemic mice on a high-fat diet	[58]
Pediococcus pentosaceus LP28 isolated from longan fruit and *Lactobacillus plantarum* SN13T	5 lean control and 30 diet-induced obese mice fed for 6 weeks with a regular diet or a high-fat diet supplemented or not with 1.25×10^9 CFU/g of a specific strain	Live LP28 reduced body weight gain and liver lipid contents, whereas heat-killed and SN13T were ineffective	[59]

Table 4.
Probiotic strains endorsed by in vitro and animal studies.

greater than 10^8 CFU/day were orally administered to the drinking water or by oral gavage of the lyophilized bacterial powder in water (in animal studies) as well as in the form of capsules or fermented milk products (in human studies). Probiotic supplementation in rat and mouse studies usually applies to both diet-induced obese individuals and lean individuals fed on a high-fat diet, thus showing the effect of probiotics in both the treatment and the prevention of several metabolic abnormalities. However, human studies are basically applied to overweight or obese healthy individuals, submitted or not to energy restriction and/or regular exercise. As regards in vitro studies, treatment of 3T3-L1 pre-adipocytes with test substances during their differentiation stage is the most common technique.

Probiotic organism	Methodology	Beneficial effect(s)	Reference
DUOLAC 7 including *S. thermophilus* KCTC 11870BP, *L. plantarum* KCTC 10782BP, L. *acidophilus* KCTC 11906BP, *L. rhamnosus* KCTC 12202BP, *B. lactis* KCTC 11904BP *B. longum* KCTC 12200BP, and *B. breve* KCTC 12201BP (5×10^{12} CFU/capsule)	A randomized, double-blinded, placebo-controlled study in 50 female aged 19–65 with BMI > 25 kg/m^2 and waist circumference > 85 cm following usual dietary intake and lifestyle receiving Bofutsushosan (3 g per administration) and probiotics (1 capsule) or Bofutsushosan and placebo twice per day for 8 weeks	Probiotics increased HDL cholesterol level and effectively modified the composition of gut microbiota *Bifidobacterium breve* was the only strain showing a significant tendency of declination of endotoxin level, so it was suggested as a promising probiotic strain specified for obesity treatment	[60]
L. rhamnosus CGMCC1.3724 (LPR) in capsules (1.62×10^8 CFU/capsule) with a mix 70:30, v/v of oligofructose and inulin (300 mg/capsule)	A double-blind, placebo-controlled, randomized trial in 125 healthy overweight men and women (age between 18 and 55, BMI between 29 and 41 kg/m^2) following a supervised diet and consuming two capsules per day or placebo for 24 weeks	LPR supplementation accentuated body-weight loss in women submitted to energy restriction; this effect persisted in the subsequent maintenance phase, when energy restriction was not further imposed	[61]
L. plantarum TENSIA (DSM 21380) isolated from the gastrointestinal tract of healthy Estonian children added to cheese milk in amounts of 1.5×10^{11} CFU/g before renneting	A randomized, double-blind, placebo-controlled, parallel-designed study in 40 subjects with metabolic syndrome following a hypocaloric diet supplemented with 50 g/day of probiotic or control cheese for 3 weeks	The hypocaloric diet supplemented with the probiotic cheese reduced BMI, arterial blood pressure, and the risk of metabolic syndrome in obese patients with hypertension	[62]
Milk fermented with or without *Lactobacillus gasseri* SBT2055 (LG2055)	Multicenter, double-blind, placebo-controlled intervention trial in which 87 subjects (BMI of 24.2–30.7 kg/m^2 and abdominal visceral fat area of 81.2–178.5 cm^2) were randomly assigned to consume 200 g/day of fermented milk with or without LG2055 for 12 weeks while maintaining their habitual mode of living	Intake of the probiotic LG2055 reduced abdominal visceral and subcutaneous fat areas as well as body weight, BMI, waist and hip circumferences, and body fat mass	[63]
Lactobacillus amylovorus and *Lactobacillus fermentum* microencapsulated in yogurt (1.39×10^9 CFU/yogurt)	A placebo-controlled, double-blind crossover clinical investigation with 28 healthy but overweight individuals (BMI between 25 and 32 kg/m^2)	Probiotic consumption altered intestinal microflora in a manner that was associated with reduced total body adiposity, an important anthropometric indicator of obesity	[64]

Table 5.
Probiotic strains endorsed by in vivo studies.

Among the analytical determinations, the most representative are changes in the body weight and the body fat content as well as main serum biochemical parameters (glucose, insulin, leptin, lipids, lipoproteins, and inflammatory indicators). Postmortem determinations, such as the liver weight or the adipose tissue histology, are also common in animal studies. Finally, since probiotics are known to increase the bacterial diversity of intestinal microflora, in vivo studies usually include viable counts in fecal samples and evaluation of intestinal survival. In fact, a lot of recent research relates gut microbiota composition with almost every chronic disease: from gastrointestinal diseases to obesity, diabetes, cancer, and even neurological and neurodegenerative disorders such as depression, autism, anxiety, and Parkinson's disease [66]. Not only does a certain microbiota predispose to suffer certain diseases, but also the incidence of a certain disorder modifies the gut microbiota of an individual. In overweight/obese subjects, *Bacteroides*, *Parabacteroides*, *Ruminococcus*, *Campylobacter*, *Dialister*, *Porphyromonas*, *Staphylococcus*, and *Anaerostipes* are the dominant genera linked to a low diversity of species, while *Faecalibacterium*, *Bifidobacterium*, *Lactobacillus*, *Butyrivibrio*, *Alistipes*, *Akkermansia*, *Coprococcus*, and *Methanobrevibacter* are predominant in lean individuals with a high bacterial diversity [67]. Apparently, the intestinal microflora of obese subjects is more efficient at extracting energy from a given diet than that of lean individuals, thus leading to increased energy storage and adiposity [65]. Moreover, beneficial intestinal microflora is known to produce short-chain fatty acids (e.g., acetate, butyrate, and propionate) from indigestible polysaccharides, which may act as energy substrates as well as regulators of satiety and food intake. Last but not least, *Lactobacilli* and *Bifidobacteria* are known to synthesize bioactive isomers of conjugated linoleic acid with antidiabetic, anti-atherosclerotic, immunomodulatory, and anti-obesity properties [68]. In other words, low bacterial diversity in obese individuals is associated with a reduction in butyrate-producing bacteria, a reduction in hydrogen and methane production, an increase in mucus degradation, and an increase in the potential to manage oxidative stress. Since intestinal microflora composition is strongly affected by dietary patterns, studies evaluating the effect of certain food components on the growth of bacteria with beneficial effect on metabolic syndrome and obesity, particularly *Akkermansia muciniphila* and *Faecalibacterium prausnitzii*, are of great interest. Increasing the intestinal population of these two species has become a real opportunity to decrease alterations associated with obesity and metabolic disorders [69]. In addition to this, high-fat diet treatment has been proven to induce metabolic changes that impair gut barrier function in rats [55].

