Unveiling the potential of natural compounds in the fight against obesity

Obesity, a complex metabolic disorder that affects nearly one billion individuals worldwide [1], necessitates the development of innovative therapeutic approaches beyond conventional lifestyle modifications and existing pharmacotherapies [2,3]. Although currently approved drugs provide modest weight loss benefits, concerns regarding their adverse effects and limited long-term efficacy persist [4,5]. Hence, there is an imperative need to investigate alternative modalities, with a burgeoning emphasis on exploring the untapped potential of natural compounds. This compelling demand for safer and more effective solutions has fueled a surge of interest in the under-explored realm of natural compounds.

Drawing upon the rich tapestry of bioactive molecules found in various plant parts, herbal remedies boast a longstanding history in traditional medicine for treating diverse ailments. Their inherent safety profiles and diverse mechanisms of action offer a potentially holistic approach to managing obesity and related metabolic disturbances. Notably, a significant portion of FDA-approved drugs, such as metformin, aspirin, and artemisinin, are derived from natural sources or their synthetic derivatives, further validating their therapeutic potential [6]. This established efficacy within conventional medicine, coupled with
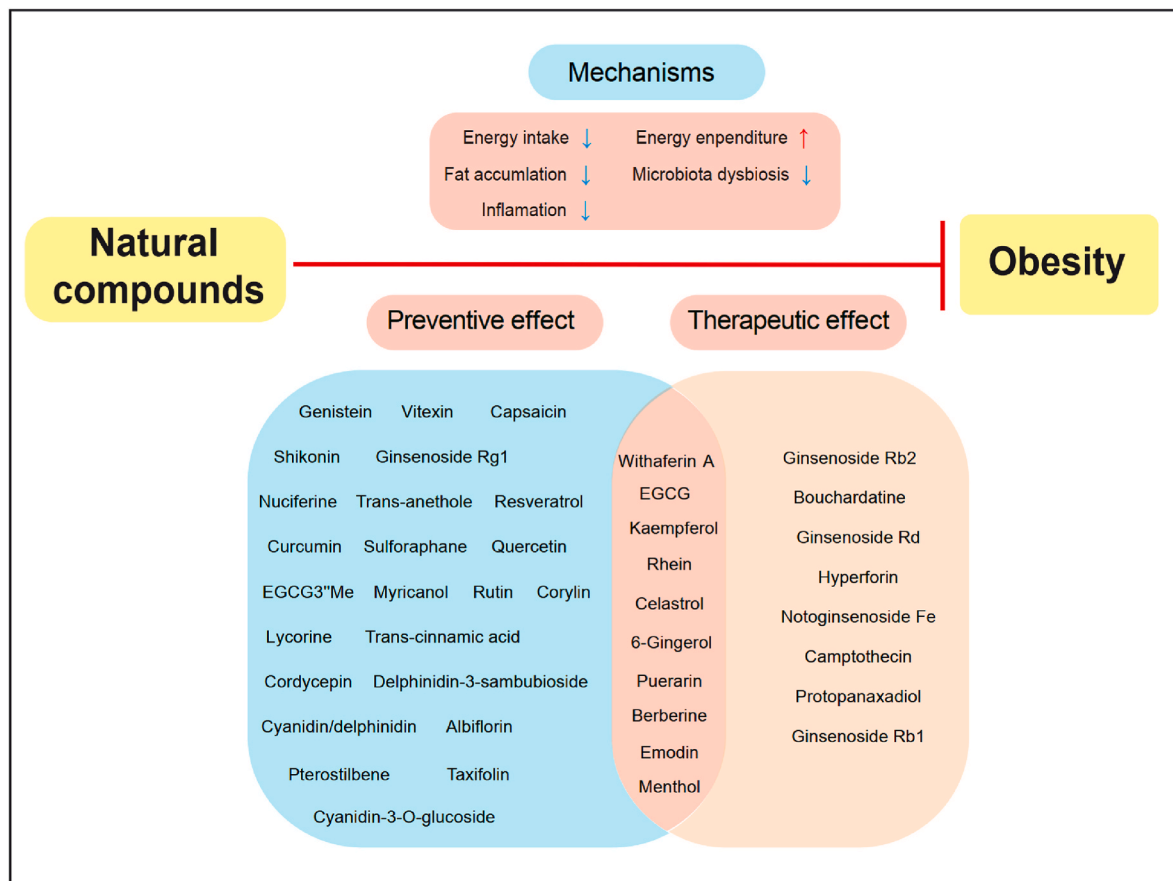

Fig. 1. Anti-obesity effects and mechanisms of natural compounds.

centuries of empirical evidence from traditional systems like Chinese medicine employing natural compounds to against obesity, warrants a closer examination of this promising avenue [7–10].

Amidst the growing interest in natural compounds for obesity management, *Zhao* et al. offer a comprehensive review of approximately 50 natural compounds and their anti-obesity efficacies in preclinical animal models [11]. Employing rigorous data extraction and standardization methods, the authors present a unique opportunity for comparative analysis by separating preventive and therapeutic effects. Significantly, the data suggests that natural compounds may be more effective in preventing obesity development. Over 34 compounds demonstrated preventive effects, with 11 suppressing body weight gain by >15 %, highlighting their potential as dietary supplements for weight control (Fig. 1). While 35 compounds exhibited therapeutic effects, only 18 could reduce body weight in obese animals, and their efficacy was generally lower compared to the preventive model. Notably, 13 compounds, including ginsenoside Rb2 and celastrol, induced more than 5 % weight loss in obese animals, showcasing promising therapeutic potential. Intriguingly, 10 compounds displayed both preventive and therapeutic effects, suggesting their suitability for further development as anti-obesity drugs. This comprehensive review not only provides valuable insights into the differential efficacies of natural compounds but also paves the way for future research, prioritizing clinical trials for the most promising candidates and guiding the development of evidence-based dietary supplements and anti-obesity medications.

The present study has demonstrated that natural compounds exert their anti-obesity effects via diverse mechanisms, encompassing reduction of fat accumulation, enhancement of energy expenditure, amelioration of inflammation, correction of gut microbiota dysbiosis, and modulation of lipid absorption. Nonetheless, the specific molecular targets *in vivo* remain largely undetermined. Therefore, further investigation aimed at elucidating these mechanisms is imperative to optimize therapeutic strategies.

Despite the promising potential of natural compounds, several challenges must be addressed before their clinical application. These include the standardization of extracts, identification of optimal dosage, evaluation of potential side effects, and rigorous clinical trials in diverse populations. Concerted efforts to overcome these hurdles are essential for translating research findings into clinical practice.

The integration of traditional knowledge, with its rich history of medicinal plant use, with modern scientific approaches, presents a promising avenue for the expedited exploration and advancement of innovative anti-obesity therapies. By fostering collaborative partnerships between scientists and traditional knowledge holders, a more inclusive and culturally attuned approach to drug development can be achieved.

CRediT authorship contribution statement

Ziwen Jia: Writing – original draft. **Sijia Lu:** Writing – original draft, Writing – review & editing. **Suzhen Chen:** Validation, Writing – review & editing. **Junli Liu:** Validation, Writing – review & editing.

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