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REDUCTION IN BODY FAT INDUCED BY CAPSAICIN, GREEN TEA AND MAGNESIUM: A PLAUSIBLE STRATEGY IN THE FACE OF THE GLOBAL OBESITY PANDEMIC?

Walter Pereira
Performance and health Science usa Corporation, Inovattis Nutrition Br, Inovattis Nutrition Br

Abstract: Obesity is considered a worldwide epidemic, characterized by the excessive accumulation of body fat, which can affect health. Several lines of research confirm that the chronic inflammation present in fatty adipose tissue is associated with metabolic diseases and heart complications. Against this backdrop, natural products such as nutraceuticals and food supplements are being used in an attempt to combat obesity and promote weight loss. Natural compounds have a proven level of evidence in terms of improving clinical parameters and helping to treat obesity. However, these are analyzed in isolation in the global database. This justifies our hypothetical opinion on the possible superior efficiency of mixed therapy of already effective compounds such as Capsaicin, Green Tea and Magnesium, analyzed simultaneously, in the control of obesity and its associated comorbidities.

INTRODUCTION

Obesity is considered a global epidemic (1). Currently, the effectiveness of weight loss approaches is limited and variable (2)making the search for alternative, yet effective and safe treatments notoriously on the rise (2). Epidemiological studies suggest that reducing body weight by at least 5% has benefits for metabolic health and cardiovascular disease (CVD) risk (3). It is widely accepted that the combination of exercise and diet are the best approaches to preventing and treating obesity, however, self-modification strategies are difficult to implement and adherence is less satisfactory in populations suffering from obesity. (4). Some anti-obesity drugs have been withdrawn from the market due to their serious adverse effects, including cardiovascular risk, mood disorders and even suicidal susceptibility (5). Agents such as the glucagon-like peptide 1 (GLP-1) analog have demonstrated anti-obesity potential (6)However, weight loss is limited and the risk of pancreatitis may increase (7). Finally, compared to the anti-obesity drugs mentioned above, bariatric surgery, such as Roux-en-Y gastric bypass or vertical gastrectomy, seems to be more effective. However, it is physically invasive, relatively expensive and its long-term effect is unclear (8). Against this backdrop, various natural products such as nutraceuticals and food supplements are being used in an attempt to combat obesity and promote weight loss (9). A number of natural compounds have a proven level of evidence in terms of improving clinical parameters and helping to treat obesity. However, these are analyzed in isolation in the global database. This justifies our hypothetical opinion on the possible superior efficiency of mixed therapy of already effective compounds such as capsaicin, green tea and magnesium, analyzed simultaneously, in the control of obesity and its associated comorbidities.

DISCUSSION - SCIENTIFIC EVIDENCE AND ISOLATED MECHANISMS OF ACTION

CAPSAICIN

Chili peppers contain active compounds capable of performing multiple functions in the body (10). Capsaicin, the main active compound in chili peppers, is recognized for its ability to perform these functions (11) as well as having antioxidant properties (12) and anti-obesity properties, as it plays a role in inhibiting adipogenesis (13). Epidemiological studies indicate that capsaicin consumption is associated with a lower prevalence of obesity (14). Snitker et al. 2009, in a double-blind study, concluded that treatment with capsaicin is safe and associated with weight loss (15). Lejeune et al, (16)investigated capsaicin in weight maintenance and showed that sustained fat oxidation and weight maintenance was greater in the intervention group compared to placebo (16). The increase in oxygen con-

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sumption (VO_2) reflects energy expenditure and plays a role in weight loss. Inoue et al (17) concluded that 10 mg/kg/pc/day of capsaicin for 4 weeks tended to reduce weight, due to a significant increase in VO2 (17). Corroborating these findings, additional clinical studies have shown that 9 mg of capsaicin for 8 weeks increased thermogenesis (18). Kang et al. (19) reported that capsaicin is associated with the inactivation of nuclear factor-κB (NF-κB) and the activation of peroxisome proliferator-activated receptor-γ (PPARγ), which can modulate the function of adipocytes in the adipose tissue of obese people, as well as suppressing the inflammatory responses of adipose tissue macrophages, which are independent of TRPV1 (19).