Together with increasing gut microbiota diversity, the production by fermentative action of those bioactive molecules involved in the metabolic pathways that trigger the metabolic syndrome has also taken a lot of interest in the last years. In particular, many studies focus on the phenolic compound bioconversion by food fermentation into other components with greater beneficial effect on the abnormalities associated with metabolic syndrome. As an example, Wang et al. [53] proved that the use of *Lactobacillus paracasei* subsp. *paracasei* strain NTU 101 in the fermentation of green tea and *Houttuynia cordata* leaves increased the levels of epigallocatechin gallate (EGCG), epigallocatechin (EGC), and chlorogenic acid, which enhanced the probiotic effect on body fat reduction. These results show the synergistic or complementary effect between the two bioactive compounds: the probiotic strain increases gut microbiota diversity and enhances intestinal absorption, while the EGCG acid promotes the lipolysis process. Zarrati et al. [70] also reported a synergistic effect between a weight loss diet and probiotic yogurt in overweight and obese individuals.

It should be noted that in order to exert their health benefits, probiotics do not necessarily have to be alive. In fact, heat-killed *Lactobacillus reuteri* GMNL 263 was as effective as live *Lactobacillus reuteri* GMNL 263 in attenuating obesity-induced

metabolic abnormalities in high-fat diet-induced rats by reducing insulin resistance and hepatic steatosis formation [55]. Also both heat-killed *Lactobacillus plantarum* strain Ln4 and freeze-dried cultured MRS broth significantly reduced lipid accumulation and stimulated glucose uptake in 3T3-L1 adipocytes [51]. Finally, Plovier et al. [56] found that pasteurization enhanced the capacity of *Akkermansia muciniphila* to reduce fat mass development, insulin resistance, and dyslipidemia in mice. It seems that a specific protein isolated from the outer membrane of *Akkermansia muciniphila* is stable at temperatures used for pasteurization and improves the gut barrier, thus being the main responsible factor of the beneficial effect of the bacteria on health.

Of all the studies analyzed, it is concluded that many microorganisms have the potential for development as therapeutic probiotics for obesity and associated disorders. However, due to the strain specificity of probiotic microbes in exerting their beneficial effects, bacterial strains of the same species have different effects on adiposity and insulin sensitivity.

3. Case study: functional food development from lulo fruit with potential effect against metabolic syndrome

The lulo fruit (*Solanum quitoense* Lam.), also known as "naranjilla," is an important native Andean crop. Grown and consumed mainly in Colombia, Ecuador, and Central America, the plant produces a spherical, 3–8-cm-diameter fruit with orange skin (epicarp) covered by short, stiff, and thorny hairs or spines. The internal structure of the fruit is similar to that of the tomato fruit: a very juicy, acidic, and translucent yellow-green pulp (mesocarp and endocarp) that is located in four compartments separated by membranous partitions [71]. In Colombia, lulo is an economically important crop which, in 2015, was grown in a total area of 10,623 ha, with a total yield of 82,354 tons and an average yield of 9.6 tons/ha [72]. Although the principal market of this crop is in the producing countries themselves, it has gained interest in recent years in national and international markets due to its organoleptic properties and its nutritional value. In fact, lulo has an intense and refreshing taste and is rich in proteins, vitamin C, fiber, and antioxidant compounds, such as all-trans-β-carotene, lutein and zeaxanthin, chlorogenic acids, and flavonol glycosides [73–76], in addition to iron, calcium, phosphorus, and some precursors of vitamin A [77] (**Table 6** [78]). In particular, fruit carotenoids present in lulo fruit have been associated to the prevention of several illnesses, including hypertension, obesity, and cardiovascular diseases [79–81]. Also the potential of lulo as an antihypertensive agent is related to its content in N1,N4,N8-tris (dihydrocaffeoyl) spermidine and N1,N8-bis (dihydrocaffeoyl) spermidine (actually bioactive amines), which are bitter active compounds with inhibitory activity against the angiotensin-converting enzyme (ACE-1) that indirectly increases the blood pressure by causing blood vessels to constrict [35]. In turn, when evaluating the antihypertensive activity of some compounds of the lulo fruit by means of chemical computation techniques, the researchers of the Natural Additives of Aroma and Color group from the Chemistry Department of the Universidad Nacional de Colombia found that this was between 10 and 20 times higher than that of the drugs traditionally used to treat hypertension.

Based on the considerations made above, the lulo fruit comes to be a promising alternative with regard to the prevention and relief of hypertension-related diseases. However, being a highly perishable fruit, technological transformation processes are indispensable to take advantage of its beneficial properties by as many consumers as possible. According to this, the group of Functional Foods of the University Institute of Food Engineering for Development of the Polytechnic

Proximates		Minerals		Vitamins	
Carb	5.9 g	Ca	8 mg	Folate	3 μg
Fiber	1.1 g	Mg	11 mg	Vit B3	1.45 mg
Protein	0.44 g	P	12 mg	Vit B5	0.22 mg
Sugars	3.74 g	K	200 mg	Vit B1	0.05 mg
Fat	0.22 g	Na	4 mg	Vit B6	0.11 mg
Water	93.05 g	Cu	0.03 mg	Vit C	3.2 mg
Energy	25 cal	Fe	0.35 mg	α-Carotene	4 μm
		Mn	0.07 mg	β-Carotene	333 μm
		Se	0.4 μg	β-Cryptoxanthin	10 μm
		Zn	0.1 mg	Lutein and zeaxanthin	299 μm
				γ-Tocopherol	0.2 mg
				α-Tocotrienol	0.01 mg
				γ-Tocotrienol	0.01 mg
				Vit A	28 μm
				Vit E	0.75 mg
				Vit K	14.6 μ

Values expressed for 100 g of fresh fruit.

Table 6.
Nutrition facts of lulo fruit.

University of Valencia (Spain), in conjunction with the group of Biodiversity Evaluation and Use of the Technological University of Chocó (Colombia), is working on the development of new functional foods from lulo fruit (*Solanum quitoense* Lam). On the one hand, a stable lulo juice with improved antioxidant properties has been obtained by means of the application of moderate high homogenization pressures (from 50 to 150 MPa) instead of traditional thermal pasteurization. The same juice has proved to be a suitable impregnation liquid for the enrichment of other fruits with a porous structure, such as Granny Smith apples. The lulo fruit itself was found to have a high impregnation capacity, which implies susceptibility to be enriched with different bioactive compounds. Finally, after fermentation with *Lactobacillus reuteri*, selected for being one of the strains with proven effect against the metabolic syndrome, the number of viable counts in lulo juice resulted to be high enough to claim that it also may exert a probiotic effect. Most relevant results in relation to these advances are shown next.

3.1 Enhancing antioxidant properties of lulo juice by means of moderate high-pressure homogenization

This section shows the effect that homogenization pressures in the range of 50–150 MPa have on main physicochemical properties, including the total content of phenols and flavonoids and the antioxidant activity measured by both DPPH and ABTS methods. To obtain the juice, washed and without peduncle lulo fruits were crushed for 10 min in a blender (Phillips Avance Collection Standmixer, 800W 2L). The liquefied product was then filtered with a stainless steel sieve of 500 μm nominal aperture. When necessary, the juice was homogenized at 50, 100 or 150 MPa in a laboratory scale high-pressure homogenizer (Panda Plus 2000, GEA-Niro Soavi, Parma, Italy).

