Integration of systematic review and data mining techniques to reveal core anti-obesity medicinal plants

Yan Jie Chester Ng
Nanyang Technological University
Kye Siong Leong
Nanyang Technological University
Ren-You Gan
Singapore Institute of Food and Biotechnology Innovation (SIFBI)
Xian Yang
University of Manchester
Linda LD Zhong (linda.zhong@ntu.edu.sg)
Nanyang Technological University

Research Article

Keywords: Data Mining, Medicinal Plants, Herbal Formula, Obesity, Hierarchical Clustering, Apriori Association

Posted Date: March 23rd, 2023

DOI: https://doi.org/10.21203/rs.3.rs-2656902/v1

Abstract

Background: Obesity is a complex chronic disease that can lead to a variety of health problems. Despite its increasing frequency, there is still a lack of safe and effective treatment options. Traditional Chinese Medicine (TCM) herbal treatment is gaining medical attention as a potential alternative to disease treatment. Specifically, biomolecular interactions of the usage of paired herbs could yield essentially synergistic effects on the fight against obesity.

Objective: This study aims to investigate the combination of core herbs and clustering patterns in obesity treatment using various data mining techniques.

Methods: Eight electronic databases were searched from inception until December 2021 and 34 Randomized Control Trials (RCTs) were identified. Subsequently, 96 different herbs were extracted from the RCTs for association analysis and hierarchical clustering. The quality assessment of the trials was conducted using the Cochrane Collaboration's Risk of Bias Tool.

Results: Association analysis identified the core herb combination of *Coptis chinensis*, *Epimedium grandiflorum*, *Salvia miltiorrhiza*, and *Poria cocos*. Hierarchical clustering also identified meaningful clustering patterns amongst herbs based on similar therapeutic effects and meridian entry.

Conclusion: Using an integrated approach of systematic review and data mining techniques has revealed core herbs for the treatment of obesity. However, more clinical trials/clinical studies are required to validate the clinical efficacy of the core herb combination.

1. Background

Obesity is a complex condition that can be caused by a variety of factors, such as environmental exposure, genetics, or lifestyle choices (1). It is characterized by abnormal fat accumulations that can affect health and can be assessed using the Body Mass Index (BMI), with a BMI≥25 indicating overweight and a BMI≥30 indicating obesity (2). Excess body fat disrupts body balance and metabolism, resulting in undesirable health complications and psychological concerns such as low self-esteem and confidence (3, 4). According to the World Health Organization, obesity has nearly tripled globally since 1975. In 2016, more than 1.9 billion adults aged 18 and older were overweight, with over 650 million of these obese (2). Hence, it is a growing public health threat that needs to be addressed.

One current treatment option is to encourage behavioral change. However, weight loss based on behavioral changes might be difficult to maintain once the body has experienced adaptive biological responses (5). The rate of relapse is high and more than 90% of people who lose weight from dieting regain it in 3-5 years (6). Another current treatment option is weight loss surgery and the use of pharmacological drugs such as Sibutramine and Orlistat, but there is the possibility of developing harmful physical side effects (7). Hence, there is a growing need to develop safer and more reliable alternatives to obesity treatment.

TCM herbal treatment is a potential alternative gaining medical recognition. It has an established history in treating various chronic diseases, and two of its main advantages are its medicinal properties and disease treatment approach (1). Exploring the use of TCM herbs could be effective for obesity as TCM herbs contain various biomolecular compounds with medicinal properties such as antioxidant and antiangiogenic capabilities (8, 9). Using multiple herbs together could produce synergistic biomolecular interactions essential in combating obesity (9). Herb-based alternative therapies are also gaining popularity and medical recognition, with increased manufacture of pharmaceuticals such as herb-based antibiotics and antimalarials (10).

Additionally, TCM adopts a holistic approach to disease treatment through evaluation and treatment of manifestations and root causes. TCM views obesity as a disease arising from *spleen and kidney deficiency and liver depression*, with phlegm, dampness, heat, and blood stasis as standard manifestations (11). Therefore, before deciding on a course of treatment, physicians will use diagnostic TCM approaches like observation, listening, questioning, and pulse analysis to determine the root cause (12). Thus, TCM could be advantageous in obesity treatment.

In recent years, data analytics has seen increased use in medical and healthcare research. Examples of application in TCM-related research include machine learning for medical diagnosis, network-based deciphering of the mechanism of action of TCM, prescription analysis, and data mining (13). Association rule analysis is one data analytics tool that seeks to provide insights on item set frequency and association rule patterns by studying variables such as support, confidence, and lift (14). Unsupervised hierarchical clustering is another data analysis tool that divides data into meaningful clusters and provides insights into cluster similarities. Through association rule analysis and hierarchal clustering, this study attempts to reveal common patterns of usage and rules that yield effective core herb combinations.

2. Methods

2.1 Literature search and data sources

This study was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (15). Eight electronic databases (PubMed, World Scientific, MEDLINE, Cochrane Library, ProQuest, CNKI, Wanfang Data and Scopus) were searched from inception until December 2021.

Keywords used included "Chinese Herbal Medicine", "Herb", "Obesity", "Overweight", "Randomized Controlled Trial" and their relevant synonyms. For different databases, search terms and relevant filters were adjusted accordingly for data retrieval. Only articles were included. The search strategy can be found in Supplementary Table A in the section titled 'Supplementary Information'. Hand-searching was also performed by examining the reference list of the retrieved studies.

2.2 Eligibility criteria

The inclusion criteria for this study are as follows: (1) RCT; (2) Participant Characteristics: Overweight or obese participants diagnosed according to the standard cutoff points for body weight, BMI, and/or waist circumference; (3) Intervention: Herbal formulas or medication consisting of two or more herbs; (4) Outcome Measures: Included body weight, BMI, and/or waist circumference as outcome measures.

The following articles were excluded: (1) Non-RCT; (2) Population: Did not specify diagnostic criteria for inclusion of obesity or overweight participants; (3) Intervention: Used a single herb ingredient or extract, or did not specify treatment details including ingredients, dosage, and frequency of herbal formula used, or identical herb composition used in the administered formulas; (4) Outcome Measure: Did not include body weight, BMI, and/or waist circumference as outcome measures.

2.3 Selection of studies and data extraction

The EndNote software was used to manage the retrieved studies. The studies were initially imported into EndNote to remove duplicates using the built-in "Find Duplicates" feature. All references with the same title and author and published in the same year and/or the same title and author and published in the same journal, would be eliminated.

A first screening was then performed by two independent screening reviewers (YJCN and KSL) based on the titles and abstracts of all articles. Irrelevant studies, such as non-clinical trials, animal studies and those without obesity-related outcomes, were excluded. Any disagreement was resolved by discussion among the two reviewers. After the first screening, preliminary included articles were screened based on their full texts. They were further assessed according to the inclusion and exclusion criteria, and the eligible studies were included in the meta-analysis. A detailed flow of this process is illustrated in Figure 1 below.

30 RCTs were identified during the data collection process. Additionally, four RCTs were identified through hand search. Subsequently, the 34 RCTs were examined, and relevant information was then extracted from the studies. Relevant information included the first author and year of publication, country of study, demographics of participants, the name of the herbal formula (if applicable) and the individual herbal composition of the formula.

The Plants for a Future (16), Global Plants (17), and Traditional Chinese Medicine Integrative Database (18) databases were used to develop a common naming knowledge base due to different naming practices in diverse studies. Subsequently, the herb nomenclature was standardized before converting the relevant data into Microsoft Excel file formats for association and hierarchical cluster analysis.

Microsoft Excel 2020 and R Studio version 4.1.0 were used for data processing and subsequent analysis in this study

2.4 Statistical analysis

2.4.1 Association analysis

The Apriori algorithm is an association rule mining algorithm that identifies frequent individual item sets in a database. Apriori algorithm-based association rule analysis provides comprehensive and intuitive results to determine association rules highlighting general trends in the database (19).

The Apriori algorithm contains an antecedent and a consequent set, both of which are a set of items. The key parameters involved in the mining of association rules are support, confidence, and lift. As shown in the formula below, X ⟶ Y is an association rule where X (left-hand side [LHS]) and Y (right-hand side [RHS]) represent the set of herb items. σ represents the frequency of an item.

$$support\ (X \rightarrow Y) = \frac{\sigma(X \cup Y)}{N}$$

$$confidence\ (X\ \rightarrow Y) = \frac{\sigma(X \cup Y)}{\sigma(X)}$$

$$lift\ (X \rightarrow Y) = confidence\frac{(X \rightarrow Y)}{\sigma(Y)}$$

$$coverage = support(X)$$

Support refers to the percentage of records that hold the union of X and Y to the total number of records (N). Confidence is the percentage of the number of transactions that contain the union of X and Y to the total number of records that include

X. It also measures the strength of the association rule. Lift is the ratio that the probability of herb Y appears in the presence of herb X to the frequency of herb Y. It also refers to the validity of the rules. Lastly, Coverage in the Apriori algorithm refers to the fraction of all records that satisfy the antecedent of a rule, represented by the support of LHS of the rule. It represents a measure of to how often the rule can be applied (20, 21).

For this study, 12 association rules were investigated. A 'for loop' was generated to find out the number of rules for various support (0.05, 0.75, 0.10) and confidence levels (0.10, 0.20). 0.30, 0.40, 0.50, 0.60, 0.70, 0.80, 0.90), and plotted onto a graph using R Studio. The minimum values of 0.05 and 0.75 for support and confidence, respectively, were selected. Amongst the association rules, the highest value was only 0.0882, and hence 0.05 was selected as the value for support. Additionally, the confidence values for overall association rules were high and all greater than 0.5, hence 0.75 was selected for the value of confidence. Applying these two parameters produced the 12 association rules.

2.4.2 Hierarchical clustering analysis

Hierarchical clustering is an unsupervised machine learning technique capable of identifying patterns from unlabeled data (22). For this study, hierarchical clustering was used to reveal meaningful classifications of herbs used in the 34 RCTs.

