

# Assessment of the efficiency of herbal formulas and finding the rules of combining herbs in the treatment of simple obesity using network meta-analysis and association rule

Phuong-Quynh N Le<sup>1</sup>, Cong-Nguyen Nguyen<sup>1</sup>, Ly-Na T Vu<sup>1</sup>, Hoang Tran<sup>1</sup>,  
Thanh-Phong Vo<sup>1</sup>, Kien-Tai H Pham<sup>1</sup>, Thi Thu Hien Nguyen<sup>2</sup>

## ABSTRACT

**Objective:** Evaluate the effectiveness of herbal formulas and finding the rules of combining herbs in the treatment of simple obesity. **Method:** Search for randomized controlled clinical trials involving herbal formulas in patients with simple obesity on the CNKI databases. The retrieval period was from 2014 to 2023. Search results were screened according to pre-established inclusion and exclusion criteria, then data were extracted. Using network meta-analysis and the association rule in R software to perform the synthesis analysis. **Results:** 61 studies were included in the analysis. The meta-analysis results revealed that three herbal formulas achieved the highest BMI reduction when combined with other treatment methods: Self-designed formulas, Wu Ling San, and Shen Ling Bai Zhu San. The synthesis analysis showed that Poria, Atractylodes, and Hawthorn were the most frequently used herbs in the decoction formulas, with common doses of 15g, 10g, and 15g, respectively. Five patterns of herb combination were identified: Atractylodes macrocephala, Crataegus pinnatifida, Citrus reticulata, Alisma orientale, and Glycyrrhiza uralensis, paired with Poria cocos, with support of 33.3%-53.3% and confidence of 83.3%-92.9%. **Conclusion:** Three herbal formulas were evaluated as achieving the highest BMI reduction when combined with other treatment methods. The linkage algorithm identified five herb combination rules in the treatment of simple obesity.

**Keywords:** The rules of combining herbs, simple obesity, network meta analysis, association rule

<sup>1</sup> University of Medicine and Pharmacy at Ho Chi Minh City, Vietnam

<sup>2</sup> Hai Phong University of Medicine and Pharmacy, Vietnam

## \* Corresponding author

Thi Thu Hien Nguyen  
Email: [ntthien@hpmu.edu.vn](mailto:ntthien@hpmu.edu.vn)

Received: April 26, 2025

Reviewed: April 29, 2025

Accepted: June 10, 2025

## INTRODUCTION

Obesity is the most prevalent metabolic disorder worldwide. In 2004, the World Health Organization (WHO) estimated that over 1 billion individuals were overweight, among whom 300 million had a body mass index (BMI) exceeding 30 kg/m<sup>2</sup> [1,2]. Substantial evidence has demonstrated the detrimental impact of obesity on health, impairing work capacity and establishing it

as a major global health concern [3]. In Singapore, healthcare expenditures related to overweight and obesity were projected to account for 1.6% of total healthcare spending in 2019 [3]. As such, obesity imposes a significant clinical, social, and economic burden.

Since the time of Hippocrates, lifestyle modifications have been recommended for individuals with obesity. By the early 20th century, several pharmacological

interventions had been introduced to facilitate weight reduction [2]. Currently, modern medicine (MM) offers a wide range of weight management strategies, including dietary control, increased physical activity, pharmacotherapy, and bariatric surgery. However, the efficacy of these approaches remains limited [4,5].

Conversely, numerous studies worldwide have demonstrated the role of traditional medicine (TM), particularly herbal medicine, in supporting obesity management. For instance, a study by Liu et al. (2022) reported superior weight reduction outcomes when Chu Shi Jiang Zhi Tang was combined with lifestyle modifications [6]. Similarly, in 2022, Yin et al. published findings on the BMI-reducing effects of Lian Chen Tang in obese individuals when integrated with lifestyle adjustments [7]. Given the increasing body of research on the weight-loss efficacy of herbal decoctions, clinicians often face challenges in selecting appropriate formulas and optimizing herbal combinations for individualized treatment. To address this, our study employs network meta-analysis and association rule mining to evaluate the effectiveness of various herbal decoctions and identify patterns in herbal combination strategies for the treatment of simple obesity. By analyzing data from previous randomized controlled trials (RCTs), this research aims to provide evidence-based recommendations for selecting optimal herbal formulas and elucidating key herb-pairing principles in obesity management within the framework of traditional medicine.

