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Novel bitter melon extracts highly yielded from supercritical extraction reduce the adiposity through the enhanced lipid metabolism in mice fed a high fat diet

Li Xu [a], Yi Xu [a], Shuang Wang [a], Qianchun Deng [b], Chun-Yan Wu [a], Xiang-Tao Chen [c], Hui-Li Wang [a, *]

[a] School of Biotechnology and Food Engineering, Hefei University of Technology, Hefei, Anhui 230009, PR China
[b] Oil Crops Research Institute, Chinese Academy of Agricultural Sciences, Wuhan, PR China
[c] School of Pharmacy, Anhui Medical University, Hefei, Anhui 230031, PR China

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ABSTRACT

Bitter melon (*Momordica charantia*) is a species of edible plant known for its medicinal value towards diabetes and obesity. Due to the various compositions of bitter melon extracts (BME), the comprehensive knowledge concerning their anti-obesity effects was insufficient. Here we first introduced supercritical extraction to BME's preparation, (supercritical extraction is a relatively advanced extraction method with a better efficiency and selectivity and expected to be extensively used in future applications) and the resultants were subjected to HPLC analysis, validating the presence of 42.60% of conjugated linolenic acid (CLnA, *cis*9, *trans*11, *trans*13-18:3) and 13.17% of conjugated linoleic acid (CLA, *cis*9, *trans*11-18:2). The BMSO (bitter melon seed oil) was then administered to the HFD mice, an obesity model established by feeding C57BL/6J mice a high fat diet. Consequently, due to the BMSO's supplementation, the HFD mice showed a significantly decreased body-weight, Lee's index, fat index and adipose size, whereas the liver weight stayed unchanged. Meanwhile, the serum FFA (free fatty acids) levels returned to normal at the dosage of 10 g/kg, and the elevated serum leptin levels were also recovered by BMSO's supplementation with moderate and high dose. These findings suggested that BMSO restored the balance between lipid intake and metabolism, which was probably mediated by leptin's variation. In summary, a detailed anti-obesity effect was described with regard to a potent CFA's (conjugated fatty acid) combination offered by BME. A potential mechanism underlying BME's beneficial effects was proposed, paving the way for the better use of BME's pharmaceutical function to serve the obesity's treatment.

1. Introduction

Obesity, a complex metabolic disorder, has become one of the main health and public issues in both developed and developing countries [1,2]. In the US, over one-third adults and 16.7% children were obese in 2009–2010, which costs up to 200 billion US dollars annually [3]. What's more, in economically advanced countries, socioeconomic inequalities in overweight and obesity continue to widen [4]. Meanwhile, there were about 200 million people who were affected by obesity in 2007 in China [5]. Given its associations with many life-threatening chronic diseases, such as insulin resistance, type II diabetes, reproductive system diseases and even cancers [6, 7], it's urgent to find safe and effective therapies for obesity and its complications. Especially, the search for the cost effective and safe preparations to address the obesity issue needs to be highlighted more.

As a species of medicinal and edible plant, the medicinal value of bitter melon (*Momordica charantia*, Linn, Cucurbitaceae) [8] has gradually drawn great attention. It has been evaluated as anti-diabetic agent in several clinical tests [9], a potent agent prohibiting the proliferation of sleeping sickness [10], an agent impairing the prostate cancer progression [11] and its anti-obesity effect was also studied and accepted [12–14]. Nonetheless, the reports pertaining to the concrete fat-reducing effects were usually contradictive, partially due to the inconsistent compositions of BME, which was obtained using various extraction methods. These

* Corresponding author.
E-mail address: wanghl@hfut.edu.cn (H.-L. Wang).

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methods mostly included the conventional Soxhlet extraction [15], hexane extraction [16], as well as acetoacetic acid extraction [17]. Compared with the conventional methods used to obtain BMSO, supercritical CO_2 extraction has a range of advantages: the supercritical fluid has a higher diffusion coefficient and lower viscosity; repeated reflux provides complete extraction; the selectivity of supercritical fluid is higher, etc [18]. It's reasonable to deduce that the supercritical extraction could lead to a BMSO with higher yields and varied constituents.

The etiology of obesity was generally associated with abnormal changes of several tissues, such as adipocyte, serum and liver [19], and the impaired energy homeostasis played essential roles in obesity's development. As for the energy balance between intake and expenditure, leptin's regulatory roles received the increasing attention [20]. Leptin is the primary signal from energy storage and functions negatively on energy intake [21], and Chen et al. [22] showed that the increased leptin signaling could facilitate the transformation of white adipocytes into fat-burning cells. In obese model, the activity of leptin was inhibited, mainly via the "leptin resistance", a mechanism characterized by the reduced hypothalamic susceptibility towards leptin's presence. Additionally, the leptin resistance was frequently accompanied by the increased circulating leptin level [21]. Thus, leptin could bridge central nervous system and peripheral tissues in energy regulation, and whether its function was improved upon a novel BMSO's administration, needs a concise investigation.