The Manhattan distance metric calculates the distance between real-valued vectors and is effective on high-dimensional datasets with discrete or binary attributes (23). The study data set is a high-dimensional one, which justifies the application of the Manhattan distance metric (24).

$$d(i,j) = \left|X_{i1} - X_{j1}\right| + \left|X_{i2} - X_{j2}\right| + \cdots + \left|X_{in} - X_{jn}\right|$$

The value of k = 9 was selected because it produced meaningful cluster sizes ranging from one to three herbs. This closely matches the study objective to interpret herb pairings. Lastly, the average linkage method was selected, as it balances single- and complete linkage clustering by eliminating the effect of outliers in cluster grouping, which could be the closest (chaining effect) or the furthest point (25).

2.5 Risk of bias assessment

To ascertain the validity of eligible randomized trials, two review authors assessed potential risks based on their independent judgement .The risk of bias assessment was carried out using Review Manager 5.4 software (26). Random sequence generation (selection bias), allocation concealment (selection bias), selective reporting (reporting bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias) and other bias were all investigated. Within each of the 34 RCTs, each domain was then assigned a "low," "high," or "unclear" risk of bias.

3. Results

3.1 Study characteristics

For this study, we refer to Horng *et al's* classification of age groups (27). The age groups are as follows: (baby: 0-2 years, Young Adults: 3–39 years, middle-aged adults: 40-59 years and Old Adults: 60–99 years). For classification, the average age group was used. The Baby age group was not represented in any of the 34 RCTs. Middle-aged adults had the highest representation (22 RCTs), followed by young adults (9 RCTs) and old Adults (3 RCTs). The results are depicted in Figure 2

(A). Figure 2 (B) shows the percentage representation of male and female participants. Females had a higher representation (65%) than males (35%). The geographical distribution of the 34 RCTs is shown in Figure 2 (C). 25 studies were from Asia (Japan, China, India, Thailand, Korea, Taiwan), 3 from Oceania (Australia), 3 from North America (USA), 1 from Europe (France), 1 from Central Africa (Cameroon), and 1 from the Middle East (Iran).

3.2 Herbal Composition

This study examined 34 RCTs in total. Supplementary Table B contains a summary of the herbs utilized in the preceding investigations.

3.3 Distribution of herbs used

The 34 RCTs yielded 96 distinct herbs and the top 20 herbs by usage frequency are displayed in Figure 3 above. Ten herbs have a relative frequency greater than 0.10. (*Coptis chinensis, Poria cocos, Rheum palmatum, Glycyrrhiza glabra, Atractylodes lancea, Atractylodes macrocephala, Coix lacryma-jobi, Ephedra sinica, Paeonia lactiflora, Salvia miltiorrhiza*).

3.4 Association analysis

Using the Apriori algorithm, the following diagrams (Figures 4, 5, 6, and Table 1) were generated. They can be found in the following sections.

3.4.1 Association rules of herb pairings

Herb prescriptions in clinical practice are usually a combination of multiple herbs. Aside from establishing synergistic biomolecular interactions, the toxicity of other prescribed herbs could be reduced, boosting the prescription's safety (28). For this study, herb pairings were investigated. The Apriori algorithm derived 12 association rules from the herbal formulations utilized in the 34 RCTs. The association rules were plotted with lift (y-axis) against support in a scatter plot (x-axis). The confidence value determined the color of each regulation. Figure 4 depicts the scatter plot, while Table 1 describes the 12 association rules.

Table 1: Summary of 12 rules obtained from Apriori association analysis.

Rule	LHS => RHS	Support	Confidence	Coverage	Lift	Count
1	*Forsythia suspensa => Glycyrrhiza glabra*	0.05882353	1.00	0.05882353	6.800000	2
2	*Cinnamomi cortex => Paeonia lactiflora*	0.05882353	1.00	0.05882353	8.500000	2
3	*Scutellaria baicalensis => Rheum palmatum*	0.08823529	1.00	0.08823529	5.666666	3
4	*Epimedium grandiflorum => Salvia miltiorrhiza*	0.05882353	1.00	0.05882353	8.500000	2
5	*Epimedium grandiflorum => Coptis chinensis*	0.05882353	1.00	0.05882353	4.250000	2
6	*Epimedium grandiflorum => Poria cocos*	0.05882353	1.00	0.05882353	4.857143	2
7	*Anemarrhena asphodeliodes => Salvia miltiorrhiza*	0.05882353	1.00	0.05882353	8.500000	2
8	*Anemarrhena asphodeliodes => Coptis chinensis*	0.05882353	1.00	0.05882353	4.250000	2
9	*Pueraria montana lobata => Poria cocos*	0.05882353	1.00	0.05882353	4.857143	2
10	*Atractylodes macrocephala => Poria cocos*	0.08823529	0.75	0.11764706	3.642857	3
11	*Salvia miltiorrhiza => Coptis chinensis*	0.08823529	0.75	0.11764706	3.187500	3
12	*Panax ginseng => Poria cocos*	0.08823529	1.00	0.08823529	4.857143	3

Table 1 shows that the lift values of the 12 rules range from 3.19 to 8.50, with all being greater than 1. Hence, the likelihood of selecting the antecedent (LHS) and consequent (RHS) acupoints in the same formula was significantly greater than that of selecting the consequent (RHS) acupoint alone.

Similarly, the dot values for all 12 rules' confidence ranged between 75% and 100%. Hence, the likelihood of selecting the subsequent (RHS) acupoint when the antecedent (LHS) acupoint is reasonably high for each rule. The dot values for the rule support levels range from 5.58 percent to 8.82 percent, suggesting that the frequency of each antecedent (LHS) acupoint occurring in the formula ranges from 5.58 percent to 8.82 percent.

From our analysis, the highest support level was 0.0833. The rules with the highest support level were rules 3, 4, 10, 11 and 12. The highest confidence level was 1.00 and the corresponding rules were rules 1, 2, 3, 5, 6, 7, 8, 9 and 12. The highest lift value was 9.00 and the corresponding rules were rules 5 and 8. Hence, evaluating these three parameters suggests the presence of a core list of herb combinations for the treatment of obesity.

Lastly, the coverage values ranged from 0.0588 to 0.1176. From our analysis, the rules with the highest coverage value of 0.1176 were rules 10 and 11, hence suggesting that the combinations of [*Atractylodes macrocephala* => *Poria cocos*] and [*Salvia miltiorrhiza* => *Coptis chinensis*] were the most often applied rules.

3.4.2 Core herb combinations

Figure 5 shows a group matrix diagram that was generated. Similar rules were gathered and depicted in various sizes of circles, illustrating the general distribution of the association rules. The LHS is represented by the X-axis, whereas the RHS is represented by the Y-axis. The varying sizes of the circles show the levels of support, while the color represents the lift. Hence, the larger the circle the larger the support, the darker the circle the higher the lift (strength).

To visualize the association rules, a network diagram was also created. This is depicted in Figure 6 below. The colored circles represent the rules, while the preceding and following arrows are the LHS and RHS, respectively. The color depth of the circles represents the lift value (strength of the relationship) of the rules, while the size of the circles represents the support.

Salvia miltiorrhiza, Paeonia lactiflora, Rheum palmatum, Glycyrrhiza glabra, Poria cocos, and *Coptis chinensis* were selected as the six core herbs in Figure 5. These herbs were commonly used with other herbs. *Poria cocos* with *Panax ginseng, Atractylodes macrocephala* and *Coptis chinensis* with *Salvia miltiorrhiza* are a few examples of pairings.

Figure 6 depicts a primary network comprised of seven herbs (*Anemarrhena asphodeloides, Salvia miltiorrhiza, Coptis chinensis, Epimedium grandiflorum, Poria cocos, Atractylodes macrocephala, Panax ginseng*). Visual analysis identifies four herbs as the network's core herbs (*Coptis chinensis, Epimedium grandiflorum, Salvia miltiorrhiza, and Poria cocos*). As a result, they are more likely to be used in conjunction with other herbs.

3.5 Hierarchical clustering analysis

Based on the item frequency plot generated in Figure 3, the top 20 herbs of highest usage frequency in obesity treatment were used to create a cluster dendrogram. The cluster numbers were manually annotated adjacent to the colored clusters for ease of visual inspection. This is depicted in Figure 7 below.

According to TCM theory, there are different approaches for classifying herbs. For this study, the herbs were categorized by therapeutic effect and/or meridian entry for cluster analysis. Meridian entry is defined as the orientation of the medicinal action to the meridian/channel via which the therapeutic action occurs. There are twelve meridians in the human body according to the meridian and collateral theory. They are the lung meridian (LU), large intestine meridian (LI), stomach meridian (ST), spleen meridian (SP), heart meridian (HT), small intestine meridian (SI), bladder meridian (BL), kidney meridian (KI), pericardium meridian (PC), triple energizer meridian (TE), gallbladder meridian (GB) and the liver meridian (LV).

Cluster 1: This cluster consists of *Alisma plantago-aquatica (Zexie), Polygonum multiflorum (Heshouwu),* and *Atractylodes lancea (Cangzhu). Alisma plantago-aquatica (Zexie)* and *Atractylodes lancea* have a main function to dry dampness. *Atractylodes lancea* builds on this main function to dry dampness to fortify the spleen. On the other hand, *Polygonum multiflorum* has a main function to tonify, and it serves to tonify the blood to fortify the liver.

Cluster 2: This cluster consists of *Anemarrhena asphodeloides (Zhimu), Salvia miltiorrhiza (Danshen), Zingiber officinale (Shengjiang)* and *Astragalus membranaceus (Huangqi)*. *Astragalus membranaceus* and *Zingiber officinale* target the lung meridian (LU) and spleen meridian (SP). They have a common therapeutic effect to dry dampness, while *Astragalus membranaceus* can induce diuresis to alleviate edema and *Zingiber officinale* can resolve phlegm. Next, *Salvia miltiorrhiza* can activate blood and dispel (blood) stasis. Lastly, *Anemarrhena asphodeloides* is able to clear heat, tonify Yin and moisten dryness.

