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Effect of the consumption of a synbiotic diet mousse containing *Lactobacillus acidophilus* La-5 by individuals with metabolic syndrome: A randomized controlled trial

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ABSTRACT

This study aimed to evaluate the impact of a synbiotic diet mousse containing *Lactobacillus acidophilus* La-5 and the prebiotics inulin and fructooligosaccharides on anthropometric and blood pressure measurements, biochemical, inflammatory, haematological, and immunological parameters of volunteers with metabolic syndrome (MetS). In a randomized, double-blind, placebo-controlled trial, forty-five volunteers with MetS were assigned into two groups, each receiving 40 g/day of: synbiotic diet mousse (SDM) (n = 23) and placebo diet mousse (PDM) without pro- and prebiotics (n = 22). All the evaluated parameters were measured at the beginning and after 8 weeks of intervention. The daily intake of SDM and PDM led to significant reductions of total cholesterol and HDL-cholesterol, as well as of immunoglobulins (A and M), and interleukin-1β in both groups ($p < .05$). These results suggest that the presence of the probiotic and prebiotic ingredients in the diet mousse did not show any additional effects on the parameters evaluated in volunteers with MetS.

1. Introduction

The metabolic syndrome (MetS) has received a great deal of attention from the scientific community in recent years. This is largely influenced by the increase in the prevalence of MetS in the last two decades especially in countries with increased calorie consumption and decreased physical activities (Mazidi, Rezaie, Kengne, Mobarhan, & Ferns, 2016). In general, MetS is a group of risk factors comprising obesity (particularly abdominal obesity), insulin resistance, atherogenic dyslipidaemia, and hypertension, which are associated with increased risk of cardiovascular disease (CVD) and type 2 diabetes mellitus (Grundy et al., 2005; Kakafika, Liberopoulos, Karagiannis, Athyros, & Mikhailidis, 2006). Moreover, subjects with these features usually present prothrombotic and proinflammatory states (Grundy et al., 2005). Clinical and epidemiological studies have indicated that low-grade inflammation may contribute to the development of metabolic disorders associated with obesity (Cani & Hul, 2015). In this sense, MetS is known to be a low grade systemic inflammatory condition (Synetos et al., 2016).

It has been shown that an intestinal dysbiosis could also be associated to MetS. In this context, a number of studies using animal models and clinical trials have reported a relationship between the composition of the intestinal microbiota and MetS risk factors, including obesity and diabetes (Larsen et al., 2010; Ley et al., 2005; Tremaroli & Bäckhed, 2012). In general, the composition of the microbiota of obese subjects has been characterized by an increased *Firmicutes/Bacteroidetes* ratio (Jonkers, 2016; Ley, Turnbaugh, Klein, & Gordon, 2006; Turnbaugh et al., 2009). Nevertheless, according to Scavuzzi et al. (2015), there is still no consensus as to the mechanisms relating intestinal microbiota modifications and the potential metabolic changes. On the other hand, these researchers reported that mechanisms possibly involve gut barrier alterations and low-grade inflammation.

The pathogenesis of MetS may have several origins; however, diet and lifestyle are considered important aspects that may influence the susceptibility of humans to MetS (Kovatcheva-Datchary & Arora, 2013). Thus, dietary approaches to manipulate the intestinal microbiota, in

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particular the use of probiotic microorganisms and/or prebiotic compounds, have demonstrated health-improving effects on the host. Therefore, these approaches were proposed for MetS management (Bernini et al. 2016; Kovatcheva-Datchary & Arora, 2013; Scavuzzi et al., 2015). It is noteworthy that studies evaluating the impact of probiotics on obesity-related inflammation are limited and mainly based on animal studies (de Moreno de LeBlanc & Perdigon, 2010; Gøbel, Larsen, Jakobsen, Mølgaard, & Michaelsen, 2012).

Some researchers reported beneficial effects of the consumption of probiotic, prebiotic, and synbiotic products on parameters related to MetS (Barreto et al., 2014; Bernini et al., 2016; Gøbel et al., 2012). Akkasheh et al. (2016) showed significant decreases in serum insulin concentrations and the homoeostasis model of assessment of insulin resistance (HOMA-IR) after the daily consumption of one probiotic capsule containing *Lactobacillus acidophilus* YAB, *Lactobacillus casei* TD_2, and *Bifidobacterium bifidum* B12 during 8 weeks. Studies have also investigated the possible role of probiotic bacteria and prebiotic fibres on different risk factors of MetS, such as the reduction of CVD risk (Al-Sheraji et al., 2012; Gøbel et al., 2012). Along these lines, a meta-analysis of randomized controlled trials conducted by Guo et al. (2011) showed that the consumption of probiotics led to a decrease in the total cholesterol and the LDL-C in individuals with high, borderline high, and normal cholesterol levels.

Recently, inflammatory processes have also been considered as biomarkers in clinical trials with MetS patients (Brito-Luna et al., 2016; Karaman, Aydin, Geçkinli, Çetinkaya, & Karaman, 2015; Panahi et al., 2016). Barreto et al. (2014) observed that the consumption of fermented milk containing *Lactobacillus plantarum* Lp 115 led to a significant decrease in IL-6 levels in patients with MetS after 90 days of study.

It is noteworthy that probiotic beneficial effects, as well as mechanisms of action, are considered as strain specific. In addition, it has been suggested that different food matrices in which the probiotic bacteria are incorporated may influence their functionality, and, consequently, their potential health effects (Forssten, Sindelar, & Ouwehand, 2011; Sanders & Marco, 2010). Besides, there are indications that synbiotic products may be more effective than either probiotics or prebiotics alone (Sanders & Marco, 2010).

