



Complementary and Alternative Therapies for Weight Loss: A Narrative Review

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Abstract

Despite various strategies, overweight and obesity problems are still increasingly prevalent worldwide with serious health outcomes. Consequently, the continuous demand for more effective, safe and acceptable therapies for reducing body weight is also escalating—including complementary and alternative therapies (CATs). The aim of this review is to provide a summary of the most commonly- and recently-used CATs, with evaluation of their safety and efficacy for weight loss. Electronic scientific databases such as Scopus, PubMed and EBSCO Host were explored for articles that reported CATs for overweight and obesity treatment from 2015 to December 2019. Only systematic reviews, meta-analysis and randomized controlled trials (RCTs) published in English were included. Studies whereby CATs were not utilized for reducing body weight were excluded. Eight systematic reviews and meta-analyses and 11 additional RCTs with 765 participants (50.2% overweight and 49.8% obese) related to hypnotherapy, acupuncture and dietary supplements met the inclusion criteria. Their results suggested that spirulina, chitosan, probiotic, EPA + DHA, vitamin D, fiber, and herbal extract supplementation may all provide small reductions in body weight (ranging from 1-10 kg). Interestingly, hypnotherapy and acupuncture reported significantly greater reduction in body weight compared with placebo ($p < 0.001$ and $p < 0.0001$, respectively). Nonetheless, the evidence is still relatively limited and not encouraging to provide a definitive conclusion due to the methodological shortcomings and the presence of adverse events in chitosan and fiber supplementation. Hence, studies of this nature need to be further replicated and improved to corroborate the efficacy and safety of the CATs to combat weight issues.

Keywords

complementary therapies, dietary supplements, obesity, overweight, weight loss

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Introduction

Overweight and obesity are chronic diseases that have become global epidemics. According to the World Health Organization (WHO),¹ the occurrence of overweight and obesity is increasing at an alarming rate with 39% of worldwide adults aged 18 years and older were overweight and 13% were obese in 2016. This global calamity did not only affect high-income countries, but were also high in developing countries especially among urban dwellers.² The increased prevalence of overweight and obesity have led to an increase in potentially life-threatening diseases such as cardiovascular diseases, diabetes, musculoskeletal disorders and some cancers, which can enhance the burden of diseases and the mortality rate.¹

The WHO defines “overweight” and “obesity” as a body mass index (BMI) greater than or equal to 25 and 30, respectively.

These problems are assumed to be the result of imbalanced energy between caloric intake and daily energy expended.³ Therefore, obesity treatments have focused on lifestyle changes such as calorie-restricted diet and increasing physical activity. However,

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these conventional approaches are not completely effective, with high drop-out rates during interventions and almost 70% of individuals failed to maintain their weight loss after the interventions.^{4,5} According to Greaves et al.,⁶ they mostly resume their previous habits such as overeating, unhealthy dietary intakes and physical inactivity. In addition, busy daily schedules, sedentary working lifestyle and the plentiful availability of unhealthy foods made lifestyle modifications unachievable.⁷ These outcomes have consequently led to further demands in exploring complementary and alternative therapies (CATs) to combat their weight problems and the proliferation of dietary supplements in the market.

Complementary and alternative therapies or medicines refers to “a group of varied medical and healthcare systems, practices and products that are not considered to be a part of any conventional medicine in the healthcare system.”⁸ The National Center for Complementary and Alternative Medicine (NCCAM) classified CATs into 5 categories which are biologically based, energy, manipulative and body-based, mind-body therapies and whole medical systems. Commonly used CATs for reducing weight includes biological based therapies such as dietary supplements as well as manipulative and body-based (acupuncture, acupressure, etc.) and mind-body therapies (hypnotherapy). The escalating acceptance of CATs has been associated with concerns of risks for obesity-related and social pressure which demand slender, lean and more muscular figure in today’s world.⁹ Despite the abundance of non-pharmacological therapies such as diets, cognitive behavioral interventions, exercise and CATs, the claim of their effectiveness is still arguable. Due to a lack of evidence and methodological problems in existing literature, the safety of these therapies especially the herbal or dietary supplements also remains uncertain. Hence, exploring additional curative options to combat overweight and obesity apart from existing pharmacological treatments becomes paramount. The purpose of the present review is to provide a summary of the most commonly- and recently-used CATs, with emphasis on their safety and efficacy for reducing body weight.

Methods

The present review was conducted in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines¹⁰ to identify all randomized controlled trials (RCTs), systematic reviews and meta-analyses of RCTs of any type of CATs for overweight and obesity treatment. Three electronic databases such as Scopus, PubMed, and EBSCO Host have been used to search related articles published in English from 2015 to December 2019. The combination of keywords and terms used for literature search were as follows: “complementary therapy” OR “alternative therapy” OR “complementary medicine” OR “alternative medicine” OR “acupuncture” OR “acupressure” OR “hypnotherapy” OR “hypnosis” OR “homeopathy” OR “herbal supplement” OR “dietary supplement” OR “herbal medicine” AND “weight loss” OR “weight reduction” AND “obesity” OR “overweight” OR “weight problem.”

Included articles must be RCTs using approaches on CATs alone or as an adjunct with a conventional method for reducing body weight.