Homogenization pressure	Brix	pH	ρ (g/cm^3)	K (Pa sn)	n
0 MPa	6.57 ± 0.12^a	3.13 ± 0.02^a	1.04 ± 0.02^a	0.39 ± 0.12^a	0.44 ± 0.06^b
50 MPa	6.4 ± 0.4^a	3.12 ± 0.02^a	1.06 ± 0.04^a	0.9 ± 0.4^b	0.37 ± 0.04^a
100 MPa	6.33 ± 0.15^a	3.18 ± 0.03^a	1.07 ± 0.02^a	0.79 ± 0.02^{ab}	0.37 ± 0.03^a
150 MPa	6.4 ± 0.4^a	3.15 ± 0.02^a	1.09 ± 0.02^a	1.3 ± 0.5^b	0.34 ± 0.04^a

$^{abc...}$ *different superscripts in the same column indicate statistically significant differences ($p < 0.05$).*

Table 7.
Effect of homogenization pressure on pH, soluble solid content (brix), apparent density (ρ), and rheological properties of lulo juice.

As it can be observed in **Table 7**, neither the soluble solid content nor the pH or the density of the lulo juices was significantly affected by homogenization pressure. On the contrary, the consistency index (K) increased significantly after the homogenization step, which is directly related to particle size reduction. As regards the average size of particles, it was maximum in the non-homogenized juice (251 ± 5 μm) and minimum in the juice homogenized at 150 MPa (57.94 ± 0.14 μm). Therefore, homogenization increased the amount of solids in suspension and, consequently, the stability of the cloud.

As regards the antioxidant properties of lulo juice, the fruit's own transformation into juice significantly reduced both total phenol and total flavonoid contents, which were probably separated from the juice together with the bagasse during the filtration step. However, the concentration of such compounds increased slightly (from 1.03 ± 0.16 to 1.28 ± 0.07 mg GAE/g for phenols and from 0.35 ± 0.24 to 0.570 ± 0.011 mg QE/g for flavonoids) after juice homogenization at 150 MPa and the subsequent reduction in the average particle size. Similar trends were observed when analyzing the total antioxidant activity by both the ABTS and the DPPH methods and when quantifying spermidine by HPLC analysis. For the latter compound, concentration increased from 1.86 ppm in non-homogenized lulo juice to 2.04 ppm in lulo juice homogenized at 150 MPa.

Regarding the ability of the homogenized lulo juice treated at 150 MPa to impregnate Granny Smith apples sliced, it was found to be similar to that of an isotonic sucrose solution. In this way, the bioactive compounds present in lulo juice may become part of the vacuum impregnated fruit composition. To be more precise, around 0.22 m^3 of lulo juice homogenized at 150 MPa could be incorporated to every m^3 of fresh apple.

3.2 Lulo fruit as a food matrix for vacuum impregnation and food property improvement

In this section, impregnation properties of lulo fruit are discussed. Vacuum impregnation being a matrix engineering technique allows to introduce desirable compounds into the porous structure of foods by applying a pressure gradient [14]. Among the impregnation parameters, the volume of the external liquid that can be incorporated into the cellular tissue in a controlled way (i.e., X, in m^3/m^3) stands out, which informs about the feasibility of incorporating physiologically active compounds into its porous structure for the formulation of new products with enhanced functional properties. Hence, unpeeled lulo fruit was cut into 5 mm thick slices and immersed in an isotonic sucrose solution (a_w = 0.994 ± 0.003). Vacuum impregnation was carried out in a pilot plant scale equipment located at the University Institute of Food Engineering for Development of the Universitat Politècnica de

València (Spain). This equipment consists of a stainless steel vacuum chamber connected to a liquid ring pump (SIHI model LOHE-25007). The vessel containing the impregnating solution was placed into the vacuum chamber, and the lulo samples were immersed in the liquid by means of a pneumatic arm operated by a compressor (COMBA, 1,5 HP de 25 L). The working conditions were set at 50 mbar for 10 min and atmospheric pressure for 10 min more. In each trial, the weight change of the samples was recorded according to the procedure described by [82], thus allowing to calculate the characteristic impregnation parameters of the lulo fruit.

As it is shown in **Table 8**, the different batches analyzed behaved in a similar way during the vacuum impregnation step. Positive values of parameters X_1 (between 1 and 5%) and X (between 8.6 and 16%) indicate that the impregnating liquid entered the porous structure after both the vacuum and the atmospheric steps. Likewise, positive values of parameters γ_1 (between 3.9 and 7.1%) and γ (between 2.9 and 6.6%) indicate a volumetric expansion of the lulo matrix after both the vacuum and the atmospheric steps. Compared to other fruits and vegetables [83], the volume fraction of fresh lulo that was filled with the impregnating solution at the end of the process (X, in $m^3/100\ m^3$) was significantly lower than that of Granny Smith apple (21.0 ± 0.9) or Soraya aubergine (64 ± 2) but considerably higher than that of Chandler strawberry (6.4 ± 0.3), Hayward kiwifruit (0.7 ± 0.5), or Bulida apricot (2.2 ± 0.2). Despite such differences, the lulo matrix can be considered as suitable to be enriched with other active compounds by means of the vacuum impregnation technique.

3.3 Probiotic food development from lulo fruit

The growing number of consumers with lactose intolerance, high cholesterol levels, and/or following vegetarian or vegan diets has encouraged the recent use of fruits and vegetables as probiotic carriers in the development of new functional foods. Fruit and vegetable juices are especially suitable for the growing of probiotic microorganisms since they inherently contain beneficial nutrients and have taste profiles that are pleasing to all the age groups [84]. In addition, due to their fast passage through the digestive tract, the viability of probiotic cells in the juices is hardly affected by the harsh acidic environment of stomach [85]. However, these food matrices do not always fulfill the pH or the essential amino acids and vitamins required for the optimum growth of most LAB with proven probiotic effect. This section evaluates the possibility of using the non-homogenized lulo juice as a medium for the growth of *Lactobacillus reuteri* CECT 925T. For this purpose, the lulo juice obtained by the procedure described above was pasteurized at 75°C for

Batch	X_1	γ_1	X	γ	ε_e
1	5 ± 7^a	5 ± 4^a	8.8 ± 1.6^a	3 ± 3^a	6 ± 4^a
2	2.1 ± 1.8^a	6 ± 5^a	10 ± 3^a	5 ± 4^a	6 ± 5^a
3	2 ± 4^a	5 ± 2^a	11 ± 2^{ab}	3.7 ± 0.9^a	8 ± 2^a
4	1 ± 1.4^a	3.9 ± 0.9^a	16 ± 6^b	6.6 ± 1.0^a	9 ± 6^a
5	2.5 ± 1.3^a	7.1 ± 1.0^a	8.6 ± 0.9^a	2.9 ± 0.8^a	6.3 ± 1.2^a

$^{abc...}$ different superscripts in the same column indicate statistically significant differences ($p \leq 0.05$).
X_1 and X stand for the volume fraction of fresh sample impregnated at the end of the vacuum step and at the end of the atmospheric step, respectively; γ_1 and γ stand for the relative volume deformation of fresh sample at the end of the vacuum step and at the end of the atmospheric step, respectively; ε_e stands for the effective porosity.