GREEN TEA

Habitual tea consumption can have positive effects on anthropometric variables. This was shown in a large cross-sectional study of 1210 adults (20). In addition, cohort studies suggest that a higher intake of green tea catechins is associated with a lower increase in BMI in women followed over a 14-year period (21). Adipose tissue is made up of adipocytes, classified into two main categories: brown adipose tissue (BAT) and white adipose tissue (WAT) (22)and plays a crucial role in energy metabolism (23). TAM is characterized by its high mitochondrial content, through the uncoupling protein 1 (UCP1), which is important for thermogenesis (24). The TAB, on the other hand, serves as a storage site for lipids in the form of triglycerides (TG), which can be used during periods of energy demand (25). Experimental studies have shown the effects of green tea extract on visceral fat and hepatic triacylglycerol (26)while others confirm that it can induce a significantly higher expression of UCP1 in brown adipocytes, due to its high content of catechins, which is reflected in thermogenesis (27). AMP-activated protein kinase (AMPK) regulates energy homeostasis and fatty acid oxidation in the liver (28). Obesity, caused by energy imbalance, not only aggravates metabolic disorders, but also reduces AMPK activity (29). Increased AMPK activity reduces hepatic triglycerides (TG) and negatively regulates lipogenic genes, as well as stimulating β-oxidation of fatty acids (28, 30). Green tea extract activates AMPK (31)and negatively regulates the expression of cells that positively regulate UCP2 expression, activating AMPK in the liver (32). Kim et al (33)reported that EGCG can inhibit lipid accumulation in mature adipocytes, exerting an anti-obesity effect through the expression of UCP1 (33). Complementary studies have concluded that green tea can prevent obesity by increasing energy expenditure, as well as increasing fatty acid oxidation (34).

MAGNESIUM

Physical inactivity has been associated with an increased risk of various diseases and is considered one of the main causes of preventable death (35, 36). Reduced amounts of muscle mass are associated with increased mortality (37). Recent studies suggest that magnesium intake may regulate the expression of inflammation and muscle mass, which are risk factors for cardiometabolic diseases (38). Magnesium (Mg) is involved in important processes, and its deficiency is associated with metabolic conditions such as sarcopenia, osteoporosis, neuromuscular disorders and arrhythmias (38). Chronically low levels of Mg induce inflammation through the imbalance of calcium homeostasis, oxidative stress and mitochondrial apoptosis, which results in the activation of cytokines (39). Studies in adult populations suggest an inverse association between magnesium intake and cardiometabolic risk, including inflammation and muscle loss (40). A large meta-analysis included 24,473 adults and suggested that magnesium