## MATERIALS AND METHODS

### Literature Search Strategy

A systematic search was conducted using the CNKI electronic database. Only studies published in English and Chinese between

2014 and 2024 were considered. The search strategy employed the Boolean operator “AND” to combine the keywords obesity, random, and group, while the “NOT” operator was used to exclude studies containing the terms mice, rat, children, and diabetes. The search strategy was refined through multiple iterations to ensure comprehensive retrieval of relevant studies.

### Selection criteria

#### *Inclusion Criteria*

Study selection was performed based on the PICOS framework, with the following criteria:

1. Participants: Adults ( $\geq 18$  years) diagnosed with simple obesity.
2. Intervention: All intervention groups had to receive traditional medicine (TM) treatments, either herbal formulas alone or in combination with other therapeutic modalities.
3. Comparison: Studies were required to include a control group for comparison with the intervention group.
4. Outcomes: The primary outcome was BMI reduction, presented as mean  $\pm$  standard deviation (SD).

#### *Exclusion Criteria*

1. Participants: Studies involving children, animals, or those addressing other metabolic disorders were excluded.
2. Outcomes: Studies that did not report BMI changes or failed to present results in the required statistical format were excluded.
3. Study Design: Only randomized controlled trials (RCTs) evaluating herbal formulas for the treatment of simple obesity were included. Studies with non-RCT designs, incomplete data, duplicate publications, or redundant analyses were excluded.

### Data Collection and Analysis

#### *Data collection*

Only randomized controlled trials (RCTs) were included in this evaluation. Studies were independently screened according to the inclusion and exclusion criteria. The screening process was conducted as follows:

1. Identification: Retrieved studies were imported into EndNote X9 for reference management. Duplicate studies were identified and removed.

2. Title and Abstract Screening: Titles and abstracts of all retrieved studies were reviewed. Studies that did not meet the inclusion criteria were excluded.

3. Full-Text Review: After the initial screening, full texts of the remaining studies were thoroughly analyzed to determine their eligibility for inclusion in the final analysis.

4. Final Selection: Studies that met all criteria were confirmed for inclusion. Any discrepancies between reviewers during the selection process were resolved through discussion or consultation with a third party.

The extracted data included:

- Study characteristics (author names, year of publication).
- Sample characteristics (sample size per group, mean age and standard deviation, traditional medicine syndromes).
- Intervention details (intervention techniques used in the control and treatment groups, formula ingredients).
- Intervention duration (measured in months, with 4 weeks considered equivalent to 1 month).
- Outcome measures (mean BMI and standard deviation for each group before and after treatment).

#### *Network Meta-Analysis and Association Rule Mining*

To analyze the network meta-analysis of the included randomized controlled trials

(RCTs), we utilized the R software, which allowed us to assess and compare the effectiveness of different interventions systematically. The results of the analysis were expressed in terms of effect size, with a 95% confidence interval (CI) to ensure statistical robustness and accuracy. Specifically, for body mass index (BMI) data, we measured the mean difference (MD) before and after the intervention and reported the corresponding 95% confidence interval (CI) to evaluate the effect of the treatment.

In addition to network meta-analysis, we applied association rule mining to uncover potential patterns in herbal combinations. The Apriori algorithm, a widely used method in association rule mining, was employed in the R software to develop an association rule model aimed at identifying frequently co-occurring herbal prescriptions. This algorithm is particularly useful for extracting meaningful relationships between herbs based on prescription data, thereby helping to identify potential synergistic effects in Traditional Chinese Medicine (TCM).

The key parameters for the association rule analysis were configured to ensure meaningful and reliable pattern extraction. The minimum support threshold was set at 1%, ensuring that only frequently occurring herbal combinations were considered. The minimum confidence threshold was established at 10%, reflecting the reliability of the associations identified. Additionally, the lift value was set to be greater than 1, indicating that the discovered associations had a stronger-than-random correlation and were of practical significance in Traditional Chinese Medicine research.