Table 8.
Vacuum impregnation response of lulo fruit slices (5 mm thick).

2.5 min before being inoculated with 4 mL/L of MRS broth containing the active microorganism in a concentration of 10^8 CFU/mL. After 24 hours of incubation at 37°C, viable counts in the juice were of the order of 10^6 CFU/mL. Although this value was high enough to make an EU-based health claim [86], it was significantly lower to that obtained in mandarin juice inoculated with either *Lactobacillus salivarius* spp. *salivarius* CECT 4063 or *Lactobacillus acidophilus* CECT 903 [87].

In a further step, the lulo juice containing the probiotic was employed as impregnating liquid for the vacuum impregnation of Granny Smith apple slices (5 mm thick). In this way, the probiotic was introduced into a solid matrix without disturbing its organized cellular structure. However, since only 20% of the initial volume of the apple is filled with the impregnation liquid during the vacuum impregnation step, the probiotic content in the impregnated apple was not greater than 10^5 CFU/g. Subsequent lyophilisation of the vacuum impregnated apples did not increase the *Lactobacillus reuteri* content as expected by water removal and subsequent weight loss, it being lower than 10^6 CFU/g in the liophylized sample. Probiotic counts in both the lulo juice and the impregnated apple snack could be improved by adding certain ingredients (e.g., prebiotics, cryprotectants, soygerm powder, yeast extract, etc.) and/or applying specific processing technologies that can improve microorganism survival such as microencapsulation or sublethal homogenization. In any case, it should be interesting to evaluate through both in vivo and in vitro studies the antihypertensive activity of *Lactobacillus reuteri* in the products designed, since it could be enhanced due to a synergistic effect with the spermidine from the lulo juice.

4. Market and consumer trends toward functional foods

Revolution in living standard, eating habits, and increased health awareness has shifted consumer's acceptance toward nutritious, healthy, and disease-preventive food with wider health benefits. Consumer is becoming more and more conscious about the role of food in life extension, well-being, and prevention of chronic diseases [87].

Specific consumer characteristics, such as demographic background or personal motivation to participate in pro-health activities, play a remarkable role in functional food acceptance and consumption. Some sociodemographic characteristics such as gender, education, and age are the most important factors related to the acceptance of functional food. In addition, apart from health benefits, the carrier and the origin of functional components play an important role in making the decision to purchase functional products, consumers being more likely to purchase those functional components found naturally in foods. Other factors, such as organoleptic attributes, convenience, or label information, are found to be essential for consumer's acceptance. In his study, Kraus [88] concludes that consumers are not willing to sacrifice taste and general pleasure of eating and also states that naturalness of a product is very important.

Particularly for probiotics, a major challenge for these products is product acceptability by consumers with regard to sensory criteria. Traditionally, health benefits of probiotics were based in the consumption of fermented dairy products; however, lactose intolerance, cholesterol content, and allergic milk proteins have limited the growth of dairy probiotics. Besides, the increase in vegetarian consumers in both developed and developing countries has also contributed to a growing demand for plant-based probiotic products [87]. According to Panghal et al. [89], fruits are healthy and refreshing and have good taste and flavor profile and can be suitable for probiotics. They are an ideal medium to develop functional foods and have more nutritional values due to the presence of various phytochemicals, antioxidants, no cholesterol, vitamins, mineral content, and dietary fibers. Besides,

economic reasons for the developing countries also require the search for an alternative to dairy products with good nutrients along with health-promoting factors, e.g., fruits, vegetables, cereal, legume, etc., and products which lack cholesterol content but are rich in protein, starches, minerals, fiber, vitamins, and antioxidants.

Nowadays an increasing trend in the Western society is consumer interest and focus toward natural and organic products, where the use of synthetic additives is limited. It has been suggested that natural ingredients with strong antioxidant activity could be used to design novel functional beverages. An increased interest relies upon the fortification with polyphenols due to their beneficial role against cardiovascular diseases, type 2 diabetes, and obesity, among other conditions. The combination of prebiotics, and also phenols with probiotic microorganisms, represents an innovative biotechnology to enlarge the functional food market and especially beverages [90].

According to Grand View Research [91], the global functional food market was higher than 129 billion dollars (US) in 2015, and it is expected to increase up to 250 billion in 2024. Growing consciousness among consumers on their health and proper diet, together with the prospect of reducing or even eliminating nutrition-related diseases, is responsible of this market trend. Society is becoming more and more conscious on the impact that changing dietary patterns may have in the incidence of type 2 diabetes, coronary heart disease, cancer, periodontal disease, and obesity. In this regard, functional foods are believed to play an outstanding role. In addition, increasing healthcare cost, along with the desire of improving later years among the geriatric population, has driven the growth of the functional food industry worldwide.

The global functional food market includes that of carotenoids, dietary fibers, fatty acids, minerals, prebiotics and probiotics, vitamins, minerals, phytochemicals, enzymes, and antioxidants in general. Market revenue of all these products separately is also expected to increase in the coming years. For example, dietary fibers, which are considered to prevent obesity and diabetes, are expected to grow by 8.4% in the next 8 years. Other phytochemicals, such as flavonoids, held a share of over 30% in terms of market value. Although these have been commonly consumed in their natural form, consumer's habits have led to their use in the form of functional food products which are aimed at preventing diet-related chronic diseases including those related to the metabolic syndrome. North America accounts for the largest market in flavonoids, the Asia Pacific demand was over 110 million US Dollars in 2015, and Europe is expected to grow, although at a slower pace. In any case, prevalence of diabetes, obesity, and chronic diseases is likely to propel demand for these nutritional foods and beverages in Europe.

With regard to probiotics, there is also a growing concern on awareness in their functional health benefits against different conditions, including those related to the metabolic syndrome such as obesity or type 2 diabetes [92]. The global probiotic market was thought to be worth 35.5 billion dollars in 2016, with predictions of this increasing up to 65 billion dollars by 2024 [93]. As reported by Lumina intelligence [92], a survey of Ganeden on consumers concluded that almost 80% of consumers preferred to consume probiotics in food and beverage products than in supplements. This is of special value taking into account that consumer preference is a key currency for measuring product success and predicting upcoming tendencies. North America demand for probiotics is expected to increase by 7.9% from 2016 to 2025, whereas the European market will grow at a pace of 7.3%. As for Asia Pacific countries, the probiotics industry is also expected to increase significantly.

Probiotics have achieved a prominent position in the global food market. Among the countries that have shown growth in the probiotic market, Europe represents the largest and fastest growing market, followed by Japan. Currently, there is a wide range of probiotic products offered by companies such as BioGaia Biologics AB, Christian Hansen A/S, ConAgra Functional Foods, Danisco, Groupe Danone, or Lifeway [87].