Cluster 3: Cluster 3 consists of *Panax ginseng (Renshen), and Citri reticulatae pericarpium (Chenpi).* The main function of the herbs in these two clusters is to target the spleen meridian and tonify the spleen. In addition, both herbs are also able to promote the smooth flow of Qi within our body.

Clusters 4, 5 and 9: Cluster 4 consist of *Scutellaria baicalensis (Huangqin) and Rheum palmatum (Dahuang).* Cluster 5 consists of *Phellodendron amurense (Huangbai).* Cluster 9 consists of *Coptis chinensis (Huanglian).* The main therapeutic effect of the herbs in these three clusters is to clear heat. Building on the main therapeutic effect, *Scutellaria baicalensis,* *Coptis chinensis* and *Phellodendron amurense* can clear heat and dry dampness, while *Rheum palmatum* can clear heat to purge fire and cool the blood.

Cluster 6: Cluster 6 consists of Cinnamomum *verum (Guizhi), Glycyrrhiza glabra (Gancao),* and *Paeonia lactiflora (Baishao).* These three herbs are key components of a well-known TCM formula "Gui-Zhi-Tang". This formula is usually paired with other spleen tonifying and/or dampness draining herbs in the treatment of "deficient obesity" (29)

Clusters 7 and 8: Cluster 7 consists of *Ephedra sinica (Mahuang) and Coix lacryma-jobi (Yiyiren).* Cluster 8 consists of *Poria cocos (Fuling),* and *Atractylodes macrocephala (Baizhu)*. The main therapeutic effect of the herbs in these three clusters is to dry dampness. Building on the main therapeutic effect, these herbs have specialized effects to target different aspects of dampness. *Ephedra sinica* can induce diuresis to alleviate edema. *Coix lacryma-jobi* and *Poria cocos* can induce diuresis to drain dampness. *Atractylodes macrocephala* is also known in Traditional Chinese pharmacy as a "key herb to fortify the spleen*".*

Hence, these observed therapeutic effects and Meridian entry of the above top 20 herbs are in line with TCM views of obesity.

3.6 Risk of bias assessment

Figure 8 depicts the risk of bias assessment for the 34 RCTs. A green circle represents a low risk of bias, a yellow circle represents an unclear risk of bias, and a red circle represents a high risk of bias.

Figure 9 depicts the risk of bias graph. It displays a summary of each risk of bias item as a proportion of all included studies. Visual analysis shows the 34 RCTs having an overall low risk of bias.

4. Discussion

Obesity is a major risk factor for a variety of health issues, including cardiovascular disease, type 2 diabetes mellitus, cancer, osteoarthritis, and depression (3, 30). Aside from medical complications, obesity may result in increased economic costs such as direct costs such as medical treatment and indirect costs such as decreased productivity and quality of life (2). RCTs on TCM herbal treatment for obesity have shown its efficacy in the treatment of obesity in recent years. As a result, this study was carried out to investigate novel combinations and prescription regularities in the treatment of obesity.

This study adopts a unique approach to data mining by incorporating systematic review, association analysis, and hierarchical clustering. The use of RCTs rather than individual patient data in this study avoided the potential limitation that individual patient data in TCM is often not uniform in terms of TCM diagnoses and efficacy reporting. To the best of our knowledge, this is the first study to evaluate multiple herbs and likely core patterns of usage in the treatment of obesity in both prescription formulae and pharmaceuticals. Risk of bias analysis also shows that the studies have a low overall risk of bias, indicating that the RCTs analyzed had a stronger research design overall (31).

However, one potential drawback could be that eligible studies were only sourced from English and Chinese language databases. As a result, research from other language databases may be underrepresented, and the conclusions may be overgeneralized. Hence, future research could explore using different language databases to include a broader range of papers for analysis.

In terms of demographics, a skew in representation towards Middle-aged individuals (64.7%) was observed. Females were also more represented (65%) than males (35%). This finding is consistent with research published by the International

Union of Nutritional Sciences, which revealed that obesity rates peak around the middle years of life (around 40 years old). Obesity was also found to affect more women than men in most countries (32).

Additionally, the Baby age group was not represented, which could be related to the fact that obesity in this age range is uncommon. The presence of early-onset obesity could be attributed to rare hereditary illnesses such as Prader-Willi Syndrome rather than environmental or behavioral causes (33).

Geographically, there is a significant skew in distribution, with 26 RCTs coming from the Asia region (76.5%). This may be explained by TCM's origins. TCM is the oldest medical system in Asia, and it was the only medical profession in China until the early nineteenth century. Over time, TCM has also found its way into various Asian cultures, such as Kampo (Japan) and Koryo medicine (Korea) (34, 35). Due to their long-standing heritage, Asian countries are likely to have conducted more research into TCM use. Hence, to minimize the under-representation of TCM use in other countries, future studies could include and investigate TCM herbal use in other non-Asian countries.

Our study has identified *Coptis chinensis, Epimedium grandiflorum, Salvia miltiorrhiza*, and *Poria cocos* as core herbs in obesity treatment. Usage of these core herbs has also been documented in animal and cellular studies, showing the potential of TCM for obesity treatment. A summary of their mechanisms of action (MOA) is summarized in Table 2 below.

TCM herbs, as demonstrated in recent research, include a variety of biomolecular components that may be useful in addressing obesity-related processes. For example, Ning *et al* discovered that Palmatine, found in *Coptis chinensis,* exhibits hypolipidemic and anti-adipogenic activities, which may result in anti-obesity effects. Jung et al. also demonstrated that Tanshinone I derived from *Salvia miltiorrhiza* could inhibit the AMPK signaling pathway and regulate early adipogenic transcription factors, potentially inhibiting early adipogenesis and having anti-obesity effects.

Table 2: Summary of similar studies and the MOA of the tested herb/combination

Herbs	Main bioactive compounds	Dosage	Test subject	Anti-obesity mechanisms	References
Coptis chinensis	Palmatine	3.5, 7 or 10.5 mg/kg	Golden Syrian hamsters	1. Up-regulation of LDLR, CYP7A1 mRNA, and protein expression 2. Down-regulation of ASBT mRNA and protein expression 3. Enhancement of fecal excretion of TC and TBA	Ning 2015 (36)
	Palmatine	Weak inhibition by 39.5% at a concentration of 50 μM	3T3-L1 adipocytes	1. Mediates inhibition of cellular triglyceride accumulation in 3T3-L1 adipocytes 2. Inhibited adipogenesis by downregulating PPAR-γ and C/EBP-α expression.	Choi 2014 (37)
	Berberine	IC_{50} value of 51.4 μM			
	Epiberberine	IC_{50} value of 56.8 μM			
	Coptisine	IC_{50} value of 39.2 μM			
	Magnoflorine	IC_{50} value of 68.8 μM			
	Jatrorrhizine hydrochloride	20 and 100 mg/kg body Jatrorrhizine hydrochloride	Obese mice	1. Reduces the expression levels of genes that inhibit lipogenesis (SREBP-1c and FAS) 2. Upregulates the expression levels of genes involved in promoting lipid metabolism (PPAR-γ and CPT1A)	Yang 2016 (38)
Poria cocos	Water-insoluble polysaccharide (WIP)	1.0 g/kg and 0.5 g/kg of WIP	Obese mice	1. Regulation of gut microbiota through the increase of butyrate-producing bacteria 2. Gut butyrate levels increased, enhanced gut mucosal integrity, activation of the intestinal PPAR- γ pathway	Sun 2019 (39)
	Poria cocos Gold-nanoparticles (PC-AuNP)	25 mg/kg of biosynthesized PC-AuNP	Obese rats	1. High and low dosage PC-AuNPs treatment significantly reduced leptin and resistin levels, and elevated the adiponectin levels in obese rats 2. Decreased levels of inflammatory	Li 2020 (40)

				cytokinesElevated the TBARS level and reduced the antioxidant glutathione level. 3. Effectively increased the urea and creatinine status and decreased the levels of ALT, AST and ALP levels	
Epimedium grandiflorum	Icariin	20 mg/kg icariin	Male C57BL/6N mice	1. Activation of the PI3K/Akt pathway by icariin partially inhibited the NF-κB activation. 2. Icariin could induce Akt phosphorylation by activating the PI3K pathway	Xu 2010 (41)
	Isopentenyl flavonoids, icariin, and icariside	IC_{50} value of 0.1 mg/ML	Rat intestinal cells	1. Suppressed α-amylase. 2. Had hypoglycemic effects	Kim 2002 (42)
Salvia miltiorrhiza	Tanshinone I	2 mg/kg or 5 mg/kg of body weight	Obese mice	1. Inhibits early adipogenesis by improving glucose metabolism and insulin sensitivity. 2. Impairing MCE through cell cycle arrest (Inhibition of ERK, p38, PI3K/Akt signaling and activation of AMPK pathway) 3. Downregulation of C/EBPβ, JMJD2B, and cell cycle genes 4. Regulating expression of early adipogenic transcription factors (GATAs and Kruppel-like factors)	Jung 2020 (43)
	Salvianolic acid B, tanshinone I, tanshinone IIA, cryptotanshinone, and danshensu (salvianolic acid A)	6 and 30 mg/kg/week of body weight	Obese mice	1. Suppresses white adipocyte accumulation but did not impact brown adipose tissue. 2. Reduces body weight through early adipogenesis/lipogenesis reduction	Wu 2022 (44)
	Tanshinone IIA	10 μM concentration	3T3-L1 Preadipocytes	1. Inhibits the mRNA and protein expressions of both C/EBP-α and PPAR-γ during 3T3-L1 adipocyte differentiation. 2. Lowers cellular levels of C/EBP-α and PPAR-γ by transcriptional repression.	Park 2017 (45)

		3. Reduces the phosphorylation of STAT-3/5 during 3T3-L1 adipocyte differentiation

However, in addition to individual MOAs for obesity treatment, the established core network of *Coptis chinensis, Epimedium grandiflorum, Salvia miltiorrhiza,* and *Poria cocos* may have synergistic effects that have yet to be identified and clinically confirmed. Past studies have also shown that the heterogeneity of patient conditions may lead to differing herb interactions amongst patients, making it difficult to determine optimal usage conditions and potential harmful side effects (11). Although the herbal formulae and combinations used in the RCTs were found to provide some weight loss, a different herb combination may cause unknown harmful side effects or have wholly different therapeutic benefits. Hence, more research into the unique core network is advised before clinical use.