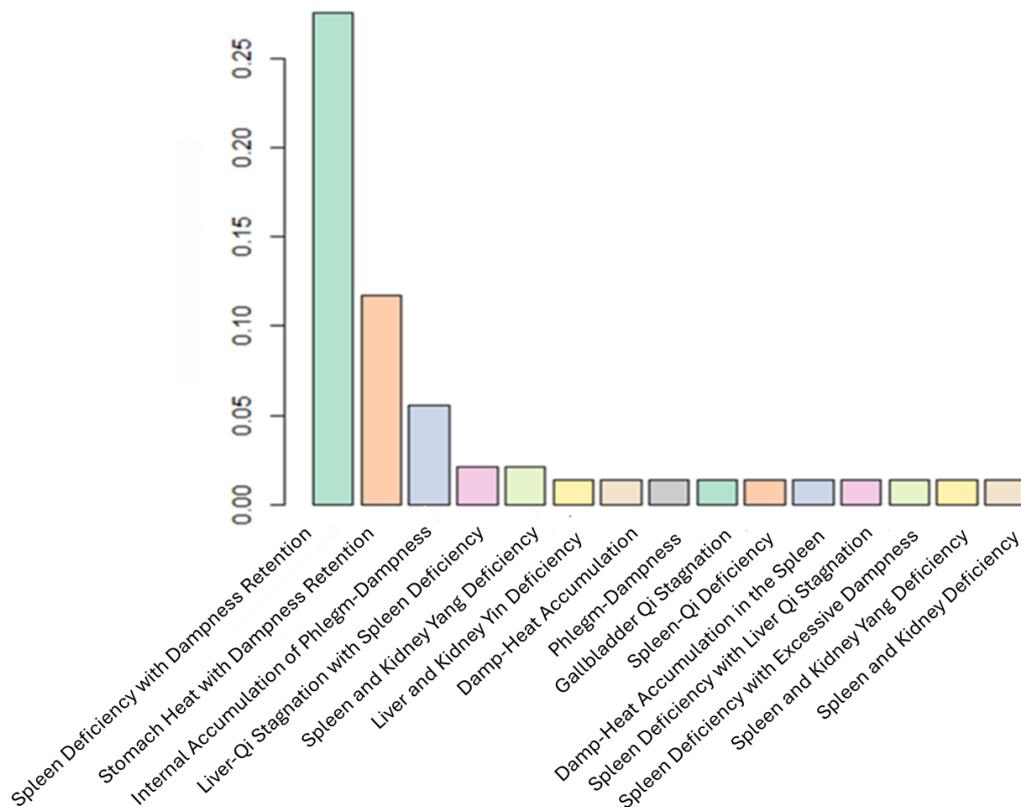
## RESULTS

### Characteristics of Included Studies

A total of 61 RCTs meeting the inclusion and exclusion criteria were identified from CNKI, covering the period from 2014 to 2024. The sample sizes in these studies ranged from 20 to 109 patients, with participant ages spanning from 26.87 to 75.02 years (15 studies did not report participant ages). The study durations varied from 1 to 6 months.

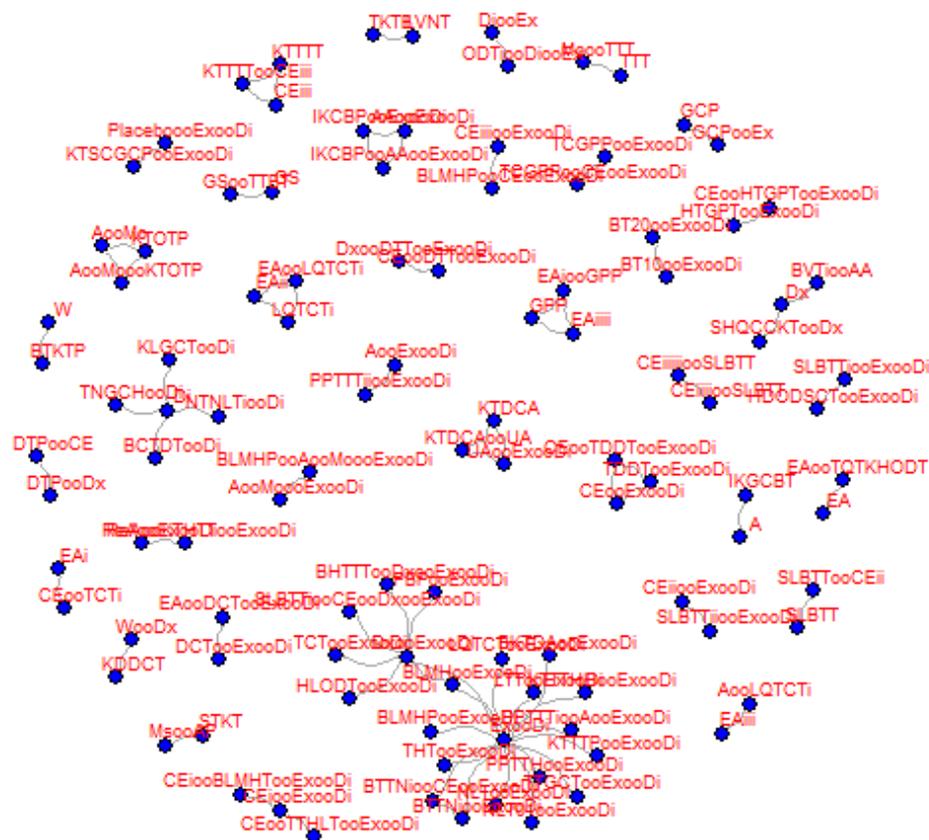
Among the 61 included studies, 52 trials employed a two-arm intervention design, while 9 trials used a three-arm intervention design, resulting in a total of 113 intervention arms and 108 different intervention methods. Notably, 75 intervention arms involved the use of herbal decoctions with fully detailed formula compositions.