5. Conclusions

The huge increase in obesity and consequently of physiological disorders associated with this has led to a massive increase in research work conducted in this area over the past 10 years. The relationship between diet and the incidence of metabolic syndrome is clearly contrasted. Although this relationship is tremendously complex and it is hardly affected by other variables related to lifestyle, specific works establish phytochemicals and probiotics as two of the active components present in food, which have the greatest effect on prevention and in the reduction of symptoms associated with metabolic syndrome.

Currently, the technological development achieved by the food industry allows both the design and development of specific foods that include active components in their composition as well as the application of specific techniques that increase the functional value of natural foods. The use of these advances in the right direction can be decisive in the solution of health problems related to obesity. Specifically, the applications of moderate homogenization pressures or food formulation techniques, such as vacuum impregnation, are presented as possibilities to develop liquid and/or solid foods that combine the presence of phytochemicals and probiotics with demonstrated effectiveness against obesity in natural foods such as lulo fruit.

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Conflict of interest

Authors of this book chapter state that they do not have conflict of interest to declare.

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References

[1] World Health Organization. 10 Facts on Obesity [Internet]. 2017. Available from: https://www.who.int/features/factfiles/obesity/en/ [Accessed: December 15, 2018]

[2] Park SY, Seong KS, Lim SD. Anti-obesity effect of yogurt fermented by *Lactobacillus plantarum* Q180 in diet-induced obese rats. Korean Journal for Food Science of Animal Resources. 2016;**36**(1):77-83. DOI: 10.5851/kosfa.2016.36.1.77

[3] Kaur J. A comprehensive review on metabolic syndrome. Cardiology Research and Practice. 2014;**2014**:1-21. DOI: 10.1155/2014/943162

[4] Esser N, Legrand-Poels S, Piette J, Scheen AJ, Paquot N. Inflammation as a link between obesity, metabolic syndrome and type 2 diabetes. Diabetes Research and Clinical Practice. 2014;**105**(2):141-150. DOI: 10.1016/j.diabres.2014.04.006

[5] Monteiro R, Azevedo I. Chronic inflammation in obesity and the metabolic syndrome. Mediators of Inflammation. 2010;**2010**:1-10. DOI: 10.1155/2010/289645

[6] Faloia E, Michetti G, De Robertis M, Luconi MP, Furlani G, Boscaro M. Inflammation as a link between obesity and metabolic syndrome. Journal of Nutrition and Metabolism. 2012;**2012**: 1-7. DOI: 10.1155/2012/476380

[7] Liang Y, Hou Y, Niu H, Lu M, Xue L, Sun Q. Correlation of high-sensitivity C-reactive protein and carotid plaques with coronary artery disease in elderly patients. Experimental and Therapeutic Medicine. 2015;**10**(1):275-278. DOI: 10.3892/etm.2015.2486

[8] Flannagan KS, Ramírez-Zea M, Roman AV, Das AK, Villamor E. Adipose tissue polyunsaturated fatty acids and metabolic syndrome among adult parents and their children. Nutrition, Metabolism, and Cardiovascular Diseases. 2018;**28**(12):1237-1244. DOI: 10.1016/j.numecd.2018.08.008

[9] Retondario A, Fernandes R, Rockenbach G, Alves MA, Bricarello LP, Trindade EBSM, Vasconcelos FAG. Selenium intake and metabolic syndrome: A systematic review. Clinical Nutrition. 2019;**38**(2):603-614. DOI: 10.1016/j.clnu.2018.02.021

[10] Guarnizo-Poma M, Urrunaga-Pastor D, Montero-Suyo C, Lazaro-Alcantara H, Paico-Palacios S, Pantoja-Torres B, et al. Association between serum vitamin B12 levels and metabolic syndrome in a euthyroid population. Diabetes and Metabolic Syndrome: Clinical Research and Reviews. 2018;**12**(6):943-948. DOI: 10.1016/j.dsx.2018.05.022

[11] Urrunaga-Pastor D, Guarnizo-Poma M, Macollunco-Flores P, Lazaro-Alcantara H, Paico-Palacios S, Pantoja-Torres B, et al. Association between vitamin D deficiency and insulin resistance markers in euthyroid non-diabetic individuals. Diabetes and Metabolic Syndrome: Clinical Research and Reviews. 2019;**13**(1):258-263. DOI: 10.1016/j.dsx.2018.09.008

[12] Ford ES, Mokdad AH, Giles WH, Brown DW. The metabolic syndrome and antioxidant concentrations findings from the third National Health and nutrition examination survey. Diabetes. 2003;**52**(9):2346-2352

[13] Cardona-Velásquez S, Guzmán-Vivares L, Cardona-Arias JA. Systematization of clinical trials related to treatment of metabolic syndrome, 1980-2015. Endocrinología, Diabetes y Nutrición. 2017;**64**(2):82-91. DOI: 10.1016/j.endien.2016.09.004

[14] Betoret E, Betoret N, Vidal D, Fito P. Functional foods development: Trends and technologies. Trends in Food Science & Technology. 2011;**22**(9):498-508. DOI: 10.1016/j.tifs.2011.05.004

[15] Chen JP, Chen GC, Wang XP, Qin L, Bai Y. Dietary fiber and metabolic syndrome: A meta-analysis and review of related mechanisms. Nutrients. 2018;**10**(1):17. DOI: 10.3390/nu10010024

[16] Morrison DJ, Preston T. Formation of short chain fatty acids by the gut microbiota and their impact on human metabolism. Gut Microbes. 2016;**7**(3):189-200. DOI: 10.1080/19490976.2015.1134082

[17] Tassinari S, Azuero A, Arreaza D, Rueda-Rodríguez MC, Castañeda-Cardona C, Rosselli D. Suplementos nutricionales como modificadores del riesgo cardiovascular en componentes del síndrome metabólico en adultos. Revista Colombiana de Cardiología. 2017;**24**(3):277-285. DOI: 10.1016/j.rccar.2016.09.013

[18] Traber MG, Buettner GR, Bruno RS. The relationship between vitamin C status, the GUT-liver axis, and metabolic syndrome. Redox Biology. 2019;**21**:1-10. DOI: 10.1016/j.redox.2018.101091

[19] Iwaniak A, Darewicz M, Minkiewicz P. Peptides derived from foods as supportive diet components in the prevention of the metabolic syndrome. Comprehensive Reviews in Food Science and Food Safety. 2018;**14**:63-81. DOI: 10.1111/1541-4337.12321

[20] Khan MI, Anjum FM, Sohaib M, Sameen A. Tackling metabolic syndrome by functional foods. Reviews in Endocrine & Metabolic Disorders. 2013;**14**(3):287-297. DOI: 10.1007/s11154-013-9270-8

[21] Zemel MB. Role of calcium and dairy products in energy partitioning and weight management. The American Journal of Clinical Nutrition. 2004;**79**(5):907S-912S. DOI: 10.1093/ajcn/79.5.907S

[22] Shi H, Halvorsen YD, Ellis PN, Wilkinson WO, Zemel MB. Role of intracellular calcium in human adipocyte differentiation. Physiological Genomics. 2000;**3**(2):75-82. DOI: 10.1152/physiolgenomics.2000.3.2.75