For systematic review or meta-analysis, only the most recent versions were included. The eligible articles must also be available in full-text, published in peer-reviewed journals and presented reports involving respondents with a BMI of ≥ 25 and were aged 18 and older. Among the CATs types, herbal and dietary supplements, acupuncture and hypnotherapy were included. Apart from that, studies that did not utilize or identify the effectiveness of CATs for overweight and obesity were excluded. Pre-clinical studies, narrative reviews, scoping reviews, conference proceeding, book, book series, letters, editorial commentaries and case studies were also excluded. Additionally, manual hand-searches were conducted through the reference list of retrieved articles to increase the inclusiveness of search strategy.

Data Extraction

Irrelevant and duplicate articles were removed after the screening of all titles and abstracts of retrieved studies following the inclusion criteria. Next, the main contents of all the remaining articles were examined thoroughly based on the: 1) research objective—the effectiveness of CATs to reduce weight; 2) study design—systematic or meta-analysis of RCTs studies, RCTs; 3) characteristics of study—sample size, duration of study, regimen of daily dose; 4) outcome measures—weight loss, BMI; and 5) overall findings. Subsequently, articles that are not based on empirical data, protocol and pilot studies were eliminated.

Results

The keyword-based searching through relevant databases and cross-referencing generated 3,492 results after excluding the duplicates. One hundred and two articles were retrieved for full-text review after screening the titles and abstracts to eliminate unrelated articles. Finally, a total of 19 articles; 8 systematic reviews and meta-analyses based on the results of RCTs and 11 additional RCTs which met all the inclusion criteria were assessed throughout the review. Figure 1 depicts the flow of the literature search process.

The examined studies were published between 2015 and 2019. Eleven RCTs studies explored the efficacy of different CATs approach including hypnotherapy, acupuncture as well as various dietary supplements to reduce weight among overweight and obese participants. Participants were mostly recruited from the general population via newspaper and social media advertisements,¹¹⁻¹⁷ while 4 studies obtained their participants through referrals from hospital,¹⁸ outpatient clinic^{19,20} and clinical centers.²¹ The sample sizes ranged from 18 to 146, with a total of 765 participants (50.2% overweight and 49.8% obese). The duration of the interventions varied between 3 weeks and 12 months. In most studies, the participants were asked to follow a low-calorie diet and exercise regularly.^{11,13,15,18,19} Five studies entailed a non-dieting approach in which participants required to maintain their dietary habits^{14,16,17,20,21} and one study instructed participants to perform exercise moderately without dietary restrictions.¹²

Eight review articles were identified from 2015 to 2019 which described the effectiveness of CATs related to acupoint embedment and dietary supplements on weight loss in obese and overweight participants. Most of them showed that there

