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Capsaicin and evodiamine ingestion does not augment energy expenditure and fat oxidation at rest or after moderately-intense exercise

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ARTICLE INFO

Article history:
Received 17 May 2013
Revised 12 August 2013
Accepted 13 August 2013

Keywords:
Thermogenesis
Humans
Catecholamines
Fatty acids
Triglycerides
Capsaicin
Energy expenditure
Evodiamine

ABSTRACT

Capsaicin and evodiamine are 2 thermogenic agents recognized for their ability to stimulate the sympathetic nervous system. We hypothesized that both capsaicin and evodiamine would be effective at increasing thermogenesis and lipid oxidation during rest and exercise. In a randomized, cross-over design, 11 men ingested 500 mg of cayenne pepper (1.25 mg capsaicin), 500 mg evodiamine, or placebo at rest following 30 minutes of energy expenditure assessment using open-circuit spirometry. Energy expenditure was assessed again prior to commencing approximately 30 minutes of treadmill exercise at 65% peak oxygen consumption. Energy expenditure was assessed for another 30 minutes of the post-exercise period. Heart rate, blood pressure, core temperature, and venous blood samples were obtained 30 minutes before supplement ingestion, 1 hour after supplement ingestion, immediately post-exercise, and 45 minutes post-exercise. Serum markers of lipid oxidation (glycerol, free fatty acids, glucose, epinephrine, and norepinephrine) were determined spectrophotometrically with enzyme-linked immunosorbent assay. Two-way analyses of variance with repeated measures were performed for each dependent variable ($P \leq .05$) with Supplement and Test as main effects. Statistical analyses revealed significant main effects for Test for hemodynamics, energy expenditure, serum catecholamines, and markers of fat oxidation immediately post-exercise ($P < .05$). No significant interactions between Supplement and Test were noted for any criterion variable ($P > .05$). These results suggest that acute ingestion of 500 mg of cayenne (1.25 mg capsaicin) or evodiamine is not effective at inducing thermogenesis and increasing fat oxidation at rest or during exercise in men.

1. Introduction

Dietary weight loss supplements are growing in popularity as a means to enhance weight loss efforts in the United States. The majority of these products supposedly contain special agents that possess thermogenic capabilities which are alleged to increase the body's metabolism. Capsaicin and evodiamine are herbal compounds that can be found in a

Abbreviations: 45PE, 45 minutes post-exercise; ATP, adenosine tri-phosphate; FFA, free fatty acids; GERD, gastroesophageal reflux disease; IPE, immediate post-exercise; PE, pre-exercise; PS, pre-supplement; REE, resting energy expenditure; RER, respiratory exchange ratio; TRPV1, transient receptor potential channel vanilloid subfamily member 1; VO_{2peak}, peak oxygen consumption.

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http://dx.doi.org/10.1016/j.nutres.2013.08.007

number of over-the-counter weight loss products due to their potential capabilities of increasing metabolic activity.

Capsaicin (*Capsicum frutescens*), which is the active, pungent component of chili peppers, works to speed up the body's metabolism by provoking the activity of the sympathetic nervous system [1]. Capsaicin is considered to be a vanilloid receptor agonist, specifically of transient receptor potential channel vanilloid subfamily member 1 (TRPV1) [2,3]. The TRPV1 is a receptor located on primary sensory neurons, and is activated by various ligands as well as natural irritants [3,4]. Activation of TRPV1 by capsaicin ultimately leads to an increase in blood pressure, body temperature, and heart rate shortly after ingestion [5,6]. Additionally, ingestion of capsaicin stimulates sustained fat oxidation for adults after weight loss when compared to a placebo group [7]. Energy expenditure has also been observed to rise above basal after acute ingestion of capsaicin in multiple studies [7-11]; however, this is not a consistent finding [12-14]. In rats, capsaicin increases swimming endurance through the increase of fatty acid utilization due to enhanced adrenaline secretion caused by capsaicin [15].