Most of the included studies focused on the following Traditional Medicine syndrome patterns: Spleen Deficiency with Dampness Retention (19 studies), Stomach Heat with Dampness Retention (8 studies), and Internal Accumulation of Phlegm-Dampness (4 studies). The distribution of syndrome patterns assessed in the RCTs is illustrated in Figure 1.



*Fig. 1. Distribution of syndrome patterns*

### Results of Network Meta-Analysis on the Effectiveness of Herbal Decoctions in BMI Reduction

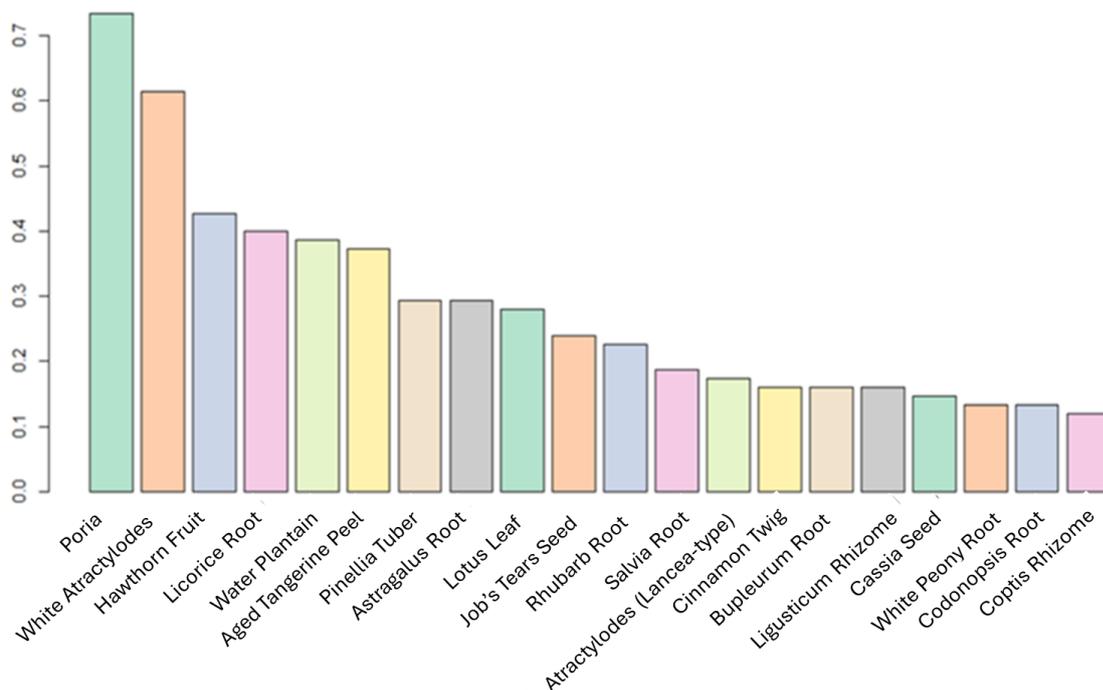


**Fig. 2.** Network Diagram Representing the Intervention Arms Included in the Analysis

The network model for this study was constructed using data from all intervention arms included in the analysis of BMI reduction outcomes. The results of the network meta-analysis (NMA) indicated that the most effective intervention for BMI reduction was a customized herbal formula consisting of *Astragalus membranaceus* (Huang Qi, 20g), *Poria cocos* (Bai Ling, 20g), *Atractylodes macrocephala* (Bai Zhu, 30g), *Bupleurum chinense* (Chai Hu, 15g), *Citrus aurantium* (Zhi Shi, 15g), *Alisma plantago-aquatica* (Ze Xie, 10g), *Citrus reticulata pericarp* (Chen Pi, 15g), *Pinellia ternata* (Ban Xia, 9g), *Zingiber officinale* (Sheng Jiang, 9g), *Morus alba* leaf (Sang Ye, 30g), *Nelumbo nucifera* leaf (He Ye, 30g), *Crataegus pinnatifida* (Shan Zha, 30g), *Paeonia rubra* (Chi Shao, 15g), *Atractylodes lancea* (Cang Zhu, 10g), *Coix lacryma-jobi* (Yi Yi Ren, 15g), *Glycyrrhiza uralensis* (Gan Cao, 9g), and *Rheum palmatum* (Da Huang, 5g). This formula was administered in combination with thread embedding therapy, dietary adjustments, and physical exercise, yielding the highest estimated effectiveness in BMI reduction.