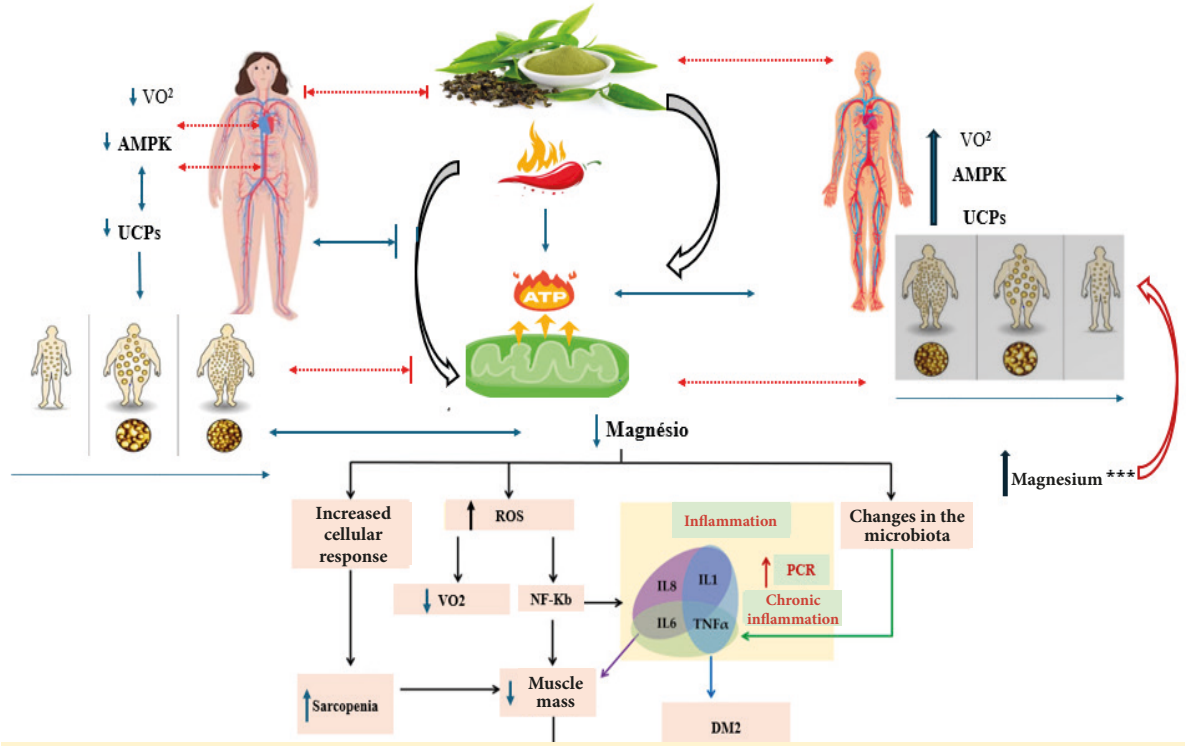

Figure 1. Possible synergistic mechanisms of mixed capsaicin, green tea and magnesium supplementation on cardiovascular health markers and muscle mass.

can positively regulate health through improved muscle activity (41). These findings are reinforced by experimental studies in which magnesium deficiency increased inflammation and reduced protein synthesis. (42-44). Other studies corroborate these inferences. A 20-year longitudinal study of 4,497 Americans concluded that lower magnesium intake was associated with greater systemic inflammation (45). Meta-analyses, including studies with more than 30,000 volunteers, have confirmed these statements (40, 41). From the age of 30, muscle mass tends to decrease at a rate of 1% per year (46). The reduction in muscle mass reduces the ability to perform activities and promotes general dependence in those affected (47)increasing the number of falls, hospitalizations and mortality (48). The imbalance between the production of free radicals and antioxidant defenses is a predictor of muscle mass loss (49). Increased ROS production in the muscles contributes to age-related muscle atrophy (50)and proteolysis through the ubiquitin-proteasome system, resulting in atrophy (51). Inflammation affects the anabolic-catabolic balance in skeletal muscle cells, causing a shift towards catabolism, atrophy and progression of sarcopenia, which is a major contributor to functional decline and frailty (52). Both TNF-α and IL-6 induce NF-kB activation, which in turn activates genes implicated in inflammation, leading to muscle loss (53).

CONSIDERATIONS

The combination of physical exercise and a low-calorie diet are the best strategies for preventing obesity and improving muscle mass. However, self-modification proposals are difficult to implement and have lower adherence in sick populations. In addition, loss of muscle mass is positively correlated with mortality and is common in individuals suffering from obesity, the elderly and those

with chronic degenerative diseases. Various lines of research have confirmed that the chronic inflammation present in fatty adipose tissue is directly associated with metabolic diseases and cardiac complications in both obesity and catabolic situations. On the other hand, numerous natural compounds have proven to improve clinical and body parameters and can help treat obesity and sarcopenia. However, these are generally analyzed in isolation in the global database. This justifies our hypothetical opinion on the possible superior efficiency of mixed therapy of already effective compounds such as Capsaicin, Green Tea and Magnesium, analyzed simultaneously, in the control of obesity and its associated comorbidities.

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