As seen in past animal studies, TCM herbs could be a potential source of novel therapeutics for obesity treatment. Biomolecular compounds in herbs have been shown to influence pathways and produce anti-obesity effects. Hence, future studies could also investigate efficient biomolecular extraction methods to produce novel herb-based pharmaceuticals.

5. Conclusion

With obesity on the rise, there is an increasing need to develop safer and more dependable obesity treatment options. TCM's synergistic effect of herbs and a holistic therapeutic approach may have benefits in treating obesity, and it may be worthwhile to explore and use TCM as a treatment option.

Our study has revealed the core herb combination of *Coptis chinensis, Epimedium grandiflorum, Salvia miltiorrhiza,* and *Poria cocos* as potential herbs in the treatment of obesity through association analysis. Hierarchical clustering has also shown patterns of herb classification through therapeutic effect and meridian entry. Nonetheless, the identified core herb combination warrants further research to determine its MOA and long-term clinical efficacy before future clinical use.

Declarations

Ethics approval and consent to participate.

Not Applicable.

Consent for publication

Not Applicable.

Availability of Data and Material

The dataset(s) supporting the conclusions of this article is(are) included within the article (and its additional file(s)).

Competing interests

The authors declare that they have no competing interests.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author Contributions

YJCN is the first author of this study, involved in designing the research plan, literature searching, screening all articles, and drafting the manuscript. Subsequently, YJCN and KSL worked independently to extract the data, assess potential risks of bias for all included studies using the Cochrane tool for assessing risk of bias. YJCN then conducted the data analysis, generated the figures, and created the tables. The manuscript was revised and finalized by YJCN, KSL, RYG, YX and LLDZ. RYG, YX and LLDZ mentored, supervised, and provided critical feedback throughout.

Acknowledgements

Not Applicable.

References

1. Xu L, Zhao W, Wang D, Ma X. Chinese medicine in the battle against obesity and metabolic diseases. Frontiers in physiology. 2018;9:850.
2. Organisation WH. Obesity and overweight 2021 [Available from: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight.
3. Wardle J, Cooke L. The impact of obesity on psychological well-being. Best practice & research clinical endocrinology & metabolism. 2005;19(3):421-40.
4. Bell JA, Carslake D, O'Keeffe LM, Frysz M, Howe LD, Hamer M, et al. Associations of body mass and fat indexes with cardiometabolic traits. Journal of the American College of Cardiology. 2018;72(24):3142-54.
5. Apovian CM, Aronne LJ, Bessesen DH, McDonnell ME, Murad MH, Pagotto U, et al. Pharmacological management of obesity: an Endocrine Society clinical practice guideline. The Journal of Clinical Endocrinology & Metabolism. 2015;100(2):342-62.
6. Mark AL. Dietary therapy for obesity is a failure and pharmacotherapy is the future: a point of view. Clinical and Experimental Pharmacology and Physiology. 2006;33(9):857-62.
7. Li M-F, Cheung BM. Rise and fall of anti-obesity drugs. World journal of diabetes. 2011;2(2):19.
8. Fan T-P, Yeh J-C, Leung KW, Yue PY, Wong RN. Angiogenesis: from plants to blood vessels. Trends in Pharmacological Sciences. 2006;27(6):297-309.
9. Williamson EM. Synergy and other interactions in phytomedicines. Phytomedicine. 2001;8(5):401-9.
10. Benzie IF, Wachtel-Galor S. Herbal medicine: biomolecular and clinical aspects. 2011.
11. Li C, Zhang H, Li X. The mechanism of traditional Chinese medicine for the treatment of obesity. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy. 2020;13:3371.
12. Jiang M, Lu C, Zhang C, Yang J, Tan Y, Lu A, et al. Syndrome differentiation in modern research of traditional Chinese medicine. Journal of ethnopharmacology. 2012;140(3):634-42.
13. Poon J, Poon SK. Data analytics for traditional Chinese medicine research: Springer; 2014.
14. Lu P-H, Keng J-L, Kuo K-L, Wang Y-F, Tai Y-C, Kuo C-Y. An Apriori algorithm-based association rule analysis to identify herb combinations for treating uremic pruritus using Chinese herbal bath therapy. Evidence-Based Complementary and Alternative Medicine. 2020;2020.
15. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Bmj. 2021;372.
16. PFAF. Plants For A Future. 1989.
17. JSTOR. Global Plants.

18. Xue R, Fang Z, Zhang M, Yi Z, Wen C, Shi T. TCMID: traditional Chinese medicine integrative database for herb molecular mechanism analysis. Nucleic acids research. 2012;41(D1):D1089-D95.
19. Hsieh P-C, Cheng C-F, Wu C-W, Tzeng I, Kuo C-Y, Hsu P-S, et al. Combination of acupoints in treating patients with chronic obstructive pulmonary disease: an apriori algorithm-based association rule analysis. Evidence-Based Complementary and Alternative Medicine. 2020;2020.
20. Guo Y, Wang M, Li X. Application of an improved Apriori algorithm in a mobile e-commerce recommendation system. Industrial Management & Data Systems. 2017;117(2):287-303.
21. CRAN. Calculate Coverage for Rules 2022 [Available from: https://rdrr.io/cran/arules/man/coverage.html.
22. Guo F, Tang X, Zhang W, Wei J, Tang S, Wu H, et al. Exploration of the mechanism of traditional Chinese medicine by AI approach using unsupervised machine learning for cellular functional similarity of compounds in heterogeneous networks, XiaoErFuPi granules as an example. Pharmacological Research. 2020;160:105077.
23. Kumar V, Chhabra JK, Kumar D. Performance evaluation of distance metrics in the clustering algorithms. INFOCOMP Journal of Computer Science. 2014;13(1):38-52.
24. Bühlmann P, Van De Geer S. Statistics for high-dimensional data: methods, theory and applications: Springer Science & Business Media; 2011.
25. Yim O, Ramdeen KT. Hierarchical cluster analysis: comparison of three linkage measures and application to psychological data. The quantitative methods for psychology. 2015;11(1):8-21.
26. Collaboration TC. Review Manager Version 5.4.1. 2020.
27. Horng W-B, Lee C-P, Chen C-W. Classification of age groups based on facial features. Journal of Applied Science and Engineering. 2001;4(3):183-92.
28. Xia P, Gao K, Xie J, Sun W, Shi M, Li W, et al. Data mining-based analysis of Chinese medicinal herb formulae in chronic kidney disease treatment. Evidence-Based Complementary and Alternative Medicine. 2020;2020.
29. Li J. 2016.
30. Visscher TL, Seidell JC. The public health impact of obesity. Annual review of public health. 2001;22(1):355-75.
31. Viswanathan M, Patnode CD, Berkman ND, Bass EB, Chang S, Hartling L, et al. Assessing the risk of bias in systematic reviews of health care interventions. Methods guide for effectiveness and comparative effectiveness reviews [Internet]. 2017.
32. Sciences IUoN. The Global Challenge of Obesity and the International Obesity Task Force. 2015.
33. Han JC, Lawlor DA, Kimm SY. Childhood obesity. The lancet. 2010;375(9727):1737-48.
34. Griffiths SM, Chung VC, Tang JL. Integrating traditional Chinese medicine: experiences from China. Australasian Medical Journal (Online). 2010;3(7):385.
35. Yu F, Takahashi T, Moriya J, Kawaura K, Yamakawa J, Kusaka K, et al. Traditional Chinese medicine and Kampo: a review from the distant past for the future. Journal of International Medical Research. 2006;34(3):231-9.
36. Ning N, He K, Wang Y, Zou Z, Wu H, Li X, et al. Hypolipidemic effect and mechanism of palmatine from Coptis chinensis in hamsters fed high-fat diet. Phytotherapy Research. 2015;29(5):668-73.
37. Choi JS, Kim J-H, Ali MY, Min B-S, Kim G-D, Jung HA. Coptis chinensis alkaloids exert anti-adipogenic activity on 3T3-L1 adipocytes by downregulating C/EBP-α and PPAR-γ. Fitoterapia. 2014;98:199-208.
38. Yang W, She L, Yu K, Yan S, Zhang X, Tian X, et al. Jatrorrhizine hydrochloride attenuates hyperlipidemia in a high-fat diet-induced obesity mouse model. Molecular Medicine Reports. 2016;14(4):3277-84.
39. Shan-Shan S, Kai W, Ke M, Li B, Hong-Wei L. An insoluble polysaccharide from the sclerotium of Poria cocos improves hyperglycemia, hyperlipidemia and hepatic steatosis in ob/ob mice via modulation of gut microbiota. Chinese journal of natural medicines. 2019;17(1):3-14.