The second most effective intervention was the Five-Ling Powder (Wu Ling San) combined with dietary adjustments and physical exercise, demonstrating significant BMI reduction. The third most effective intervention was the Shen Ling Bai Zhu San formula, administered alongside thread embedding therapy, dietary adjustments, physical exercise, and modern pharmacological treatments, which also showed substantial effectiveness in BMI reduction.

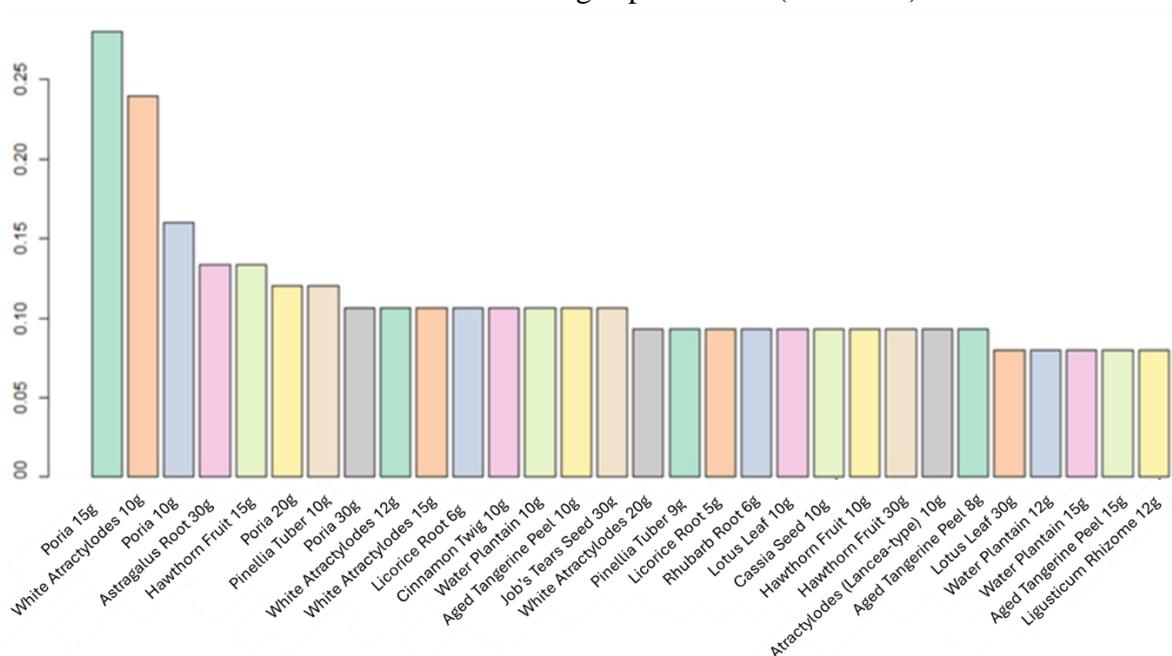
### Proportion of Herbs Used



**Fig. 3.** Proportion of Herbs Used in Herbal Decoctions

Figure 3 illustrates the proportion of herbs used in the studied herbal decoction formulas. Among the analyzed formulas:

- 73.33% contained Poria cocos (Bai Ling)
- 61.33% contained Attractylodes macrocephala (Bai Zhu)
- 42.66% contained Crataegus pinnatifida (Shan Zha)