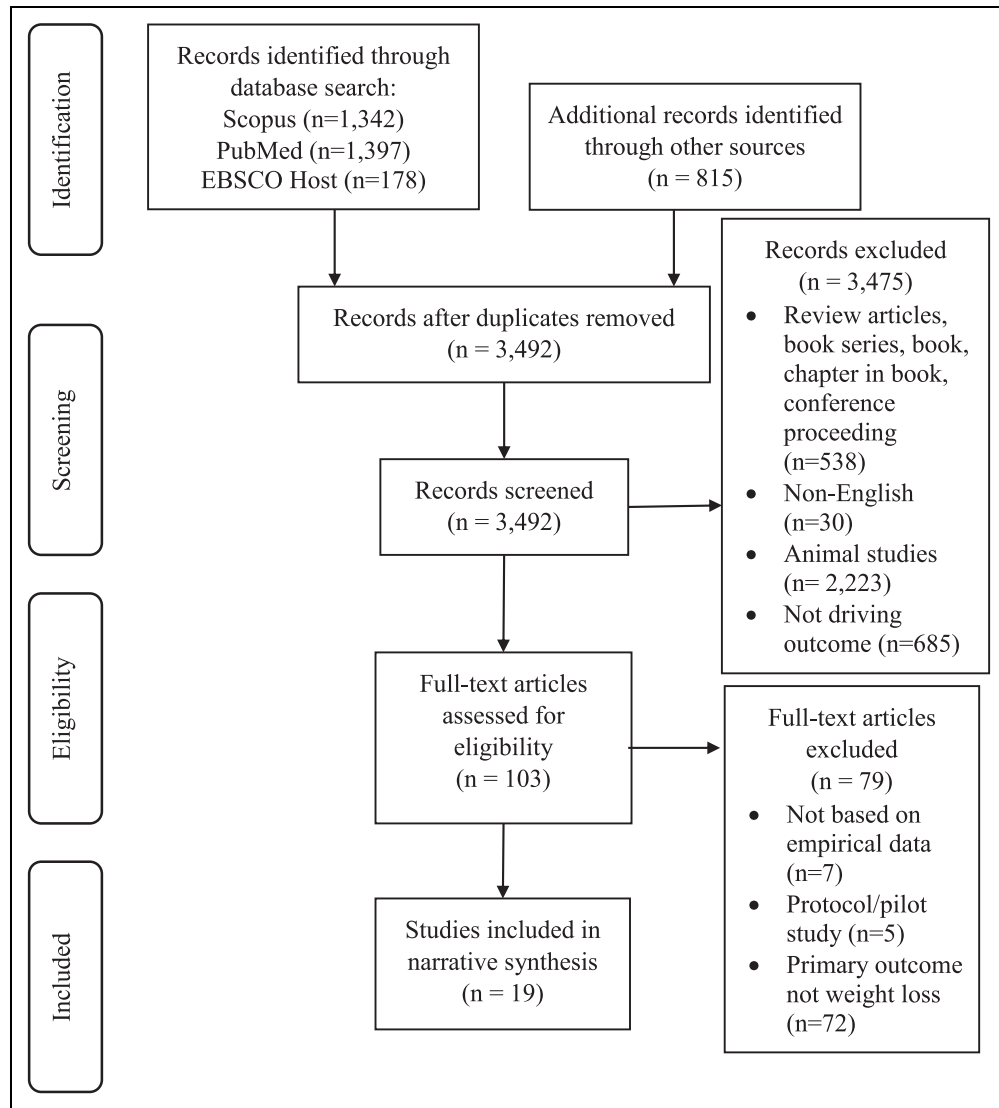


Figure 1. Flow diagram of selection studies (adapted from Moher et al¹⁰).

was a significant relationship between acupuncture or dietary supplementation and improvement of body weight loss among participants.²²⁻²⁶ Meanwhile, 3 studies reported that there were no intergroup or intragroup differences on body weight after dietary supplementations.²⁷⁻²⁹ The authors also highlighted other associated risk factors of obesity and adverse events reported after CATs approach or supplementation. The identified findings of all the studies are summarized in Tables 1 and 2.

Dietary Supplements

The most commonly identified method for combating weight loss is the use of dietary supplements. Despite the abundance of the dietary supplements in the market and favorable effects in reducing weight, the effectiveness of these products remains to be ascertained.

Spirulina. Spirulina belongs to the family *Oscillatoriceae*, spiral blue-green microalgae and filamentous cyanobacterium which has been used as food or food supplement for various health concerns.³⁰ A systematic review²⁵ and 2 RCTs^{12,17} found that spirulina supplementation significantly reduced body weight among obese and overweight participants. Additionally, a study by Hernández-Lepe et al¹² identified that *Spirulina maxima* supplementation improves the effect of exercise among obese participants. However, there is considerable doubt on which types of spirulina were most effective as they assessed different types of Spirulina such as *maxima* and *platensis*. Overall, there were no adverse events reported after supplementation, thus encouraging further studies.

Chitosan. Chitosan is an aminated polysaccharide, product of chitin deacetylation which is derived from crustaceans.³¹ It has been widely used as dietary supplements due to its properties such as antioxidant activity,³² anti-obesogenic³³ and

Table 1. Systematic Reviews and Meta-Analyses of Complementary and Alternative Therapies for Weight Loss.

Author, year	Type of CATs	CATs duration/regimen of daily dose	Main findings	Comments
Cho et al, 2019	Acupuncture (acupoint embedment)	<ul style="list-style-type: none"> • 5 to 12 weeks • Arm 1; Acupoint embedment once every 1 or 2 weeks • Arm 2; Sham acupuncture (control group) 	<ul style="list-style-type: none"> • Arm 1 showed significant reduction in BW (2.97 kg; $p < 0.0001$) compared to Arm 2. 	<ul style="list-style-type: none"> • Adverse events including bruise, soreness and cramp, patchy skin induration and erythema were reported.
Sheng et al, 2019	Acupuncture [acupoint catgut embedding (ACE)]	<ul style="list-style-type: none"> • 4 to 12 weeks • Arm 1; ACE once or 2 times per week and once per 10 days. • Arm 2; Either electroacupuncture or manual acupuncture as control. 	<ul style="list-style-type: none"> • Those in Arm 1 showed significant decrease in BW (5.20 kg; $p = 0.01$) compare to control group. 	<ul style="list-style-type: none"> • Overall quality of included studies was poor (small sample size, clinical heterogeneity).
Moradi et al, 2019	Dietary supplements, Spirulina	<ul style="list-style-type: none"> • 6 to 12 weeks • Arm 1; Spirulina supplementation (range 1 to 4.5 g/day). • Arm 2; Placebo 	<ul style="list-style-type: none"> • Intergroup difference between intervention and control group in BW (1.56 kg; $p = 0.069$). 	<ul style="list-style-type: none"> • Varied dose of supplementation. • Short study duration
Mofrad et al, 2019	Dietary supplements, psyllium	<ul style="list-style-type: none"> • 2 to 48 weeks • Arm 1; Psyllium supplementation (range 1.7 to 15 g/day). • Arm 2; Placebo 	<ul style="list-style-type: none"> • No significant BW reduction benefits was seen after psyllium supplementation ($p = 0.268$). 	<ul style="list-style-type: none"> • Varied dosage and forms of supplementation. • Adverse events such as flatulence, bloating, indigestion, nausea and vomiting were reported.
Moraru et al, 2018	Dietary supplements, chitosan	<ul style="list-style-type: none"> • 4 to 52 weeks • Arm 1; Chitosan supplementation (range 0.34 to 3.4 g/day). • Arm 2; Placebo 	<ul style="list-style-type: none"> • Supplementation of chitosan slightly reduce BW (1.01 kg; $p = 0.003$). 	<ul style="list-style-type: none"> • Adverse events such as constipation and diarrhea were reported.
Borgeraas et al, 2017	Dietary supplements, probiotic	<ul style="list-style-type: none"> • 3 to 12 weeks • Arm 1; Probiotic supplementation (range 1.0×10^9 to 4.8×10^{11} CFU/day). • Arm 2; Placebo 	<ul style="list-style-type: none"> • Those receiving probiotic supplementation showed larger weight reduction (0.60 kg; $p = 0.02$). 	<ul style="list-style-type: none"> • Small number of sample sizes in most included studies.
Li et al, 2016	Dietary supplements, calcium	<ul style="list-style-type: none"> • 12 weeks to 6 years • Calcium supplementation range from 1000 to 2100 mg/day. • Arm 2; Placebo 	<ul style="list-style-type: none"> • No significant differences in BW ($p = 0.02$) between Arm 1 and Arm 2. 	<ul style="list-style-type: none"> • Varied age range, BMI and study duration.
Onakpoya, Sullivan & Heneghan, 2015	Dietary supplements, cactus pear	<ul style="list-style-type: none"> • 6 weeks to 2 years • Arm 1; Cactus pear dosage varied from 400 mg to 15 g/day. • Arm 2; Placebo 	<ul style="list-style-type: none"> • No significant difference in weight reduction between Arm 1 and Arm 2. 	<ul style="list-style-type: none"> • Varied in study design and methodology. • Small effect sizes.