[23] Zheng H, Lenard NR, Shin AC, Berthoud HR. Appetite control and energy balance regulation in the modern world: Reward-driven brain overrides repletion signals. International Journal of Obesity. 2009;**33**(S2):S8-S13. DOI: 10.1038/ijo.2009.65

[24] Kobori M. Dietary quercetin and other polyphenols: Attenuation of obesity. In: Watson RR, Preedy VR, Zibadi S, editors. Polyphenols in Human Health and Disease. Vol. 1. Oxford, UK: Academic Press; 2014. pp. 163-175. DOI: 10.1016/B978-0-12-398456-2.00014-1

[25] Pastor-Villaescusa B, Sánchez-Rodriguez E, Rangel-Huerta OD. Polyphenols in obesity and metabolic syndrome. In: Martí del Moral A, Aguilera-García CM, editors. Obesity: Oxidative Stress and Dietary Antioxidants. Oxford, UK: Academic Press; 2018. pp. 213-239. DOI: 10.1016/B978-0-12-812504-5.00011-8

[26] Sharma H, Kumar P, Deshmukh RR, Bishayee A, Kumar S. Pentacyclic triterpenes: New tools to fight metabolic syndrome. Phytomedicine. 2018;**50**:166-177. DOI: 10.1016/j.phymed.2018.09.011

[27] Wang S, Moustaid-Moussa N, Chen L, Mo H, Shastri A, Su R, et al. Novel insights of dietary polyphenols and obesity. Journal of Nutritional Biochemistry. 2014;**25**(1):1-18. DOI: 10.1016/j.jnutbio.2013.09.001

[28] Williams DJ, Edwards D, Hamernig I, Jian L, James AP, Johnson SK, et al.

Vegetables containing phytochemicals with potential anti-obesity properties: A review. Food Research International. 2013;**52**(1):323-333. DOI: 10.1016/j.foodres.2013.03.015

[29] Mallappa RH, Rokana N, Duary RK, Panwar H, Batish VK, Grover S. Management of metabolic syndrome through probiotic and prebiotic interventions. Indian Journal of Endocrinology and Metabolism. 2012;**16**(1):20-27. DOI: 10.4103/2230-8210.91178

[30] Arts IC, Hollman PC. Polyphenols and disease risk in epidemiologic studies. The American Journal of Clinical Nutrition. 2005;**81**(1):317S-325S. DOI: 10.1093/ajcn/81.1.317S

[31] Holubková A, Penesová A, Šturdík E, Mošovská S, Mikušová L. Phytochemicals with potential effects in metabolic syndrome prevention and therapy. Acta Chimica Slovaca. 2012;**5**(2):186-199. DOI: 10.2478/v10188-012-0029-8

[32] Richard AJ, Amini-Vaughan Z, Ribnicky DM, Stephens JM. Naringenin inhibits adipogenesis and reduces insulin sensitivity and adiponectin expression in adipocytes. Evidence-based Complementary and Alternative Medicine. 2013;**2013**:1-10. DOI: 10.1155/2013/549750

[33] Liang J, Halipu Y, Hu F, Yakeya B, Chen W, Zhang H, et al. Naringenin protects keratinocytes from oxidative stress injury via inhibition of the NOD2-mediated NF-κB pathway in pemphigus vulgaris. Biomedicine and Pharmacotherapy. 2017;**92**:796-801. DOI: 10.1016/j.biopha.2017.05.112

[34] Landa P, Kokoska L, Pribylova M, Vanek T, Marsik P. In vitro anti-inflammatory activity of carvacrol: Inhibitory effect on COX-2 catalyzed prostaglandin E2 biosynthesis. Archives of Pharmacal Research. 2009;**32**(1):75-78. DOI: 10.1007/s12272-009-1120-6

[35] Forero DP, Masatani C, Fujimoto Y, Coy-Barrera E, Peterson D, Osorio C. Spermidine derivatives in Lulo (*Solanum Quitoense* Lam.) fruit: Sensory (taste) versus biofunctional (ACE-inhibition) properties. Journal of Agricultural and Food Chemistry. 2016;**64**(26):5375-5383. DOI: 10.1021/acs.jafc.6b01631

[36] Hsu CL, Yen GC. Induction of cell apoptosis in 3T3-L1 pre-adipocytes by flavonoids is associated with their antioxidant activity. Molecular Nutrition & Food Research. 2006;**50**(11):1072-1079. DOI: 10.1002/mnfr.200600040

[37] González-Castejón M, Rodriguez-Casado A. Dietary phytochemicals and their potential effects on obesity: A review. Pharmacological Research. 2011;**64**(5):438-455. DOI: 10.1016/j.phrs.2011.07.004

[38] Yang JY, Della-Fera MA, Nelson-Dooley C, Baile CA. Molecular mechanisms of apoptosis induced by ajoene in 3T3-L1 adipocytes. Obesity. 2006;**14**(3):388-397. DOI: 10.1038/oby.2006.52

[39] Karim N, Jia Z, Zheng X, Cui S, Chen W. A recent review of citrus flavanone naringenin on metabolic diseases and its potential sources for high yield-production. Trends in Food Science and Technology. 2018;**79**:35-54. DOI: 10.1016/j.tifs.2018.06.012

[40] Yang M, Jiang ZH, Li CG, Zhu YJ, Li Z, Tang YZ, et al. Apigenin prevents metabolic syndrome in high-fructose diet-fed mice by Keap1-Nrf2 pathway. Biomedicine and Pharmacotherapy. 2018;**105**:1283-1290. DOI: 10.1016/j.biopha.2018.06.108

[41] Cho S, Choi Y, Park S, Park T. Carvacrol prevents diet-induced obesity by modulating gene expressions involved in adipogenesis

and inflammation in mice fed with high-fat diet. Journal of Nutritional Biochemistry. 2012;**23**(2):192-201. DOI: 10.1016/j.jnutbio.2010.11.016

[42] Son MJ, Rico CW, Nam SH, Kang MY. Effect of oryzanol and ferulic acid on the glucose metabolism of mice fed with a high-fat diet. Journal of Food Science. 2011;**76**(1):4-7. DOI: 10.1111/j.1750-3841.2010.01907.x

[43] Pongchaidecha A, Lailerd N, Boonprasert W, Chattipakorn N. Effects of curcuminoid supplement on cardiac autonomic status in high-fat-induced obese rats. Nutrition. 2009;**25**(7-8):870-878. DOI: 10.1016/j.nut.2009.02.001

[44] González-Ortiz M, Méndez-Del Villar M, Martínez-Abundis E, Ramírez-Rodríguez AM. Effect of resveratrol administration on metabolic syndrome, insulin sensitivity, and insulin secretion. Minerva Endocrinologica. 2018;**43**(3):229-235. DOI: 10.23736/S0391-1977.16.02550-5

[45] Rezazadeh K, Aliashrafi S, Asghari-Jafarabadi M, Ebrahimi-Mameghani M. Antioxidant response to artichoke leaf extract supplementation in metabolic syndrome: A double-blind placebo-controlled randomized clinical trial. Clinical Nutrition. 2018;**37**(3):790-796. DOI: 10.1016/j.clnu.2017.03.017