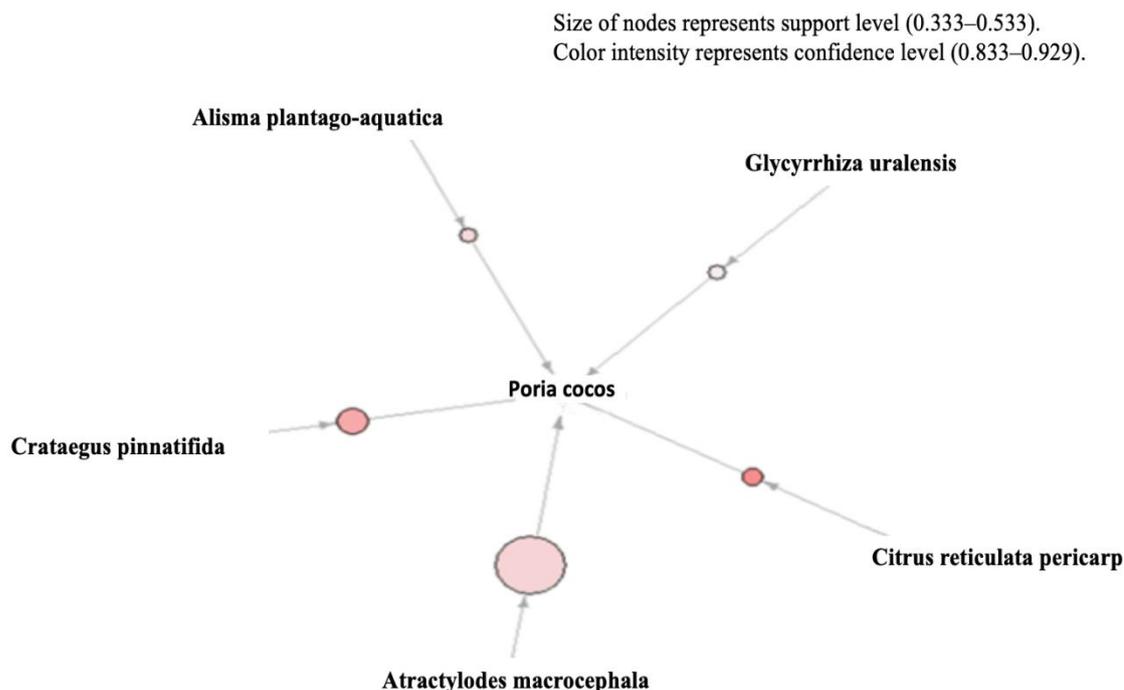


**Fig. 4.** Proportion of Herbs and Their Dosages Used

To provide a more comprehensive analysis, we examined both the herb composition, and the dosage used. As depicted in Figure 4:

- *Poria cocos* (Bai Ling) and *Atractylodes macrocephala* (Bai Zhu) were used at doses of 10g, 15g, and 20g.
- The most commonly used dosage for Bai Ling was 15g.
- The most commonly used dosage for Bai Zhu was 10g.
- *Crataegus pinnatifida* (Shan Zha) was used at doses of 10g, 15g, and 30g, with 15g being the most frequently used dosage.

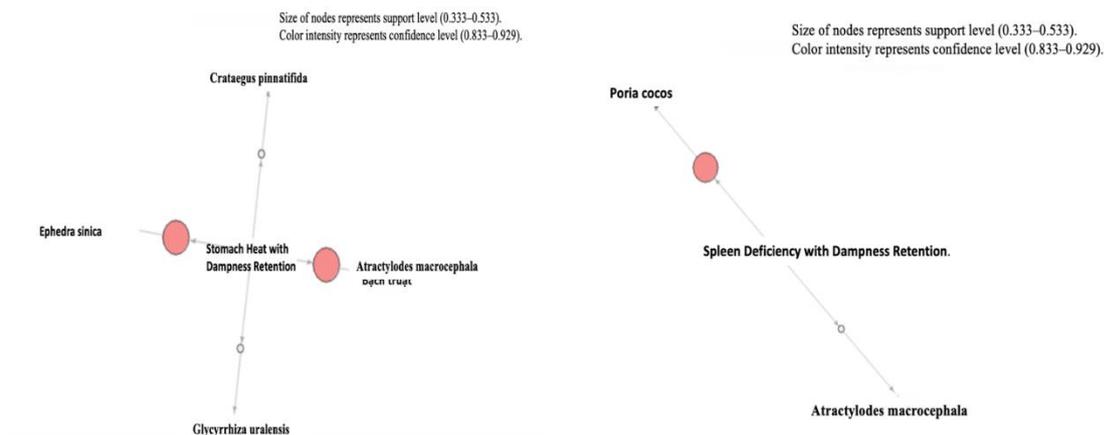
### Herbal Combination Patterns



**Fig. 5.** Herbal Combination Patterns

Figure 5 illustrates the herbal combination rules, with a support level of 33.3%–53.3% and a confidence level of 83.3%–92.9%. The analysis shows that *Atractylodes macrocephala* (Bai Zhu), *Crataegus pinnatifida* (Shan Zha), *Citrus reticulata pericarp* (Chen Pi), *Alisma plantago-aquatica* (Ze Xie), and *Glycyrrhiza uralensis* (Gan Cao) are all commonly paired with *Poria cocos* (Bai Ling).

