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Prospects

Prospects about the Use of Açaí *(Euterpe oleracea Mart.)* on the Modulation of the Inflammation and Energetic Metabolism in Overweight and Obese Individuals

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Abstract

The adiposity excess has as consequences metabolic complications which could predispose to the onset of chronic diseases concomitantly to induction of an inflammatory condition of low intensity by means of the secretion and expression of inflammatory cytokines in adipose tissue. These cytokines (IL-2, IL-4, IL-13, IL-15 e IFN-γ) may be involved in the regulation of energetic metabolism and food intake, contributing or minimizing the adipose tissue expansion. Some factors modulate the inflammation, such as body composition, biochemical, clinical and dietary parameters. The high intake of polyphenols, which is essential to preserve the metabolic homeostasis and control the subclinical inflammation, has been correlated to low incidence of chronical diseases. The açaí is a fruit rich in polyphenols which has been investigated due to its antioxidant and antiinflammatory effects. However, so far, its effects are not clear in humans. The perspective is that the açaí pulp intake could play beneficial effect on the inflammatory, anthropometric, metabolic and body composition states on the obesity process.

Keywords: Inflammation; Inflammatory Mediators; Obesity; Interleukin-2; Interleukin-4; Interleukin-13; Interleukin-15; Interferon-Gamma; Anthocyanins; Fruits.

Abbreviations

BMI: Body Mass Index;

CAC: Coronary arteries calcification;

COX-2: Cyclooxygenase-2;

FBR: Family Budget Research;

HDL: High Density Lipoprotein;

IFN-γ: Interferon-gamma;

IL-13: Interleukin-13;

IL-15: Interleukin-15;

IL-2: Interleukin-2;

IL-4: Interleukin-4;

JAK: *Janus kinases;*

LDL: Low density liprotein;

NF-Kβ: Nuclear factor-kappa-B;

NK: Natural killer cells;

sIL-2R: Soluble Interleukin-2 Receptor;

STAT3: Signal transducer and activator of transcription 3;

TNF-α: Tumor necrosis factor alpha;

VIGITEL: Vigilance of the risk factors and protection to chronic diseases by telephonic inques.

The overweight and obesity are complex chronic diseases, characterized by body fat excess. In the world, they affect both industrialized and developing countries [1]. About 0,5 billion dollars are spent in obesity treatment per year in Brazil [2], where a research of the Vigilance of the risk factors and protection to chronic diseases by telephonic inquest (VIGITEL), performed in 2012, revealed that more than half of population are overweight (51%) and 17% are obese [3].

The energetic imbalance, as a risk factor to obesity, could be arising from dietary patterns with high calorie intake, which becomes larger than the total energy expenditure. This calorie excess is transformed in triacylglycerol and is deposited in the white adipose tissue, causing metabolic complications which could predispose to development of chronic diseases, such as, cardiovascular diseases and type 2 diabetes [4]. Moreover, poor quality diets, with low intake of antioxidant nutrients and non-nutrients with functional effect (polyphenols, for example) chronically induce to a low intensity inflammatory state, with changes in expression of cytokines release. Therefore, obese individuals have hypertrophied adipose tissue, with increase in cytokine synthesis capacity with inflammatory action [5], for example: interleukin-2 (IL-2), interleukin-15 (IL-15) and interferon-gamma (IFN-γ), and antiinflammatory, such as interleukin-4 (IL-4), interleukin-13 (IL-13) and (IL-15).

The infiltration of macrophage, immune system cells, in the adipose tissue is able to synthetize such cytokines which activate the Nuclear factor-kappa-B (NF-Kβ) and *Janus kinases* (JNK) pathways. These inflammatory pathways inhibit the signalization of the insulin receptors by means of STAT3 via, resulting in the development of resistance to this hormone, besides reducing the fatty acids oxidation in the skeletal muscle and triggering, respectively, a type 2 diabetes and obesity framework.

Such cytokines could modulate and be modulated by anthropometric, and body and diet composition parameters; which could contribute to the obesity prevention or promotion, by means of the regulation or dysregulation of energetic metabolism.

The IL-2, which is a pro-inflammatory cytokine which promotes the production of cytokines derivative from natural killer cells (NK), such as TNF-α (tumor necrosis factor alpha) e IFN-γ [6] , recently was associated to the atherogenesis [7,8] and type 2- diabets development [910]. High concentrations of IL-2 are strongly associated to coronary arteries calcification (CAC) and the larger mortality rate [8]. Among the found studies, no one related IL-2 concentrations or its receptors to obesity, neither to the body fat distribution. However, IL-2 and sIL-2R (soluble Interleukin-2 Receptor) high concentrations are associated to coronary artery disease and diabetes, which relates to obesity. Thus, it suggests a direct relationship between obesity and IL-2 e sIL-2R high concentrations. Additionally, in according to Gaffen and Liu [6] and Ye [11] the α subunit gene of IL-2 receptor is located on chromosome 10, which is the chromosome linked to obesity and type 2 diabetes in humans. Therefore, it is assumed that obese individuals may have high concentrations of IL-2 and sIL-2R.