[46] Nishihira J, Sato-Ueshima M, Kitadate K, Wakame K, Fujii H. Amelioration of abdominal obesity by low-molecular-weight polyphenol (Oligonol) from lychee. Journal of Functional Foods. 2009;**1**(4):341-348. DOI: 10.1016/j.jff.2009.09.002

[47] González-Ortiz M, Martínez-Abundis E, Espinel-Bermúdez MC, Pérez-Rubio KG. Effect of pomegranate juice on insulin secretion and sensitivity in patients with obesity. Annals of Nutrition and Metabolism. 2011;**58**(3):220-223. DOI: 10.1159/000330116

[48] Ibero-Baraibar I, Azqueta A, De Cerain AL, Martinez JA, Zulet MA. Assessment of DNA damage using comet assay in middle-aged overweight/obese subjects after following a hypocaloric diet supplemented with cocoa extract. Mutagenesis. 2015;**30**(1):139-146. DOI: 10.1093/mutage/geu056

[49] Amin F, Islam N, Anila N, Gilani AH. Clinical efficacy of the co-administration of turmeric and black seeds (Kalongi) in metabolic syndrome-a double blind randomized controlled trial-TAK-MetS trial. Complementary Therapies in Medicine. 2015;**23**:165-174. DOI: 10.1016/j.ctim.2015.01.008

[50] FAO/WHO. Working Group Report on Drafting Guidelines for the Evaluation of Probiotics in Food. London, Ontario, Canada; 2002

[51] Lee E, Jung SR, Lee SY, Lee NK, Paik HD, Lim SI. *Lactobacillus plantarum* strain Ln4 attenuates diet-induced obesity, insulin resistance, and changes in hepatic mRNA levels associated with glucose and lipid metabolism. Nutrients. 2018;**10**(5):643. DOI: 10.3390/nu10050643

[52] Chen LH, Chen YH, Cheng KC, Chien TY, Chan CH, Tsao SP, et al. Antiobesity effect of *Lactobacillus reuteri* 263 associated with energy metabolism remodeling of white adipose tissue in high-energy-diet-fed rats. The Journal of Nutritional Biochemistry. 2018;**54**:87-94. DOI: 10.1016/j.jnutbio.2017.11.004

[53] Wang LC, Pan TM, Tsai TY. Lactic acid bacteria-fermented product of green tea and Houttuynia cordata leaves exerts anti-adipogenic and anti-obesity effects. Journal of Food and Drug Analysis. 2018;**26**(3):973-984. DOI: 10.1016/j.jfda.2017.11.009

[54] Balolong MP, Bautista RLS, Encarma NCA, Balolong EC Jr, Hallare AV, Elegado F. Evaluating the anti-obesity potential of *Lactobacillus fermentum* 4B1, a probiotic strain isolated from balao-balao, a traditional Philippine fermented food. International Food Research Journal. 2017;**24**(2):819-824

[55] Hsieh FC, Lan CCE, Huang TY, Chen KW, Chai CY, Chen WT, et al. Heat-killed and live *Lactobacillus reuteri* GMNL-263 exhibit similar effects on improving metabolic functions in high-fat diet-induced obese rats. Food & Function. 2016;**7**(5):2374-2388. DOI: 10.1039/c5fo01396h

[56] Plovier H, Everard A, Druart C, Depommier C, Van Hul M, Geurts L, et al. A purified membrane protein from *Akkermansia muciniphila* or the pasteurized bacterium improves metabolism in obese and diabetic mice. Nature Medicine. 2017;**23**(1):107-113. DOI: 10.1038/nm.4236

[57] An HM, Park SY, Lee DK, Kim JR, Cha MK, Lee SW, et al. Antiobesity and lipid-lowering effects of *Bifidobacterium* spp. in high fat diet-induced obese rats. Lipids in Health and Disease. 2011;**10**:116. DOI: 10.1186/1476-511X-10-116

[58] Fåk F, Bäckhed F. *Lactobacillus reuteri* prevents diet-induced obesity, but not atherosclerosis, in a strain dependent fashion in *Apoe*−/− mice. PLoS One. 2012;**7**(10):e46837. DOI: 10.1371/journal.pone.0046837

[59] Zhao X, Higashikawa F, Noda M, Kawamura Y, Matoba Y, Kumagai T, et al. The obesity and fatty liver are reduced by plant-derived *Pediococcus pentosaceus* LP28 in high fat diet-induced obese mice. PLoS One. 2012;**7**(2):e30696. DOI: 10.1371/journal.pone.0030696

[60] Lee SJ, Bose S, Seo JG, Chung WS, Lim CY, Kim H. The effects of co-administration of probiotics with herbal medicine on obesity, metabolic endotoxemia and dysbiosis: A randomized double-blind controlled clinical trial. Clinical Nutrition. 2014;**33**(6):973-981. DOI: 10.1016/J.CLNU.2013.12.006

[61] Sanchez M, Darimont C, Drapeau V, Emady-Azar S, Lepage M, Rezzonico E, et al. Effect of *Lactobacillus rhamnosus* CGMCC1.3724 supplementation on weight loss and maintenance in obese men and women. British Journal of Nutrition. 2014;**111**(8):1507-1519. DOI: 10.1017/S0007114513003875

[62] Sharafedtinov KK, Plotnikova OA, Alexeeva R, Sentsova TB, Songisepp E, Stsepetova J, et al. Hypocaloric diet supplemented with probiotic cheese improves body mass index and blood pressure indices of obese hypertensive patients—A randomized double-blind placebo-controlled pilot study. Nutrition Journal. 2013;**12**:138. DOI: 10.1186/1475-2891-12-138

[63] Kadooka Y, Sato M, Imaizumi K, Ogawa A, Ikuyama K, Akai Y, et al. Regulation of abdominal adiposity by probiotics (*Lactobacillus gasseri* SBT2055) in adults with obese tendencies in a randomized controlled trial. European Journal of Clinical Nutrition. 2010;**64**(6):636-643. DOI: 10.1038/ejcn.2010.19

[64] Omar JM, Chan YM, Jones ML, Prakash S, Jones PJH. *Lactobacillus fermentum* and *Lactobacillus amylovorus* as probiotics alter body adiposity and gut microflora in healthy persons. Journal of Functional Foods. 2013;**5**(1):116-123. DOI: 10.1016/j.jff.2012.09.001

[65] Kobyliak N, Conte C, Cammarota G, Haley AP, Styriak I, Gaspar G, et al. Probiotics in prevention and treatment of obesity: A critical view. Nutrition and Metabolism. 2016;**13**:14. DOI: 10.1186/s12986-016-0067-0

[66] Ghaisas S, Maher J, Kanthasamy A. Gut microbiome in health and disease: Linking the microbiome-gut-brain axis and environmental factors in the pathogenesis of systemic and neurodegenerative diseases. Pharmacology & Therapeutics. 2016;**158**:52-62. DOI: 10.1016/j.pharmthera.2015.11.012