Abbreviation: BW = body weight.

antibacterial and hypoglycemic effects for chronic diseases prevention.³¹ A meta-analysis by Moraru et al²⁶ identified 14 RCTs evaluating the effectiveness of chitosan supplementation for reducing body weight. The results suggested a slight reduction with the mean weight difference of 1.01 kg after chitosan oral supplementation up to 52 weeks compared with the placebo.²⁶ The most common adverse events reported from analyzed studies were constipation and diarrhea.

Probiotic. Probiotic refers to live organisms that occur naturally in the gut. Previous studies reported that oral supplementation of the probiotic gut may help individuals to lose weight by manipulating the gut ecosystem^{34,35,36} however there is no clear evidence on its role. A meta-analysis review of 15 studies, accounting for 957 participants (63% of women) was conducted on the use of probiotics for weight loss.²² The participants in the experimental group were reported to have a

Table 2. Randomized Controlled Trials of Complementary and Alternative Therapies for Weight Loss.

Author, year	Type of CATs	Study design	Sample (s)	CATs duration/regimen of daily dose	Main findings	Comment(s)
He et al, 2015	Acupuncture + massage therapy	Randomized, short-term clinical trial	96 obese and overweight women Arm 1; n = 56 Arm 2; n = 40	<ul style="list-style-type: none"> 3 weeks Arm 1; combined manual acupuncture + massage therapy (MAMT). Arm 2; Manual acupuncture therapy 	<ul style="list-style-type: none"> There are no significant changes between Arm 1 and Arm 2 in BW (p = 0.629) and the BMI (p = 0.525). 	<ul style="list-style-type: none"> Short-term treatment.
Dostal et al, 2016	Dietary supplement (Green tea extract)	Double-blind, randomized, placebo-controlled trial	121 postmenopausal overweight and obese women IG; n = 61 CG; n = 60	<ul style="list-style-type: none"> 12 weeks IG; Oral decaffeinated green tea extract catechin complex 4 capsules/day (~1300 mg/day catechin equivalent to ~843 mg/day EGCG) CG; Placebo 	<ul style="list-style-type: none"> No differences in changes in BMI and %BF between IG and CG (p > 0.05) 	<ul style="list-style-type: none"> GTE used in this study was decaffeinated, hence lack of significance in BMI and %BF. Caffeine content or synergism between catechins and caffeine might play a large role on their effects on body weight and adiposity.
Cho et al, 2017	Dietary supplement (YY-312)	Double-blind, randomized, placebo-controlled, parallel-group clinical trial	60 overweight adults aged between 19 to 60 years IG; n = 30 CG; n = 30	<ul style="list-style-type: none"> 12 weeks IG; 3 tablets of YY-312 (each tablet 1800 mg active herbal extract + 600 mg cyclodextrin) + weight loss diet -500 kcal CG; Placebo + weight loss diet -500 kcal 	<ul style="list-style-type: none"> Significantly greater reductions in IG compared to CG for BW (IG = 2.7 kg vs. CG = 1.0 kg), FM (IG = 1.6 kg vs. CG = 0.1 kg), WC (IG = 2.2 cm vs. CG = 0.8 cm) 	<ul style="list-style-type: none"> Small sample size Short duration of study
Zeinlian et al, 2017	Dietary supplement (Spirulina)	Randomized, double blind, placebo-controlled	64 obese individuals age between 20 to 50 years IG; n = 32 CG; n = 32	<ul style="list-style-type: none"> 12 weeks IG; 500 mg Spirulina, twice daily CG; Placebo 	<ul style="list-style-type: none"> IG significantly decreased BW, BMI compared to CG (p < 0.05). 	<ul style="list-style-type: none"> Small sample size Short duration of study
Bo Bo et al, 2018	Hypnotherapy	Prospective, randomized controlled, open-label, monocentric trial	120 severe obesity clients IG; n = 60 CG; n = 60	<ul style="list-style-type: none"> 15 weeks IG; Hypnosis + Lifestyle modifications CG (control); Lifestyle modifications 	<ul style="list-style-type: none"> BW loss was 6.5 kg in the IG compared to 5.6 kg in the CG and the difference between group was not significant. 	<ul style="list-style-type: none"> High drop-out rate (28%). Participants stayed too long (8 months) without receiving any reinforcement session.