To the best of our knowledge, no study is available in the scientific literature on the impact of a synbiotic diet dessert on subjects with MetS. The aim of this study was therefore to assess the impact of a synbiotic diet dessert (mousse) containing *L. acidophilus* La-5 and the prebiotic ingredients inulin and fructooligosaccharides (FOS) on biochemical (plasmatic glucose, TC, HDL-C, LDL-C, TG, and insulin), inflammatory (TNF-α, CD40, IL-1β, IL-6, IL-8, IL-10, and IL-12), haematological (erythrocytes, leukocytes, lymphocytes, erythrocytes, neutrophils, eosinophils, monocytes, and haemoglobin), and immunological (IgA, IgE, IgG, and IgM) parameters of volunteers with MetS.

2. Materials and methods

2.1. Production of synbiotic and placebo diet mousses

The diet desserts were produced under suitable hygiene and sanitation criteria at the Laboratory of Food Technology of the Department of Biochemical and Pharmaceutical Technology of the School of Pharmaceutical Sciences of the University of São Paulo (SP, Brazil), according to the method described by Buriti, Castro, and Saad (2010). The ingredients employed in the production of the diet desserts and their compositions are shown in Tables 1 and 2, respectively.

Diet desserts were packaged in polypropylene plastic pots for food products (100 mL of capacity) (Tries Aditivos Plásticos, São Paulo, Brazil) in portions of 40 g. The pots were sealed with metallic covers with varnish in a sealer (Delgo Metalúrgica, Cotia, Brazil). The products were stored frozen (−18 °C) and delivered to each volunteer in plastic vials labelled with the date of manufacture and of expiration. Microbiological analyses of the synbiotic product showed that the average population of *L. acidophilus* La-5 ranged between 9.2 and 9.5 log CFU (colony-forming units) per daily serving portion (40 g) during the experimental period. Therefore, the probiotic population was above the minimum recommended level (6 log CFU/g) suggested for beneficial health effects (Champagne, Ross, Saarela, Hansen, & Charalampopoulos, 2011; Health Canada, 2009; Ministero della Salute, 2013). Coliforms, *Escherichia coli*, and yeasts and moulds were not detected during the products' storage period.

Table 1
Ingredients employed in the production of synbiotic diet mousse (SDM) and placebo diet mousse (PDM).

Ingredients (g/100 g)	SDM	PDM
Skimmed milk[1]	61.7	61.7
Skimmed milk powder[2]	4.0	14.0
Sucralose[3]	1.1	1.1
Pasteurized and frozen guava pulp[4]	20.0	20.0
Emulsifier/stabilizer[5]	2.8	2.8
FOS[6]	6.0	0.0
Inulin[7]	4.0	0.0
Lactic acid[8]	0.4	0.4
Lactobacillus acidophilus La-5[9]	0.05	0.0
Total	100.0	100.0

[1] Paulista (Danone, Guaratinguetá, SP, Brazil).
[2] Molico (Nestlé, Araçatuba, SP, Brazil).
[3] Sucralose (Línea Sucralose, São Paulo, SP, Brazil).
[4] Icefruit Comércio de Alimentos (Icefruit Comércio de Alimentos, Tatuí, SP, Brazil).
[5] Cremodan Mousse 30 (Danisco, Cotia, SP, Brazil).
[6] Beneo P95 (Orafti, Oreye, Belgium).
[7] Beneo HP (Orafti, Oreye, Belgium).
[8] Purac (Purac Sínteses, Rio de Janeiro, RJ, Brazil; 85 g/100 g food-grade solution).
[9] Strain La-5 (Christian Hansen, Hoersholm, Denmark).

Table 2
Chemical composition, energy contribution of macronutrients, and total energy values (TEV) of synbiotic diet mousse (SDM) and placebo diet mousse (PDM) in 100 g of whole mousses (dry weight).

	SDM	PDM
Composition (g/100 g)		
Ash	0.90 (0.06)^{B}	1.42 (0.17)^{A}
Proteins	6.77 (0.37)^{B}	8.55 (0.33)^{A}
Simple carbohydrates	10.24 (0.97)^{B}	17.53 (1.01)^{A}
Fructans	9.63^{B,*}	0.00^{A}
Lipids	0.22 (0.05)^{A}	0.12 (0.06)^{A}
Moisture	72.24 (1.59)^{A}	72.38 (1.84)^{A}
Total	100.0	100.0
Energetic value (kJ/100 g)		
Proteins	113.30 (6.67)	143.09 (5.52)
Lipids	8.28 (2.07)	4.52 (2.26)
Simple carbohydrates	171.38 (31.07)	293.24 (16.90)
Fructans	60.46	0.00
TEV	353.42 (27.91)	440.85 (11.42)

Values are expressed as mean (standard deviation).
* Estimate based on information given by the supplier (Orafti) for the prebiotic ingredients (Beneo P95 and Beneo HP).

2.2. Participants

Sixty subjects with MetS, aged between 19 and 65, were recruited (August 2014 up to June 2015) from the ambulatory of the University Hospital (São Paulo, SP, Brazil). The present study was conducted according to the guidelines laid down in the Declaration of Helsinki and approved by the Ethical Committees involving humans of the School of Pharmaceutical Sciences of the University of São Paulo (CAAE 30539214.6.0000.0067) and of the University Hospital (Protocol Number 663.138). All subjects provided written consent form before