Comparing the combination patterns of Bai Zhu and Shan Zha with Bai Ling, it was observed that Bai Zhu exhibited a higher support level when paired with Bai Ling, whereas Shan Zha demonstrated a higher confidence level in combination with Bai Ling. Figure 6 illustrates the herbal combination patterns observed in two syndrome types: Spleen Deficiency with Dampness Retention and Stomach Heat with Dampness Retention.



**Fig. 6.** Herbal Combination Patterns in Two Syndrome Types

## DISCUSSION

### Network Meta-Analysis Results and Herbal Formula Effectiveness

The network meta-analysis (NMA) results identified a customized herbal formula as the most effective intervention for BMI reduction. This formula consisted of *Astragalus membranaceus* (Huang Qi, 20g), *Poria cocos* (Bai Ling, 20g), *Atractylodes macrocephala* (Bai Zhu, 30g), *Bupleurum chinense* (Chai Hu, 15g), *Citrus aurantium* (Zhi Shi, 15g), *Alisma plantago-aquatica* (Ze Xie, 10g), *Citrus reticulata* pericarp (Chen Pi, 15g), *Pinellia ternata* (Ban Xia, 9g), *Zingiber officinale* (Sheng Jiang, 9g), *Morus alba* leaf (Sang Ye, 30g), *Nelumbo nucifera* leaf (He Ye, 30g), *Crataegus pinnatifida* (Shan Zha, 30g), *Paeonia rubra* (Chi Shao, 15g), *Atractylodes lancea* (Cang Zhu, 10g), *Coix lacryma-jobi* (Yi Yi Ren, 15g), *Glycyrrhiza uralensis* (Gan Cao, 9g), and *Rheum palmatum* (Da Huang, 5g). When combined with other therapeutic methods, this formula exhibited the highest effectiveness in reducing BMI, followed by Wu Ling San and Shen Ling Bai Zhu San.

From the perspective of Traditional Chinese Medicine (TCM), simple obesity is classified under “Fei Bang” (肥胖, obesity

syndrome), which is characterized by “ben xu biao shi” (本虚标实, root deficiency with excess manifestation). Spleen Deficiency impairs the transformation and transportation of food and fluids, leading to dampness accumulation, which eventually transforms into phlegm and fat deposits. The most effective formula was found to strengthen the Spleen, lift Yang, resolve dampness, regulate Yin-Yang balance, and promote Qi circulation, aligning with the underlying mechanisms of Fei Bang. In addition to the customized formula, Wu Ling San, which facilitates water metabolism and dampness elimination, and Shen Ling Bai Zhu San, which strengthens the Spleen and Stomach while boosting Qi, were also found to be effective in BMI reduction.

### Herb Frequency, Dosage Patterns, and Association Rule Mining

An analysis of herb usage frequency showed that *Poria cocos* (Bai Ling), *Atractylodes macrocephala* (Bai Zhu), and *Crataegus pinnatifida* (Shan Zha) were included in over 40% of the studied formulas, consistent with the findings of Zeng et al. (2017). *Atractylodes macrocephala* (Bai Zhu) functions as a Qi-tonifying and Spleen-strengthening herb, *Poria cocos* (Bai Ling) aids in draining dampness, and *Crataegus*

pinnatifida (Shan Zha) promotes digestion and eliminates food stagnation. The most commonly used dosages for these herbs in the included studies were *Poria cocos* (Bai Ling) at 15g, *Atractylodes macrocephala* (Bai Zhu) at 10g, and *Crataegus pinnatifida* (Shan Zha) at 15g, all of which fall within the recommended dosage ranges in the Vietnamese Pharmacopoeia V. Using association rule mining, five key herbal combination patterns were identified for treating simple obesity. These findings were consistent with those reported by Zeng et al., confirming the stability of these combinations [9]. The five most frequently observed pairings included *Atractylodes macrocephala* (Bai Zhu) with *Poria cocos* (Bai Ling), *Alisma plantago-aquatica* (Ze Xie) with *Poria cocos* (Bai Ling), *Crataegus pinnatifida* (Shan Zha) with *Poria cocos* (Bai Ling), *Glycyrrhiza uralensis* (Gan Cao) with *Poria cocos* (Bai Ling), and *Citrus reticulata* pericarp (Chen Pi) with *Poria cocos* (Bai Ling). Among these, *Poria cocos* (Bai Ling) was the most frequently paired herb due to its dampness-draining properties, making it a key component in addressing the pathogenesis of Fei Bang. Notably, the confidence level for the Bai Zhu – Bai Ling combination was lower than that of Shan Zha – Bai Ling, suggesting variations in the effectiveness of different herb pairings.