(continued)

Table 2. (continued)

Author, year	Type of CATs	Study design	Sample (s)	CATs duration/regimen of daily dose	Main findings	Comment(s)
Cefalo et al, 2018	Dietary supplement (Vitamin D)	Double-blind, randomized, placebo-controlled trial	18 overweight and obese adults IG; n = 9 CG; n = 9	<ul style="list-style-type: none"> 12 weeks IG; Oral cholecalciferol 25,000 IU solution / week + hypocaloric diet counseling CG; Placebo + hypocaloric diet counseling 	<ul style="list-style-type: none"> BW in both groups decreased significantly (-7.5% in the vitamin D group and -10% in the placebo group; p < 0.05 for both) with no between-group differences 	<ul style="list-style-type: none"> Cholecalciferol supplementation combined with weight loss improves insulin sensitivity in healthy subjects with obesity. Small sample size, estimated effect size was higher
Larsen, Bibby & Hansen, 2018	Dietary supplements (Whey protein)	Randomized, single-blinded, controlled trial	41 overweight and obese participants Arm 1; n = 21 Arm 2; n = 20	<ul style="list-style-type: none"> 4 weeks Arm 1; VLCD + walking exercise training Arm 2; VCD + walking exercise training + whey protein concentrate supplement 	<ul style="list-style-type: none"> No intergroup difference for body weight between Arm 1 and Arm 2 (p = 0.47). 	<ul style="list-style-type: none"> Adverse events such as constipation and influenza were reported.
Khosravi et al, 2018	Dietary supplement (Vitamin D)	Double-blind, randomized, placebo-controlled trial	53 overweight and obese women IG; n = 26 CG; n = 27	<ul style="list-style-type: none"> 6 weeks IG; Vitamin D supplements 50,000 IU/week CG; Placebo 	<ul style="list-style-type: none"> IG showed significant reduction in BW (1.6 kg), BMI (0.6 kg/m² and WC (2.3 cm) compared to CG (p < 0.001) 	<ul style="list-style-type: none"> Short duration of study Level of vitamin D increased in control group due to increased sunlight exposure during summer season
Sedláček et al, 2018	Dietary supplements (EPA + DHA)	Parallel-group, 3-arm, blinded randomized trial	28 overweight women Arm 1; n = 11 Arm 2; n = 10 Arm 3; n = 8	<ul style="list-style-type: none"> 12 weeks Arm 1; 1500 mg/ day EPA + DHA concentrate (containing 600 mg EPA + DHA) + Lifestyle modification Arm 2; Placebo + Lifestyle modification Arm 3 (control); Placebo 	<ul style="list-style-type: none"> Arm 1 and Arm 2 significantly decreased BW, BMI and WC compared to Arm 3 (control) (p < 0.05). 	<ul style="list-style-type: none"> Small sample size Short duration of study

Abbreviations: IG = intervention group; CG = control group; BW = body weight; BMI = body mass index; VLCD = very low-calorie diet.

significantly larger weight loss than those receiving placebo (mean weight difference: -0.60 kg, 95% CI: $-1.19, -0.01$; $P = 0.02$). However, the efficacy could not be determined due to the high heterogeneity among the selected studies and most of the studies were funded by probiotic companies which may have led to reporting bias.

Calcium. Calcium is an essential mineral component of the body which is important for maintaining bone mineral homeostasis. It is promoted as a remedy to reduce lipogenesis thus suppressed body fat and weight gain^{36,37} although no definitive correlation has been reported.^{29,38} Li et al²⁷ had conducted a meta-analysis review of 33 RCTs studies, which reported that there are no differences in weight changes that were shown between intervention and control group (Mean Difference: -0.01 kg, 95% CI: $-0.02, 0.00$; $P = 0.12$) after supplementation of calcium with various sources (831-1861mg/d). However, they found that increasing calcium intake through supplementation may reduce body weight in normal BMI participants. Obviously, this has brought a considerable concern about the role of calcium on body weight among overweight or obese participants.

Psyllium. Used for varieties of reasons due to it being financially practical, availability in different flavors and various forms such as capsules, powdered drink mixes or wafers, psyllium is another popular alternative to combat weight loss. It is a non-fermented fiber supplement which consists of mixtures of polysaccharides, capable of affecting body weight by increasing satiety,³⁹ delaying gastric emptying,⁴⁰ regulating gut hormones, and improving glucose and insulin responses.⁴¹ However, data from a meta-analysis of 22 RCTs studies, which included 1,458 participants (intervention group = 730; control group = 728), indicated that there is no significant effect of psyllium supplementation on body weight in comparison with control groups. They concluded that the effectiveness of psyllium on body weight is not established due to several methodological limitations such as duration of the study, sample size, and dosage of supplementation.