Despite evidence implicating its possible effectiveness, the characteristic pungency of capsaicin may hinder its use as an anti-obesity agent in some individuals. Acute administration of capsaicin induces esophageal and gastric symptoms of heartburn in healthy individuals and gastroesophageal reflux disease (GERD) patients [16]. Acute capsaicin ingestion also hastens the time to peak heartburn symptoms and leads to greater acid reflux [17,18]. Chronic ingestion of chili peppers containing capsaicin induces GERD symptoms in otherwise healthy individuals suggesting the esophageal and gastric symptoms associated with acute capsaicin ingestion do not subside with chronic administration [19]. Furthering the problem is the positive association between obesity and the risk for GERD symptoms which may contraindicate use of capsaicin in this population [20,21]. Because of these observations, there has been an effort to identify non-pungent vanilloids capable of activating TRPV1.

Evodiamine, regarded as a "hot nature" herb in Chinese medicine, is extracted from the fruit of *Evodia rutaecarpa* and has no perceptible taste or pungency [22]. Like capsaicin, evodiamine is a TRPV1 agonist with demonstrable anti-obesity effects. In rats, evodiamine induced heat loss and heat production while also stimulating the utilization of stored food energy at a rate like that of capsaicin [22]. However, when evodia was ingested by women daily at 3 g (6.75 mg evodiamine) for 8 weeks consecutively, weight loss was not significantly more than attained with a placebo [23]. Since evodiamine has been demonstrated to be less potent than capsaicin [24], it is possible that the 6.75 mg dose of evodiamine provided in the previous study [23] was too low to elicit a thermogenic response. Although some research has been conducted in order to identify the effects of evodiamine, nothing has yet been empirically established. In fact, compared to the numerous experiments conducted to analyze the effects of capsaicin, research is limited.

Non-pungent evodiamine may be a viable alternative to capsaicin, which is intolerable in some individuals, for inducing lipid oxidation and thermogenesis via TRPV1 stimulation. Most data available for capsaicin and evodiamine with regard to weight loss and thermogenesis have been exclusively focused on long-term use with little data available regarding the acute effects of ingesting these herbs. Many, but not all, studies of capsaicin employ doses that may not be realistic due to its pungency. However, because evodiamine has no pungency associated with its ingestion, high doses of this extract may be tolerated well.

The purpose of this study was to investigate the effects a single 500 mg dose of cayenne (equivalent to 1.25 mg of capsaicin) and a single dose of 500 mg of evodiamine (100% pure evodiamine extract) had on hemodynamics, energy expenditure, and lipid oxidation at rest and after moderate-intensity exercise. We hypothesized that both supplements would acutely increase thermogenesis and lipid oxidation during rest and exercise, and that supplementation with evodiamine would lead to effects equal to or greater than those observed with capsaicin because of the higher dose administered. To test this hypothesis, hemodynamics, energy expenditure, and serum markers of lipid oxidation (glucose, triglycerides, free fatty acids, and glycerol) were measured at rest, 30 minutes after supplement ingestion, and after a single bout of moderate-intensity exercise equivalent to an energy expenditure of 500 kilocalories. This approach was based on the premise that after ingesting the supplement, hemodynamics, energy expenditure, and lipid oxidation may be affected compared to before ingesting the supplement and that an additive effect of supplementation with exercise may exist.

2. Methods and materials

2.1. *Experimental approach*

In a randomized, uniform-balanced, cross-over design, participants performed 3 separate testing sessions involving a resting and endurance exercise component after ingesting 500 mg of either placebo, cayenne pepper (1.25 mg capsaicin), or evodiamine. The mean (SD) duration between each testing session was 13 ± 7 days (Fig.).

2.2. *Participants*

Eleven apparently healthy and active men between the ages of 18 to 30 years participated in the double-blind study. Enrollment was open to men of all ethnicities. Only participants who were considered as low to moderate risk for cardiovascular disease and had no contraindications to exercise as outlined by the American College of Sports Medicine, who had not consumed any nutritional supplements other than vitamins, and who had never been involved in any weight loss regimen in the last 6 months were allowed to participate. There were no exclusionary criteria regarding exercise habits or body weight. All eligible participants were cleared for participation by passing a mandatory medical screening and provided written informed consent by signing university-approved informed consent documents and approval was granted by the Institutional Review Board for Human Subjects. Additionally, all experimental procedures involved in the study conformed to the ethical consideration of the Helsinki Code.