40. Li W, Wan H, Yan S, Yan Z, Chen Y, Guo P, et al. Gold nanoparticles synthesized with Poria cocos modulates the anti-obesity parameters in high-fat diet and streptozotocin induced obese diabetes rat model. Arabian Journal of Chemistry. 2020;13(7):5966-77.
41. Xu C-Q, Liu B-J, Wu J-F, Xu Y-C, Duan X-H, Cao Y-X, et al. Icariin attenuates LPS-induced acute inflammatory responses: involvement of PI3K/Akt and NF-κB signaling pathway. European journal of pharmacology. 2010;642(1-3):146-53.
42. Kim S-H, Kwon C-S, Lee J-S, Son K-H, Lim J-K, Kim J-S. Inhibition of carbohydrate-digesting enzymes and amelioration of glucose tolerance by Korean medicinal herbs. Preventive Nutrition and Food Science. 2002;7(1):62-6.
43. Jung DY, Kim J-H, Jung MH. Anti-obesity effects of tanshinone I from salvia miltiorrhiza bunge in mice fed a high-fat diet through inhibition of early adipogenesis. Nutrients. 2020;12(5):1242.
44. Wu Y-L, Lin H, Li H-F, Don M-J, King P-C, Chen H-H. Salvia miltiorrhiza Extract and Individual Synthesized Component Derivatives Induce Activating-Transcription-Factor-3-Mediated Anti-Obesity Effects and Attenuate Obesity-Induced Metabolic Disorder by Suppressing C/EBPα in High-Fat-Induced Obese Mice. Cells. 2022;11(6):1022.
45. Park Y-K, Obiang-Obounou BW, Lee J, Lee T-Y, Bae M-A, Hwang K-S, et al. Anti-adipogenic effects on 3T3-L1 cells and zebrafish by tanshinone IIA. International Journal of Molecular Sciences. 2017;18(10):2065.
46. Andersen T, Fogh J. Weight loss and delayed gastric emptying following a South American herbal preparation in overweight patients. Journal of Human Nutrition and Dietetics. 2001;14(3):243-50.
47. Arentz S, Smith CA, Abbott J, Fahey P, Cheema BS, Bensoussan A. Combined lifestyle and herbal medicine in overweight women with polycystic ovary syndrome (PCOS): A randomized controlled trial. Phytotherapy research. 2017;31(9):1330-40.
48. Azushima K, Tamura K, Haku S, Wakui H, Kanaoka T, Ohsawa M, et al. Effects of the oriental herbal medicine Bofu-tsusho-san in obesity hypertension: a multicenter, randomized, parallel-group controlled trial (ATH-D-14-01021. R2). Atherosclerosis. 2015;240(1):297-304.
49. Boozer C, Nasser J, Heymsfield S, Wang V, Chen G, Solomon J. An herbal supplement containing Ma Huang-Guarana for weight loss: a randomized, double-blind trial. International Journal of Obesity. 2001;25(3):316-24.
50. Cheon C, Song Y-K, Ko S-G. Efficacy and safety of Euiiyin-tang in Korean women with obesity: A randomized, double-blind, placebo-controlled, multicenter trial. Complementary Therapies in Medicine. 2020;51:102423.
51. Cho Y-G, Jung J-H, Kang J-H, Kwon JS, Yu SP, Baik TG. Effect of a herbal extract powder (YY-312) from Imperata cylindrica Beauvois, Citrus unshiu Markovich, and Evodia officinalis Dode on body fat mass in overweight adults: a 12-week, randomized, double-blind, placebo-controlled, parallel-group clinical trial. BMC complementary and alternative medicine. 2017;17(1):1-10.
52. Chung W, Ryu J, Chung S, Kim S. Effect of Qingxue Dan on obesity and metabolic biomarker: a double-blind randomized-controlled pilot study. Journal of Traditional Chinese Medicine. 2016;36(3):291-8.
53. Ding G, Yu G, Liang S, Fan C, Tong Z, Liu L, et al. Jiawei lingguizhugan tang for obesity induced by psychoactive drugs. Chinese Journal of Clinical Rehabilitation. 2006;10(43):46-8.
54. Dixit K, Kamath DV, Alluri KV, Davis BA. Efficacy of a novel herbal formulation for weight loss demonstrated in a 16-week randomized, double-blind, placebo-controlled clinical trial with healthy overweight adults. Diabetes, Obesity and Metabolism. 2018;20(11):2633-41.
55. Garrison R, Chambliss WG. Effect of a proprietary Magnolia and Phellodendron extract on weight management: a pilot, double-blind, placebo-controlled clinical trial. Alternative therapies in health and medicine. 2006;12(1):50-5.
56. Greenway F, Liu Z, Martin C, Kai-Yuan W, Nofziger J, Rood J, et al. Safety and efficacy of NT, an herbal supplement, in treating human obesity. International journal of obesity. 2006;30(12):1737-41.
57. He C, Wang W, Li B, Xu D, Chen W, Ying J, et al. Clinical research of Yiqi Sanju Formula in treating central obese men at high risk of metabolic syndrome. Zhong xi yi jie he xue bao= Journal of Chinese integrative medicine.

2007;5(3):263-7.

58. Huang Y-H, Chen S-T, Liu F-H, Hsieh S-H, Lin C-H, Liou M-J, et al. The efficacy and safety of concentrated herbal extract granules, YH1, as an add-on medication in poorly controlled type 2 diabetes: a randomized, double-blind, placebo-controlled pilot trial. PloS one. 2019;14(8):e0221199.
59. Ignjatovic V, Ogru E, Heffernan M, Libinaki R, Lim Y, Ng F. Studies on the use of "slimax", a Chinese herbal mixture, in the treatment of human obesity. Pharmaceutical biology. 2000;38(1):30-5.
60. Kim H-J, Gallagher D, Song M-Y. Comparison of body composition methods during weight loss in obese women using herbal formula. The American journal of Chinese medicine. 2005;33(06):851-8.
61. Kuamsub S, Singthong P, Chanthasri W, Chobngam N, Sangkaew W, Hemdecho S, et al. Improved lipid profile associated with daily consumption of tri-Sura-Phon in healthy overweight volunteers: an open-label, randomized controlled trial. Evidence-Based Complementary and Alternative Medicine. 2017;2017.
62. Lenon GB, Li KX, Chang Y-H, Yang AW, Da Costa C, Li CG, et al. Efficacy and safety of a Chinese herbal medicine formula (RCM-104) in the management of simple obesity: a randomized, placebo-controlled clinical trial. Evidence-Based Complementary and Alternative Medicine. 2012;2012.
63. LI S-w, Jun-hua Z, WANG Y-h. A Clinical Study on Treatment of Simple Obesity (Stomach-heat and Damp-stagnation Syndrome) by Jianfei Tiaozhi Capsule. Journal of New Chinese Medicine. 2007:02.
64. Liu L. Effects of Qiwei Baizhu Powder ( ) on Glucose and Lipid Metabolism and Intestinal Flora in Obesity Patients of Spleen Deficiency and Dampness Disturbing Type. Journal of Traditional Chinese Medicine 2020.
65. Lu C, Zhao X, Li Y, Li Y, Yuan C, Xu F, et al. Serum metabolomics study of Traditional Chinese medicine formula intervention to polycystic ovary syndrome. Journal of pharmaceutical and biomedical analysis. 2016;120:127-33.
66. Mirfeizi M, Mehdizadeh Tourzani Z, Mirfeizi SZ, Asghari Jafarabadi M, Rezvani HR, Afzali M. Controlling type 2 diabetes mellitus with herbal medicines: A triple-blind randomized clinical trial of efficacy and safety: 2 : . Journal of diabetes. 2016;8(5):647-56.
67. Nagata Y, Goto H, Hikiami H, Nogami T, Fujimoto M, Shibahara N, et al. Effect of keishibukuryogan on endothelial function in patients with at least one component of the diagnostic criteria for metabolic syndrome: a controlled clinical trial with crossover design. Evidence-Based Complementary and Alternative Medicine. 2012;2012.
68. Oben JE, Ngondi JL, Momo CN, Agbor GA, Sobgui CSM. The use of a Cissus quadrangularis/Irvingia gabonensis combination in the management of weight loss: a double-blind placebo-controlled study. Lipids in Health and Disease. 2008;7(1):1-7.
69. Pan L, Deliang L, Lei M, Zhang L, Zhou L. Preparation-containing node of Lotus Rhizome, green tea and Panax notoginseng for obese adults. Chinese Journal of Tissue Engineering Research. 2005;9(15):231-3.
70. Sengupta K, Mishra AT, Rao MK, Sarma KV, Krishnaraju AV, Trimurtulu G. Efficacy of an herbal formulation LI10903F containing Dolichos biflorus and Piper betle extracts on weight management. Lipids in health and disease. 2012;11(1):1-9.
71. Shi J, Hu Y, Wang Q. Fufang cangzhu tang for treatment of senile obesity or overweight complicated with impaired glucose tolerance–a clinical observation in 32 cases. Journal of Traditional Chinese Medicine= Chung I Tsa Chih Ying Wen pan. 2006;26(1):33-5.
72. Shi Y-L, Liu W-J, Zhang X-F, Su W-J, Chen N-N, Lu S-H, et al. Effect of Chinese herbal medicine Jinlida granule in treatment of patients with impaired glucose tolerance. Chinese Medical Journal. 2016;129(19):2281.
73. Stern JS, Peerson J, Mishra AT, Mathukumalli VSR, Konda PR. Efficacy and tolerability of an herbal formulation for weight management. Journal of medicinal food. 2013;16(6):529-37.
74. Tong X, Wu S, Lian F, Zhao M, Zhou S, Chen X, et al. The safety and effectiveness of TM81, a Chinese herbal medicine, in the treatment of type 2 diabetes: a randomized double-blind placebo-controlled trial. Diabetes, Obesity and Metabolism. 2013;15(5):448-54.

75. Tong X, Xu J, Lian F, Yu X, Zhao Y, Xu L, et al. Structural alteration of gut microbiota during the amelioration of human type 2 diabetes with hyperlipidemia by metformin and a traditional Chinese herbal formula: a multicenter, randomized, open label clinical trial. MBio. 2018;9(3):e02392-17.
76. Wang C, Cheng Z. Pinggan Yishen Ditan decoction for hypertensive obesity: a clinical observation of 31 cases. Journal of Traditional Chinese Medicine. 1993(02).
77. Xing F, Tan Y, Yan G-J, Zhang J-J, Shi Z-H, Tan S-Z, et al. Effects of Chinese herbal cataplasm Xiaozhang Tie on cirrhotic ascites. Journal of ethnopharmacology. 2012;139(2):343-9.
78. Yoo J-H, Lee E-J, Kwak C-K, Sohn E-H, Koh B-H, Song I-B, et al. Clinical trial of herbal formula on weight loss in obese Korean children. The American journal of Chinese medicine. 2005;33(05):713-22.
79. Zhou Q, Chang B, Chen X-Y, Zhou S-P, Zhen Z, Zhang L-L, et al. Chinese herbal medicine for obesity: a randomized, double-blinded, multicenter, prospective trial. The American journal of Chinese medicine. 2014;42(06):1345-56.