Opuntia ficus-indica (Cactus Pear). *Opuntia ficus-indica* (OFI) is a domesticated cactus plant mostly found in Mexico, Latin America, South Africa and the Mediterranean which has been widely used as a traditional treatment due to its antioxidant and anti-carcinogenic properties.^{42,43} OFI is rich in dietary fiber and has been suggested to promote weight loss due to fat binding and reduction in fat absorption.⁴⁴ One meta-analysis with 5 RCTs was identified, which evaluates the effectiveness of OFI for reducing body weight.²⁹ Nonetheless, no significant changes in body weight in either the intervention group or the control group (mean difference: -0.83 kg, 95%CI: $-2.49-0.83$) were detected. They also reported several adverse events after OFI supplementation such as gastric intolerance, cold and flu.

N-3 Fatty acids (EPA + DHA). The N-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) have been suggested to improve body weight among overweight and obese individuals due to their anti-inflammatory and hypolipidemic effects.^{45,46} The researchers¹⁵ identified a parallel, 3-arm RCT that tested the effects of 1.5 g EPA + DHA supplementation daily in women with BMI in the range of 25-29.9 kg/m². The result suggests that EPA + DHA supplementation after 3-month-combined lifestyle modification decreased body weight in the intervention group compared with the control group. The evidence for EPA + DHA is encouraging and further independent studies are needed to substantiate its effectiveness. No adverse events or unintended effects in participants were reported.

Whey protein. Whey protein is a fast-digested protein derived from milk which modulates several hormones that influence body weight and body composition.⁴⁷ Whey protein supplementation has been reported to boost protein balance and muscle protein synthesis.⁴⁸ A single-blinded, 4-week RCT accounting for 41 participants (intervention = 21; control = 20) was conducted on the use of whey protein for weight loss. The result suggests that whey protein is not effective for reducing body weight as there were no significant group differences were observed during pre- and post-measurements.

Vitamin D. Vitamin D is an essential element required for calcium absorption and homeostasis. This is because Vitamin D may decrease the growth and maturation of fat cell,⁴⁹ it has been hypothesized that vitamin D would have an effect on body weight and body composition. Two double-blind RCTs which included participants with a BMI of 35 kg/m² and above were identified.^{14,19} Both of the studies reported significantly greater effects for body weight reduction compared with placebo and one reported significant reductions of fat mass after supplementation.¹⁹ These are thus inspiring evidence for the usage of vitamin D for losing weight but it does require further studies. Both studies did not report any adverse effects.

Fiber. Usually consumed to keep the digestive system healthy and prevent constipation, dietary fiber has been suggested in order to give beneficial effects for reducing weight as it increased satiety.⁵⁰ In a 3-arm, parallel, blind RCT, 118 overweight participants were randomized to one of 3 group to test the effects of mixture of fiber supplementation such as konjac glucomannan, sodium alginate and xanthan gum [PolyGlycopleX (PGX)].¹⁶ The subjects in the intervention group, who were given 2 different doses of PGX (4.5 g softgels PGX and 5 g PGX granules) were reported to have lost 1 kg more than those receiving placebo ($P < 0.01$). However, the evidence was concluded to be unconvincing due to small magnitude of changes and short duration of study (12 weeks). Adverse events related to gastrointestinal system such as diarrhea, bloating and flatulence were reported.

Herbal extract powder (YY-312). YY-312 is obtained from extracts of *Imperata cylindrica* Beauvois, *Citrus unshiu* Markovich and *Evodia officinalis* Dode; and according to Korean traditional medicine, it promotes body fat reduction.⁵¹ The result of a 12-week double-blind RCT study which includes 60 overweight participants to evaluate the effectiveness of YY-312 in weight reduction, indicated that YY-312 is relatively more effective and well-tolerated than the placebo ($P = 0.049$). It proves that YY-312 positively acts as anti-obesity agents, however there is no proof for a length of time longer than 12 weeks of supplementation.

Green tea extract (GTE). Green tea extract has been widely used for a variety of ailments including treating metabolic syndromes such as obesity, diabetes and cardiovascular risk factors.⁵² Epigallocatechin-3-gallate (EGCG) is the most bioactive component in the green tea which promotes anti-obesity effects⁵³ (Kao et al, 2000). According to a double-blind RCT study on weight loss trial which involved 121 overweight and obese postmenopausal women, a consumption of 843 mg decaffeinated GTE over a minimum period of 12 weeks, was unlikely to be effective.²¹ The study reported no adverse events.

Acupuncture

Acupuncture is a traditional Chinese medical practice which involves the insertion of small needles into certain points on the skin, called acupoints.⁵⁴ Due to several possible mechanisms such as increasing metabolism, regulation of obesity-related neuropeptides and reducing triglycerides and cholesterol levels,⁵⁵ it has become a popular alternative treatment for reducing body weight. According to a systematic review and meta-analysis including 5 RCTs, acupoint embedment was found to be more effective for body weight reduction with 2.97 kg greater weight loss ($P < 0.0001$) than the sham control group.¹¹ An open, RCT, which tested the effectiveness of acupuncture report results among 56 obese women in favor of treatment with acupuncture compared with control ($P < 0.001$).²⁰ Overall, the evidence of acupuncture to reduce body weight is not convincing due to several methodological weakness such as study variation in intervention duration and the selection of acupoints in retrieved studies.