The purpose of this paper is to perform a comprehensive study on the anti-obesity effect of a novel BMSO and in further steps, investigate the underlying regulatory mechanisms involved in this advantageous effect. Besides, the function of conjugated fatty acids (CFA) was also summarized and discussed.

2. Materials and methods

2.1. BMSO's preparation

Bitter melon seeds (purchased from Chengxin Herb Corporation, Hebei province, China) collected from ripe bitter melons only, with similar size, color, and no physical damage. BMSO's preparation was carried out as suggested previously [22] with some modifications:

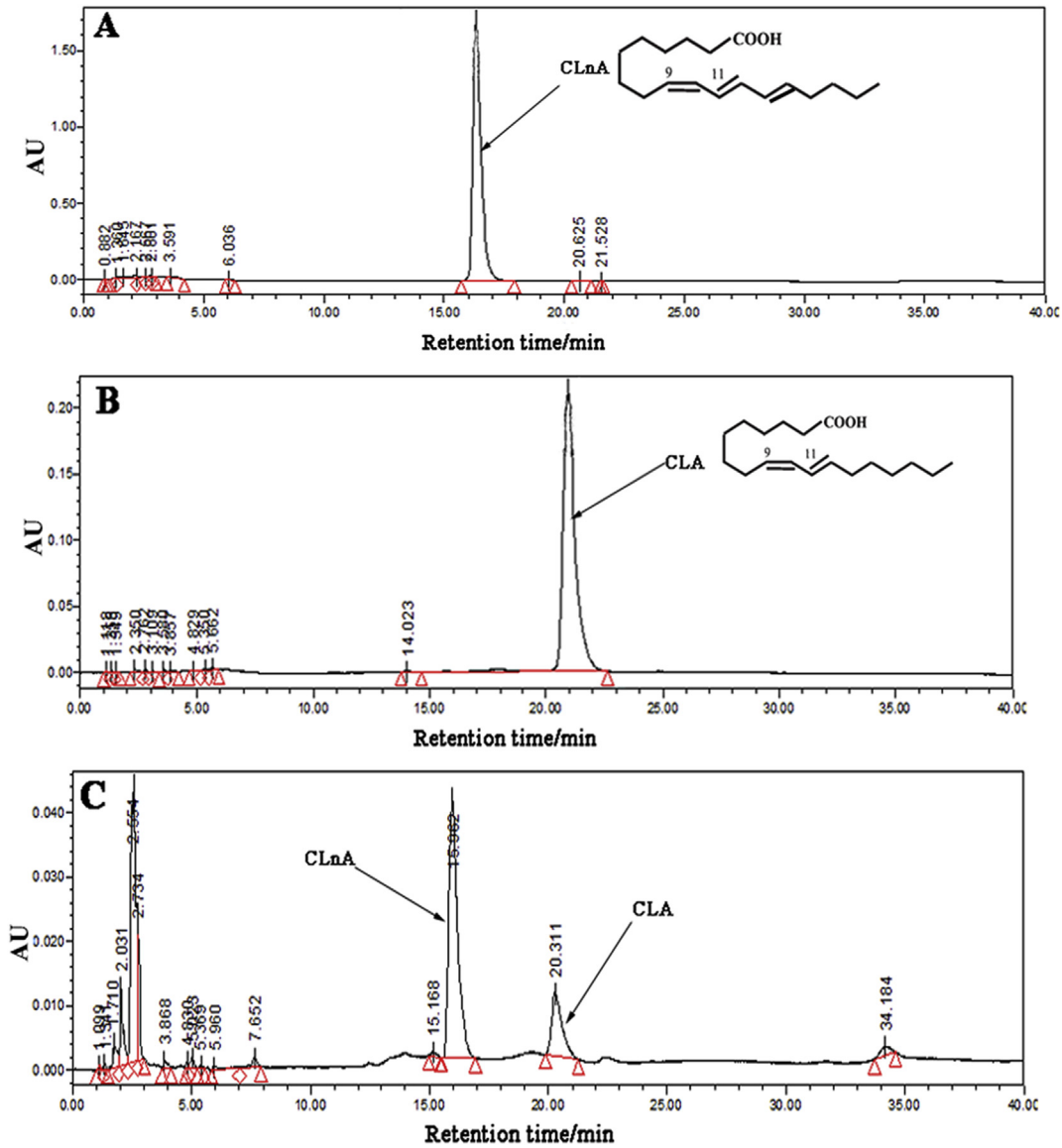

Fig. 1. HPLC analysis of polyunsaturated fatty acids. A, standard sample of CLnA (*cis*9, *trans*11, *trans*13-18:3); B, standard sample of CLA (*cis*9, *trans*11-18:2); C. BMSO(bitter melon seed oil) sample. The arrows indicated the objective characteristic peaks. Each experiment was repeated thrice, and results of a representative experiment are shown.