#### **Clinical Implications and Syndrome-Specific Herbal Combinations**

One possible explanation for the higher confidence level of the Shan Zha – Bai Ling combination compared to Bai Zhu – Bai Ling lies in the biomedical properties of *Crataegus pinnatifida* (Shan Zha). According to Kuo et al., extracts from Shan Zha have been shown to reduce both brown and white fat deposits, contributing to weight reduction in obese individuals. As a

result, Shan Zha is widely included in herbal formulas for simple obesity, not only for its digestive properties but also for its anti-obesity effects. To further investigate herbal combination rules, association rule mining identified two key herbal combinations for Spleen Deficiency with Dampness Retention, primarily Bai Ling and Bai Zhu, and four key herbal combinations for Stomach Heat with Dampness Retention, including Ma Huang, Shan Zha, Bai Zhu, and Gan Cao. These findings highlight the importance of syndrome differentiation in herbal prescriptions. Clinicians are advised to consider these pairing rules when formulating herbal treatments for simple obesity to ensure alignment with the patient's syndrome differentiation and treatment principles, thereby optimizing therapeutic outcomes.

#### **CONCLUSION**

In conclusion, based on the results of the network meta-analysis, three herbal decoction formulas, when combined with other therapeutic methods, demonstrated the highest effectiveness in BMI reduction. Additionally, association rule mining identified five key herbal combination patterns for the treatment of simple obesity, along with two combination rules specific to Spleen Deficiency with Dampness Retention and four combination rules specific to Stomach Heat with Dampness Retention. These findings provide valuable insights into herbal formulation strategies for clinical application in obesity treatment.

#### **Data availability statement**

The data that support the findings of this study are available from the corresponding author upon reasonable request.

#### **Declaration of competing interest**

The authors declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

## REFERENCES

1. Xavier F, Ana C. Obesity: epidemiology and clinical aspects. *Best Practice & Research Clinical Gastroenterology*. 2004;18(6): 1125-1146. doi:10.1016/j.bpg.2004.06.030
2. Bray GA, Heisel WE, Afshin A, et al. The Science of Obesity Management: An Endocrine Society Scientific Statement. *Endocr Rev*. 2018;39(2):79-132. doi:10.1210/er.2017-00253
3. Lam BCC, Lim AYL, Chan SL, et al. The impact of obesity: a narrative review. *Singapore Med J*. 2023;64(3):163-171. doi:10.4103/singaporemedj.SMJ-2022-232
4. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. *World Health Organ Tech Rep Ser*. 2000; 894:i-253.
5. Courcoulas AP, Christian NJ, O'Rourke RW, et al. Preoperative factors and 3-year weight change in the Longitudinal Assessment of Bariatric Surgery (LABS) consortium. *Surgery for Obesity and Related Diseases*. 2015;11(5):1109-1118. doi:10.1016/j.soard.2015.01.011
6. 刘峰. 除湿降脂方治疗成人单纯性肥胖痰湿内盛证的临床观察[D].湖南中医药大学, 2022.DOI:10.27138/d.cnki.ghuzc.2022.000171.
7. 尹东. 连陈汤治疗肥胖的临床疗效及对血清IL-6、IL-10、GLP-1及PYY的影响[D].黑龙江中医药大学, 2022.DOI:10.27127/d.cnki.ghlzu.2022.000164.
8. 张中成.刘志诚针刺治疗肥胖症的经验[J].辽宁中医杂志,2001,(04):207.DOI:10.13192/j.ljtc.2001.04.16.zhangzhch.009.
9. 曾慧妍,肖颖馥,张锦明等.基于中医辅助传承系统的中医药治疗单纯性肥胖方剂组方规律分析[J].广州中医药大学学报,2017,34(04):612-616.DOI:10.13359/j.cnki.gzxbtcm.2017.04.033.
10. Kuo DH, Yeh CH, Shieh PC, et al. Effect of shanzha, a Chinese herbal product, on obesity and dyslipidemia in hamsters receiving high-fat diet. *J Ethnopharmacol*. 2009;124(3):544-550. doi:10.1016/j.jep.2009.05.005