High concentrations of IFN-γ, which is another proinflammatory cytokine, are found in the obesity, in both models, human and rodents, while smaller concentrations result in the improvement of glucose tolerance in mice. Since IFN-γ is high in obesity, studies suggest that it is harmful to the body weight and glucose homeostasis [12, 13, 14]. In other hand, in rats, the IFN-γ suppression result in body weight reduction and the glucose homeostasis improvement, due to the increase of insulin sensitivity [14].

The IL-4 forms a part of the adipose tissue, besides exerts antiinflammatory effect on it [15]. Such cytokine is associated to the increase of insulin sensitivity and glucose tolerance, inhibiting the lipids accumulation on the adipose tissue, which leads to a decrease of weight gain and body fat [8,15,16, 17, 18]. So, it suggest that this cytokine is inversely proportional to weight gain and adiposity and, wherefore, it could contribute to the energetic metabolism regulation and, consequently, to the obesity prevention.

The IL-13 also exerts antiinflammatory effect on adipose

tissue and its concentrations are high in obesity. It reveals an adipocytes defense mechanism, which limits the inflammation and the insulin resistance by means of itself regulation. Thereby, the adipose tissue inflammation induces the IL-13 expression, which keeps the low-grade chronic inflammation and, thus, limits the obesity magnitude [19]. Moreover, it is conceivable that during an inflammation process, one of the main IL-13 functions would be restore the glucose homeostasis,that is interrupted by proinflammatory actions [20]. Then, it is considered that IL-13 could modulate the energetic metabolism in obesity, by means of the inflammatory process inhibition and the glucose metabolism modulation, minimizing the obesity clinical complications.

The IL-15 is an antiinflammatory cytokine which exerts pleiotropic functions, by means of the apoptosis stimulation and its capacity to modulate the metabolism, and proinflammatory functions, due to promotes the IFN-γ expression. A larger IL-15 RNAm expression is widely expressed in skeletal muscle tissue. So, it has a larger function as endocrine factor, which could be associated to energetic metabolism and, consequently, to body composition modulation [11,21,22]. It is believed that IL-15 is capable to modulate the body composition due to exerts direct effects on lipids and carbohydrates metabolism, as well as on the insulin sensitivity, fat acids oxidation, lipogenesis inhibition, very low density lipoprotein (VLDL) decrease and thermogenesis promotion [11,21,23, 24,25]. It is important to consider that, although, IL-15 has beneficial effects on the energetic metabolism modulation, the inhibition of its expression on the obesity process is more satisfactory, because high concentrations favor the IFN-γ expression.

The food partterns have a determinant role on the obesity risk and associated chronic diseases. In fact, an excessive nutrients intake [26].especially of saturated fat acids, could lead to adiposity tissue metabolic changes, increasing the phosphorylation of JNK and NF-Kβ pathways that induce the pro-inflammatory cytokines synthesis and insulin peripheral resistance [27]. Therefore, it is plausible to propose that the adoption of healthy eating patterns influence the inflammatory biomarkers concentrations, as a mechanism to improve the obesity clinical manifestations.

Polyphenols are known to act as antioxidants and anti-inflammatory, thus they provide potential protective effect against the obesity development. Additionally, greater intake of polyphenols dietary, particularly anthocyanins, is associated to reduced risk of hypertension, myocardial infarction, type 2 diabetes and certain cancers [28]. Food which are rich in polyphenols, are able to decrease the inflammatory mediators concentrations that are activated by NF-Kβ, in humans [29]. If the polyphenols inhibit NF–Kβ, possibly, also inhibit the cytokines of this pathway, for example, IL-15, IL-2 and IFN-γ. In a study proposed by Bobe *et al.*, the flavonoids intake decreased the IFN-γ and IL-2 concentrations.

The açaí *(Euterpe oleracea* Mart.), a typical and popular fruit of the Amazon region, has gained importance in the last years due to its benefits conferred to health, associated to its phytochemical composition and antioxidant capacity. Brazil is its main producer, consumer and exporter [5]. Rich in polyphenols, especially in anthocyanins, [30,31,32] its pulp has many functional properties. In animals model, the açaí modulated the reactive oxygen species production and presented hypocholesterolemic effects and inhibited the TNF-α and NF-Kβ expression [7, 5]. In a study in humans, proposed by Udani *et al.* [33], the pulp açaí intake (100g) during 4 weeks by overweight individuals reduced the fasting glucose, insulin and cholesterol.

Given the above, it is clear the açaí contribution on the health promotion, possibly, due to it has high antioxidant and anti-inflammatory capacity, besides act on the glucose and lipid metabolism regulation and, consequently, on the energetic metabolism. Since, the nutritional intervention with açaí related to its beneficial on the inflammatory process, is scarce in humans, it is essential perform more study with this issue. The scientific community needs more studies which evaluate the effect of the typical regional food intake on obesity and associated chronic diseases, through the modulation of inflammatory mediators, energy metabolism and body composition. Moreover, the incentive to intake of this kind of food encourages the local production generating a favorable social impact. Finally, these studies will provide new insights and clarification to the population and health professionals about the potential benefits of açaí intake and their consumption recommendation.

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