Figures

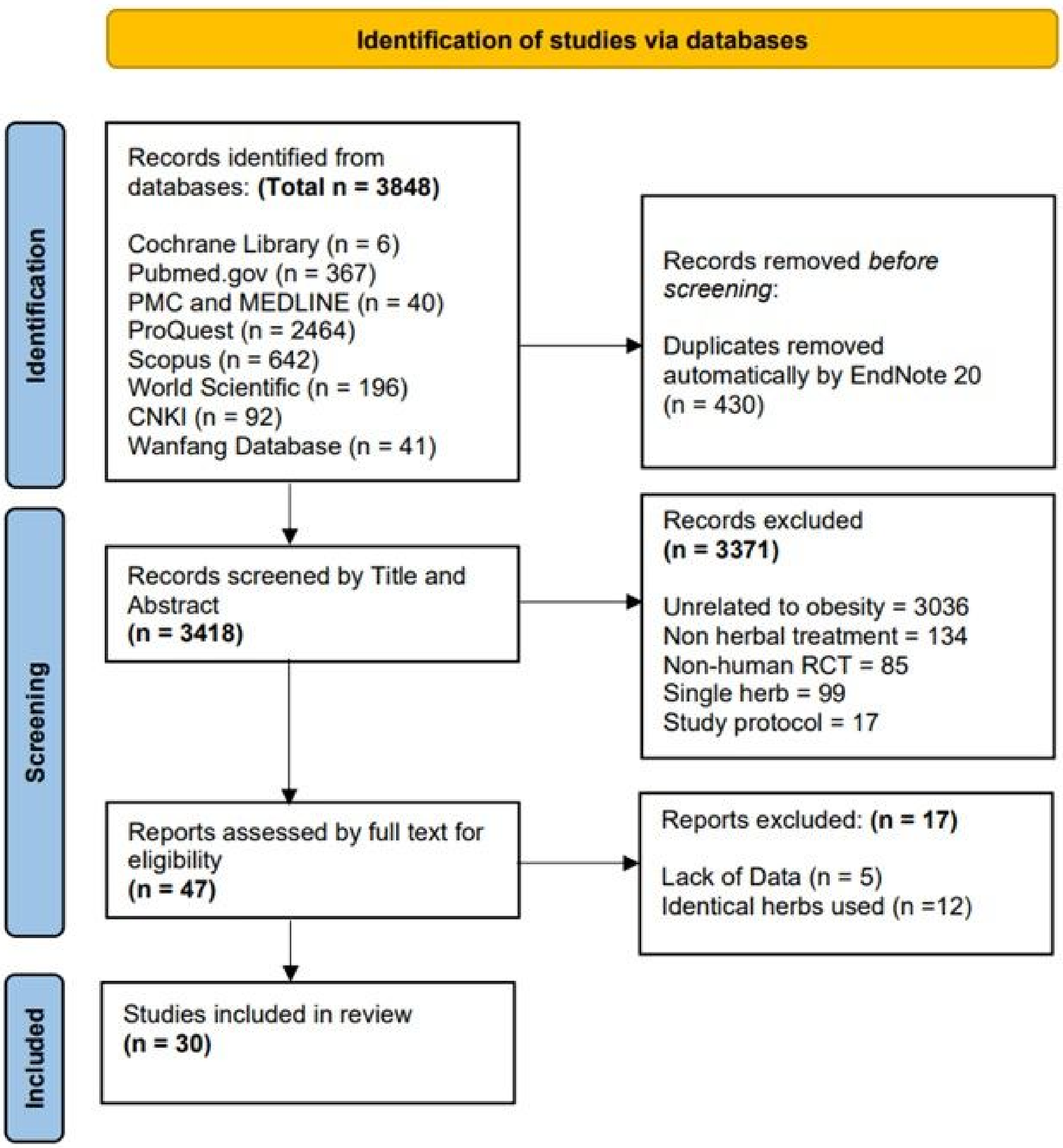

Figure 1

Flowchart of trial selection according to the PRISMA-P terminologies.

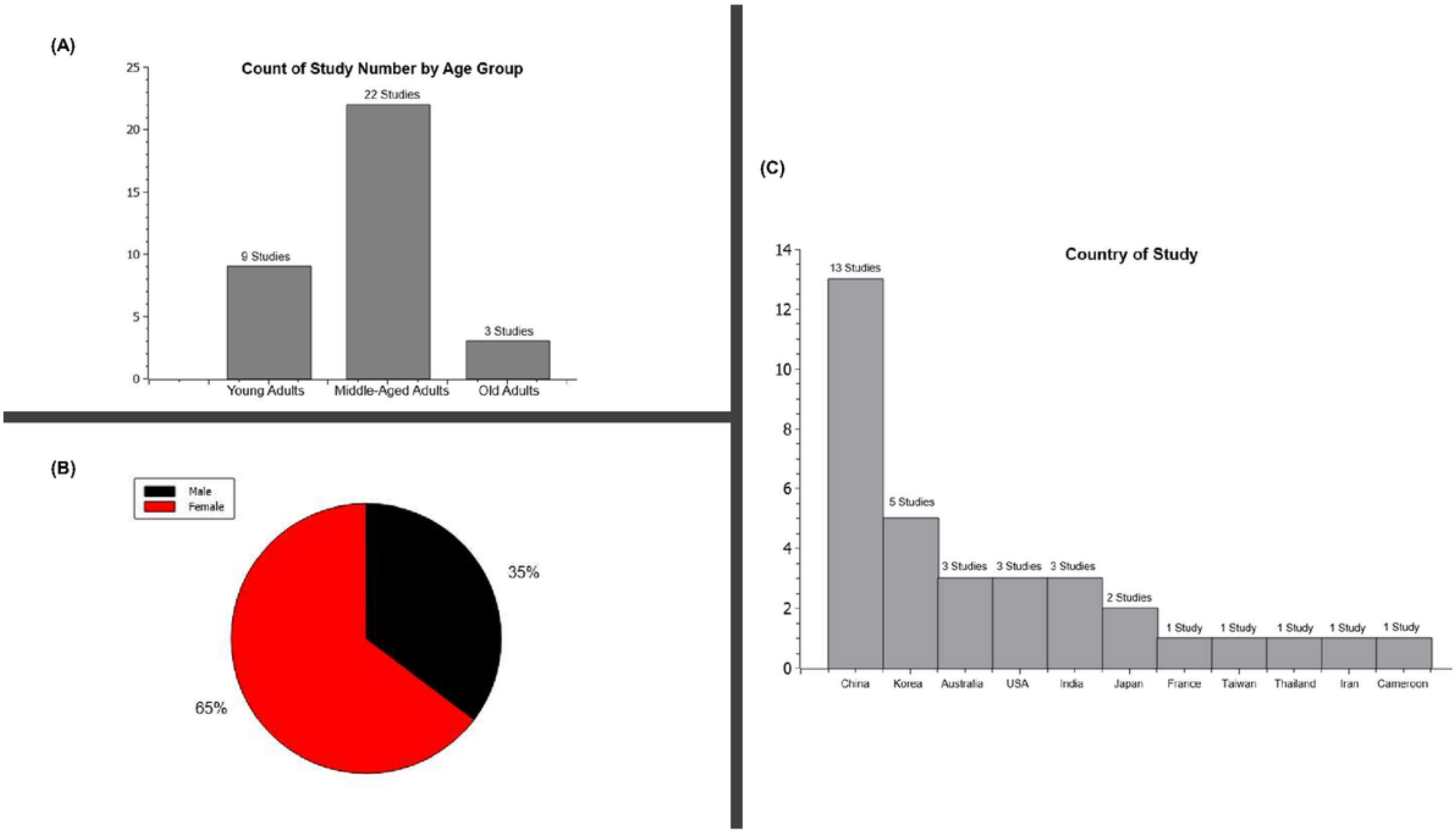

Figure 2

(A) Bar chart showing the count of study numbers by age group.

(B) Pie chart showing gender representation across the 34 RCTs.

(C) Histogram showing the distribution of the 34 RCT countries of origin.

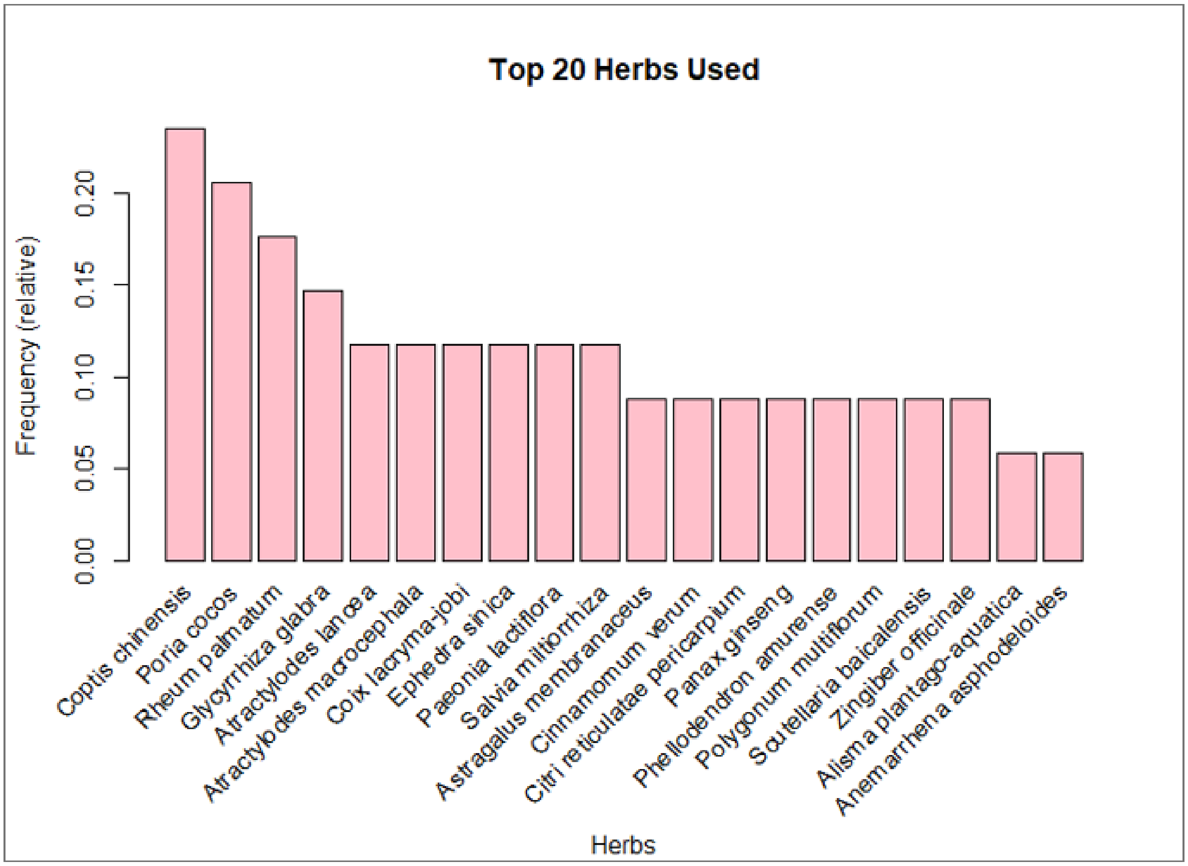

Figure 3

Item frequency plot of the top 20 herbs used in the treatment of obesity.