Hypnotherapy

Hypnotherapy is yet another promising therapy used for weight control. According to one RCT study on 120 participants with BMI ranges from 35 to 50 kg/m², the addition of hypnotherapy to conventional lifestyle modification leads to a relatively small reduction in body weight.¹⁸ However, those practicing self-hypnosis more than once per day showing greater weight loss and improved dietary intake after follow-up for 12 months ($P < 0.001$). At present, it is still unclear whether hypnotherapy is effective for reducing body weight because of limited research available.

Discussion

Overall, this review compiles the important scientific evidence on studies involving CATs that have been used for reducing weight among overweight and obese individuals. Clearly, the most common types of CATs tested were biological-based practices such as vitamins, herbal extract, foods and dietary supplements, followed by acupuncture and hypnotherapy. The findings encouragingly suggested that CATs can offer beneficial effects for weight reduction although there was no adequate evidence to support their long-term safety and effectiveness. Hypnotherapy, spirulina, chitosan, probiotic, EPA + DHA, vitamin D, fiber and herbal extract supplementation showed promising results compared with mere placebos. However, several methodological limitations such as small sample size, inconsistent long-term compliance tracking and a lack of safety evaluation seemed to have hampered more concrete outcomes. Besides, there was an increased risk of adverse effects with supplementation of chitosan and fiber. These findings were in concert with the results of Pittler and Ernst⁵⁶ who reviewed 14 different available complementary therapies and dietary supplements claimed to have significant effects on weight loss, the findings were nevertheless not adequate enough to suggest confirmed effectiveness.

Despite their unproven therapeutic potential through various investigations, dietary supplements have been commonly used to treat various diseases globally. They often vary in content and concentration of constituents and come from different manufacturers, resulting in differences in bioavailability and humans' pharmacological activity.^{57,58} The dietary supplements are expected to adhere to the regulations of the Dietary Supplement and Health Education Act (DSHEA) and comply with the Final Rule for Current Good Manufacturing Practices for Dietary Supplements which required manufacturers to determine the safety before marketed as well as to ensure that claims made regarding the product are accurate and not misleading.⁵⁹ However, the term "dietary supplements" itself cause confusion among consumers as their actual function not intended for use as drugs (treat, cure or prevent any disease) but to support or promote healthy body function.⁶⁰ The wrong expression of "dietary supplement" wording should be noted as overconsumption associated with increased risk of health problems (kidney and liver damages, iron toxicity, etc.). As claimed by Aliyu and colleagues,⁶¹ dietary supplements should not be taken to treat a health condition, especially among those who consume a normal, well-balanced diet unless recommended by a health care provider. It is due to they are not intended to supplement any diet, replace food or serve as a medicine to cure chronic diseases. Thus, consumers must be cautious about taking dietary supplements, consult with health-care providers before taking them and be cognizant of its hepatotoxic potential.

Some of the dietary supplements are widely marketed over-the-counter even though their long-term efficacy and safety for treating overweight and obesity is conflictual. According to Kazemipoor et al,⁶² the increasing demand of CATs especially

dietary supplements might be due to the which have weight-lowering effects such as suppressing appetite and increasing satiety. For instance, spirulina has been suggested to inhibit inflammatory responses, reducing cholesterol absorption thus affecting appetite.^{25,63} Besides, previous investigators have shown that some dietary supplements such as herbal extract could provide anti-obesity effects which may enhance lipolysis and decrease lipid absorption.^{64,65} However, little is known about the exact action mechanism of these ingredients in reducing body weight.

In fact, losing weight may help individual to live longer as those with a high BMI commonly associated with higher mortality driven by comorbidities such as cardiovascular diseases, certain types of cancer and arthritis.⁶⁶ As claimed by Emekcioglu,⁶⁷ improvements in several lifestyle measures (nutrition, physical activity, health care, etc.) have resulted in a significant increase in life expectancy for adults of all ages especially among people from Blue Zones (Okinawa, Sardinia, Nicoya, Icaria and Loma Linda), who have a significantly longer life-span than people in other parts of the world. Factors which are associated with longevity in these populations are eating healthy diet with high consumption of vegetables, fruits and whole grains, regular physical activity and related to the latter point consumption of herbal, namely shell ginger (*Alpinia zerumbet*).^{68,69} The high consumption of antioxidants contained in fruits and vegetables as well as in the shell ginger aid in the protection against oxidative damages and scavenging the free radicals and reactive oxygen species (ROS), which contributes significantly to prolonging human lives especially among Okinawans.^{69,70} In this context, it is believed that Okinawan diet (low calorie and fatty acid intake + high intake of vegetables and soy products + traditional Okinawa cuisine) can be considered as a cause for longevity among the population.

Of the 19 studies reviewed, most of the participants incorporated lifestyle modifications such as reducing calorie intake and increasing physical activity alongside with CATs usage or supplementation. According to Curioni and Lourenço⁷¹ the combination of hypocaloric diet and physical exercise suggested significant reduction in body weight. The dietary counseling with personalized balanced, reduced calorie diet recommendations will encourage participants to reduce their habitual intake, thus leading to losing their weight.⁷² But, due to the poor commitment and difficulties to follow the dietary restrictions, CATs supplementation may only act as an alternative to reduce weight.⁵ However, the nature of lifestyle modifications might have affected and limited the evidence of CATs efficacy for weight loss.