[67] Le Chatelier E, Nielsen T, Qin J, et al. Richness of human gut microbiome correlates with metabolic markers. Nature. 2013;**500**(7464):541-546. DOI: 10.1038/nature12506

[68] Lehnen TE, Ramos da Silva M, Camacho A, Marcadenti A, Lehnen AM. A review on effects of conjugated linoleic fatty acid (CLA) upon body composition and energetic metabolism. Journal of the International Society of Sports Nutrition. 2015;**12**:36. DOI: 10.1186/s12970-015-0097-4

[69] Patterson E, Ryan PM, Cryan JF, Dinan TG, Ross P, Fitzgerald GF, et al. Gut microbiota, obesity and diabetes. Postgraduate Medical Journal. 2016;**92**(1087):286-300. DOI: 10.1136/postgradmedj-2015-133285

[70] Zarrati M, Salehi E, Nourijelyani K, Mofid V, Zadeh MJH, Najafi F, et al. Effects of probiotic yogurt on fat distribution and gene expression of proinflammatory factors in peripheral blood mononuclear cells in overweight and obese people with or without weight-loss diet. Journal of the American College of Nutrition. 2014;**33**(6):1-9. DOI: 10.1080/07315724.2013.874937

[71] Igual M, Ramires S, Mosquera LH, Martínez-Navarrete N. Optimization of spray drying conditions for lulo (*Solanum quitoense* L.) pulp. Powder Technology. 2014;**256**:233-238. DOI: 10.1016/j.powtec.2014.02.003

[72] Ministerio de Agricultura y Desarrollo Rural de Colombia. Producción Nacional por Producto. Available from: http://www.agronet.gov.co/Paginas/ProduccionNacionalProducto.aspx

[73] Contreras-Calderón J, Calderón-Jaimes L, Guerra-Hernández E, García-Villanova B. Antioxidant capacity, phenolic content and vitamin C in pulp, peel and seed from 24 exotic fruits from Colombia. Food Research International. 2011;**44**(7):2047-2053. DOI: 10.1016/j.foodres.2010.11.003

[74] Gancel AL, Alter P, Dhuique-Mayer C, Ruales J, Vaillant F. Identifying carotenoids and phenolic compounds in naranjilla (*Solanum quitoense* Lam. Var. puyo hybrid), an Andean fruit. Journal of Agricultural and Food Chemistry. 2008;**56**(24):11890-11899. DOI: 10.1021/jf801515p

[75] Acosta Ó, Pérez AM, Vaillant F. Chemical characterization, antioxidant properties, and volatile constituents of Naranjilla (*Solanum quitoense* Lam.) cultivated in Costa Rica. Archivos Latinoamericanos de Nutrición. 2009;**59**(1):88-94

[76] González-Loaiza DI, Ordóñez-Santos LE, Venegas-Mahecha P, Vásquez-Amariles HD. Cambios en las propiedades fisicoquímicas de frutos de lulo (*Solanum quitoense* Lam.) cosechados en tres grados de madurez. Acta Agronómica. 2014;**63**(1):11-17. DOI: 10.15446/acag.v63n1.31717

[77] Vasco C, Ruales J, Kamal-Eldin A. Total phenolic compounds and antioxidant capacities of major fruits from Ecuador. Food Chemistry. 2008;**111**(4):816-823. DOI: 10.1016/j.foodchem.2008.04.054

[78] Nutrition Facts of Lulo Fruit. Available from: https://www.traditionaloven.com/foods/details/fruits-juice/naranjilla-lulo-pulp-frozen-unsweeten.html

[79] Mertz C, Gancel AL, Gunata Z, Alter P, Dhuique-Mayer C, Vaillant F, et al. Phenolic compounds, carotenoids and antioxidant activity of three tropical fruits. Journal of Food Composition and Analysis. 2009;**22**(5):381-387. DOI: 10.1016/j.jfca.2008.06.008

[80] Van Berleere M, Dauchet L. Fruits, vegetables, and health: Evidence from meta-analyses of prospective epidemiological studies. In: Mariotti F, editor. Vegetarian and Plant-Based Diets in Health and Disease Prevention. London: Academic Press; 2017. pp. 215-248. DOI: 10.1016/B978-0-12-803968-7.00013-7

[81] Yahia EM, García-Solís P, Maldonado-Celis ME. Contribution of fruits and vegetables to human nutrition and health. In: Yahia EM, editor. Postharvest Physiology and Biochemistry of Fruits and Vegetables. Duxford: Woodhead Publishing; 2019. pp. 19-45. DOI: 10.1016/B978-0-12-813278-4.00002-6

[82] Fito P, Andrés A, Chiralt A, Pardo P. Coupling of hydrodynamic mechanism and deformation relaxation phenomena during vacuum treatments in solid porous food-liquid systems. Journal of Food Engineering. 1996;**27**(3):229-240. DOI: 10.1016/0260-8774(95)00005-4

[83] Fito P, Chiralt A, Barat JM, Andrés A, Martínez-Monzó J, Martínez-Navarrete N. Vacuum impregnation for development of new dehydrated products. Journal of Food Engineering. 2001;**49**(4):297-302. DOI: 10.1016/S0260-8774(00)00226-0

[84] Rivera-Espinoza Y, Gallardo-Navarro Y. Non-dairy probiotic products. Food Microbiology. 2010;**27**(1):1-11. DOI: 10.1016/j.fm.2008.06.008

[85] Vijaya-Kumar B, Vijayendra SVN, Reddy OVS. Trends in dairy and non-dairy probiotic products—A review. Journal of Food Science and Technology. 2015;**52**(10):6112-6124. DOI: 10.1007/s13197-015-1795-2

[86] Rad AH, Torab R, Mortazavian AM, Mehrabany EV, Mehrabany LV. Can probiotics prevent or improve common cold and influenza? Nutrition. 2013;**29**(5):805-806. DOI: 10.1016/j.nut.2012.10.009

[87] Panghal A, Janghu S, Virkar K, Gat Y, Kumar V, Chhikara N. Potential non-dairy probiotic products—A healthy approach. Food Bioscience. 2018;**21**:80-89. DOI: 10.1016/j.fbio.2017.12.003

[88] Kraus A. Factors influencing the decisions to buy and consume functional food. British Food Journal. 2015;**117**(6):1622-1636. DOI: 10.1108/BFJ-08-2014-0301

[89] Panghal A, Virkar K, Kumar V, Dhull SB, Gat Y, Chhikara N. Development of probiotic beetroot drink. Current Research in Nutrition and Food Science Journal. 2017;**5**(3):257-262. DOI: 10.12944/CRNFSJ.5.3.10

[90] Corbo MR, Bevilacvqua A, Petruzzi L, Casanova FP, Sinigaglia M. Functional beverages: The emerging side of functional foods commercial trends, research, and health implications. Comprehensive Reviews in Food Science and Food Safety. 2014;**13**:1192-1206. DOI: 10.1111/1541-4337.12109

[91] Grand View Research. Available from: https://www.grandviewresearch.com/

[92] Lumina intelligence.com. Available from: https://www.lumina-intelligence.com/

[93] Global Market Insights. Available from: https://www.globalinsights.com/