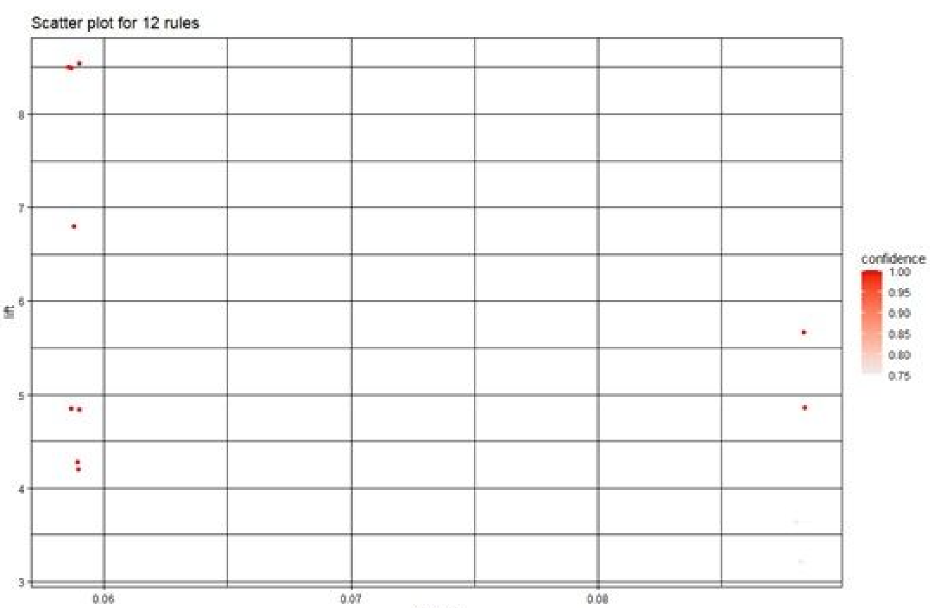

Figure 4

Scatter plot of 12 rules derived from Apriori association analysis.

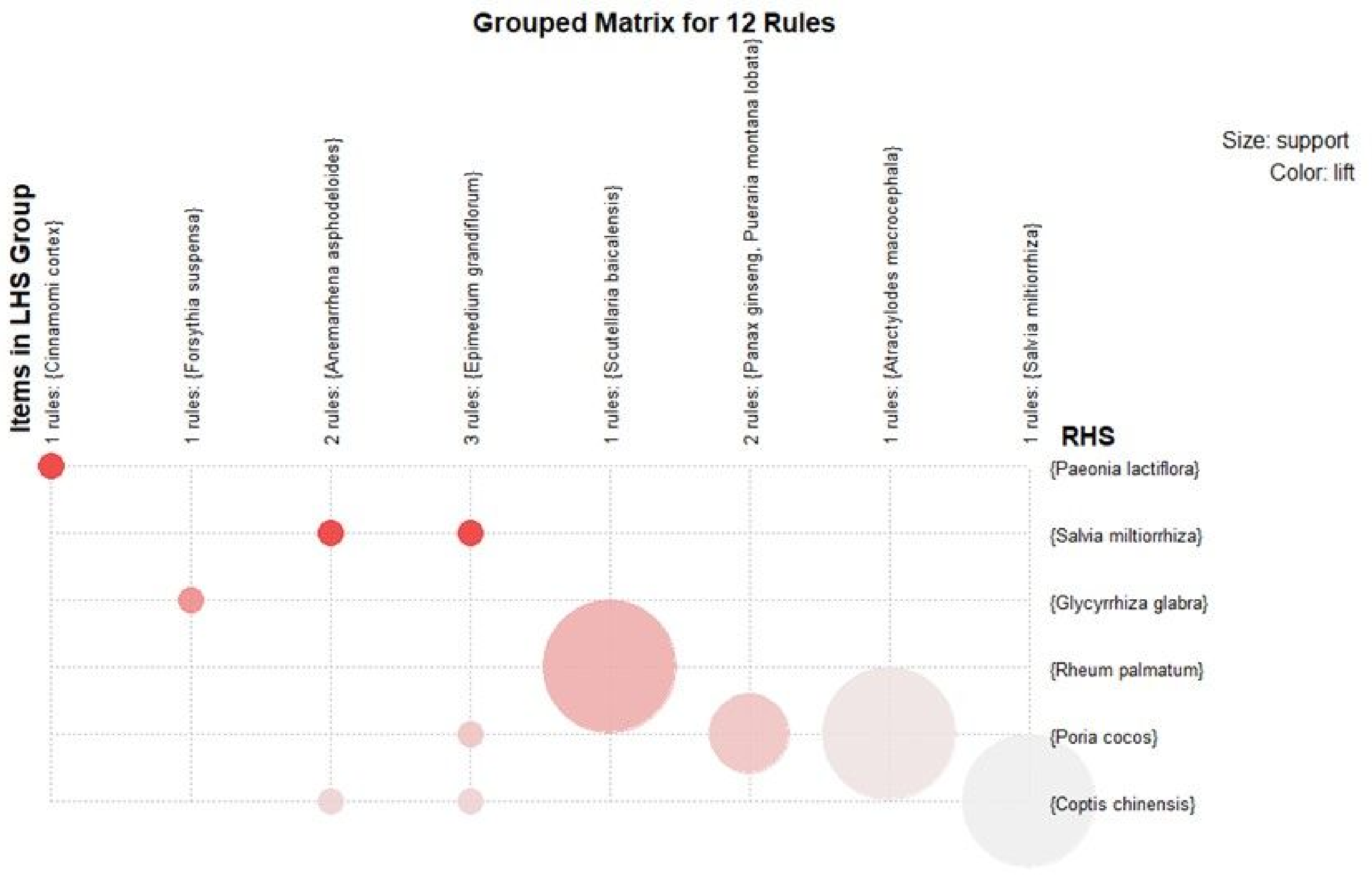

Figure 5

Group matrix for 12 rules obtained from Apriori association analysis.

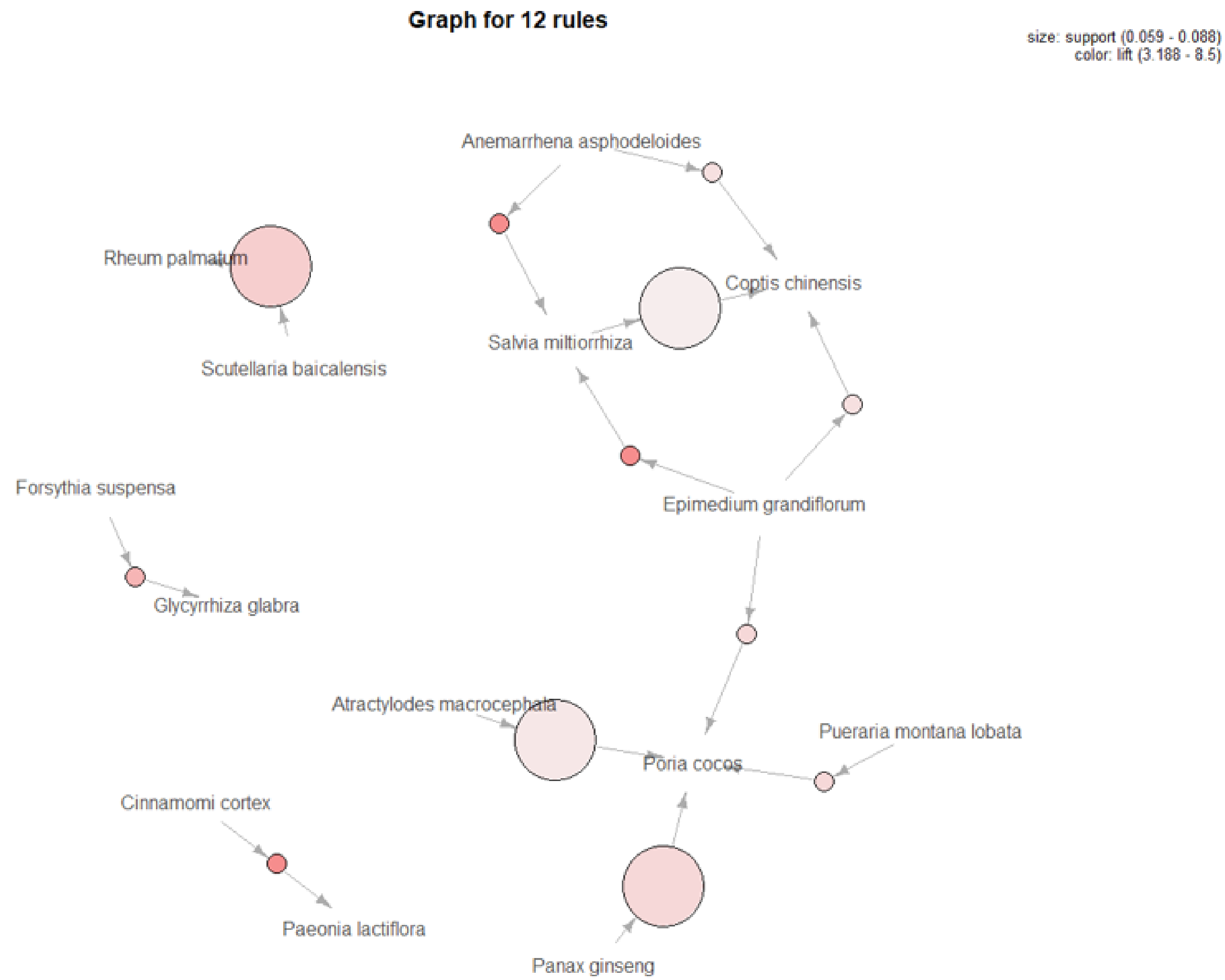

Figure 6

Network diagram for 12 rules obtained from Apriori association analysis.

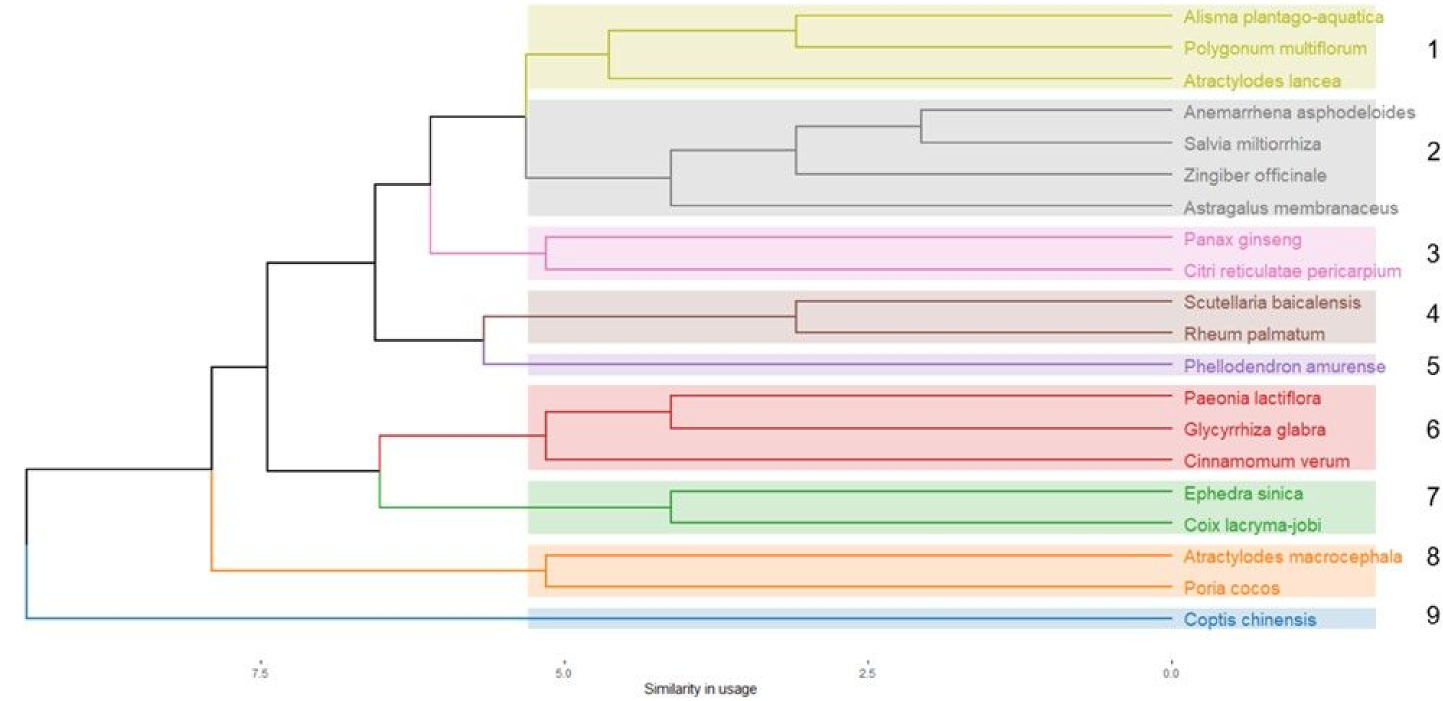

Figure 7

Cluster dendrogram of the top 20 herbs used in the treatment of obesity.

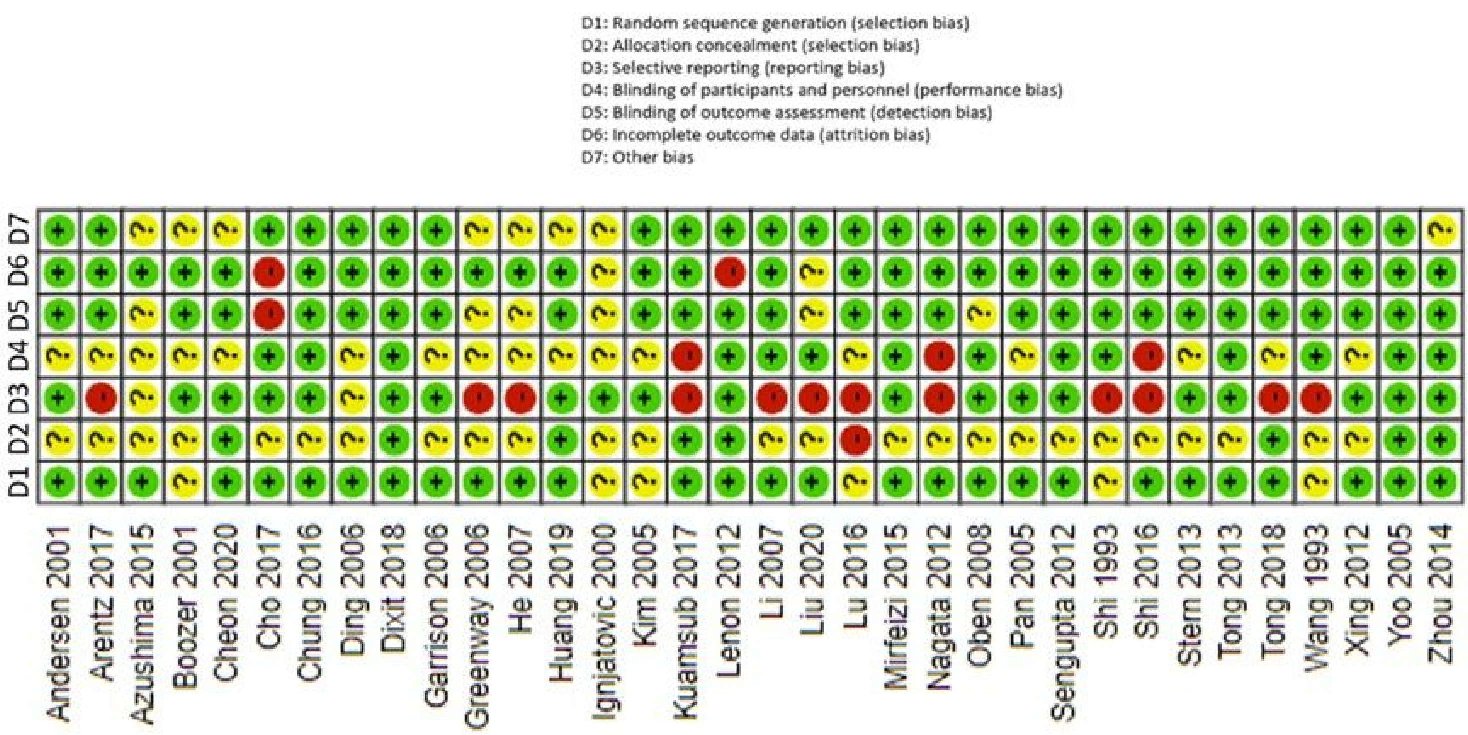

Figure 8

Risk of bias assessment for the 34 RCTs collected.

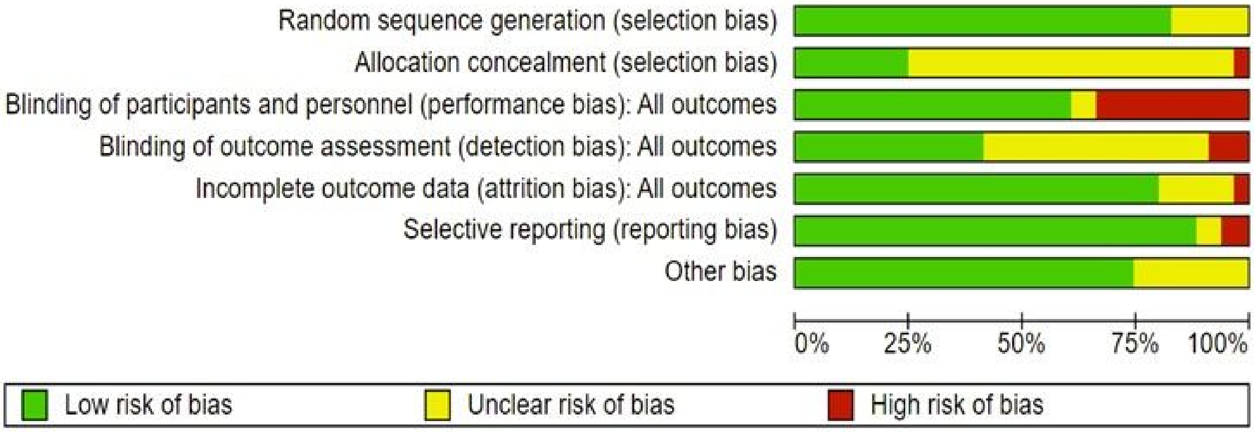

Figure 9

Risk of bias graph of the 34 RCTs used in this study.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryInformation.docx