Besides, there are no consistencies in term of the dosage and duration of supplementation between the same CATs in the reviewed studies. For instance, the findings from 2 different studies of vitamin D supplementation (25, 000 IU/week versus 60, 000 IU/week) both showed significant changes of body weight after the intervention. Different implementation of acupuncture such as types of acupuncture, acupoints, selection of needles and duration of acupuncture sessions could also result in different effects on body weight.⁵⁴ Hence, no definite

conclusion of suitable dosage of vitamin D for weight reduction could be made at the moment. According to Jeffery et al,⁷³ weight loss interventions should include long-term weight maintenance phase after initial weight loss. However, the reviewed studies only cover a maximum period of 1 year¹⁸; thus, requiring further investigation for their long-term benefits and safety.

As claimed by Santos and colleagues,⁷⁴ the safety information is disputed due to a lack of empirical evidence of efficacy and toxicity despite the widespread belief that dietary supplements are natural and safe. Indeed, there has been growing concern regarding the potential hepatotoxicity following herbal products' consumption, ranging from acute hepatitis to fulminant liver failure requiring transplantation or lead to death.⁷⁵ The most frequent single herbal ingredients involved in hepatotoxicity were *Camellia sinensis* and *Centella Asiatica* species, with 20% reported cases.⁷⁴ The various multi-ingredient products such as Herbalife, Oxy ELITE Pro and Hydroxycut have also been linked to severe liver injury cases.⁷⁶ Although the consumption of average amounts of GTE appears to be safe and harmless, this belief is often inaccurate and excessive doses have been associated with catechin-induced hepatocellular injury.⁷⁶ As a result, the European Food Safety Authorities (EFSA) and other global government authorities, including Health Canada and Norwegian Food Safety Authority (NFSA) have required that all GTE products bear a cautionary label that includes guidance on how to consume them as well as signs of the liver problem.

Establishing a causal relationship is challenging as the correlation between a single causative agent and hepatotoxicity can be extremely difficult to prove. Thus, the Roussel Uclaf Causality Assessment Method (RUCAM) was commonly used to proof of herbal product-related liver injury.⁷⁷ The RUCAM scale calculates scores which features in 7 different domains such as chronology (latency and de-challenge), risk factors, concomitant drug use, exclusion of other causes, previous information on drug's hepatotoxicity potential and response to re-challenge with a higher score indicates increased likelihood of hepatic injury due to consumption of a specific substance.⁷⁸ However, several pitfalls have questioned the reliability of this method in multi-ingredient products as RUCAM can be calculated only for a single drug each time. Of note, several adverse events induced by multi-ingredient products with a high score of RUCAM scale (highly probable) were reported.⁷⁴ For example, the intake of Herbalife supplements has been reported with acute liver injury cases.^{79,80} As Herbalife composed of complex mixtures of plants and herbs, this hinders the identification of the exact ingredient causing the hepatotoxic effects. Likewise, aloe vera, vitamin A and contamination with *Bacillus subtilis* has been considered the likely cause of directly hepatotoxic effects in in vitro tests.^{81,82}

A recent study evaluating the performance of the RUCAM scale on Oxy ELITE Pro (OEP) and critical case re-evaluation reported there are some flaws such as lack of case data transparency, hidden case data, incomplete data transfer, overt pre-existing disease and incorrect scoring of causality gradings

during the causality assessment.⁷⁸ This multi-ingredient weight loss product has been associated with several hepatotoxicity cases.⁸³ One of the reported cases concerns 7 patients who took the supplement for as short as 5 weeks to as long as 2 years before they were hospitalized.⁸³ Liver biopsy revealed a mixed pattern of hepatitis and cholestatic features and not a characteristic of auto-immune hepatitis thus suggests OEP was the probable cause of the hepatotoxicity. This issue raises whether obesity-associated liver diseases are related to herbal or dietary supplements hence, novel causality assessment tools are required. The complex nature of most products, variety types of consumption and the delayed onsets of liver damage hampers the determination of causality. Regulation standards for herbal products need to be considered so that these products' efficacy and safety have been clearly demonstrated before entering the markets.

In addition, some adverse events such as bruising, flatulence, flu, vomiting and other gastrointestinal problems were reported after the use of CATs in some studies.^{11,16,26,28,29} Some studies did not even provide detailed information regarding the safety aspects especially in regard to long-term usage of CATs. Although these alternative treatments are mostly based on natural products and are generally well-tolerated, their effectiveness and possible serious events must still be thoroughly ascertained. It has been suggested that OFI enhances hypoglycaemic in diabetic patients after oral supplementation.^{84,85} In addition, acupuncture-related complications such as pneumothorax, internal organ and central nervous system injury has been previously reported in China.^{85,86} Therefore, a safety risk assessment should be included in clinical trials in order to enhance efficacy of CATs for a long-term supplementation.

Although promising results have been shown, several limitations need to be mentioned. First, there are only a handful of studies (n = 19) that have been reviewed after searching through the databases. In general, it cannot be assured that all relevant studies have been located as relevant literature published in other languages might be missed due to prior-set inclusion criteria. Second, methodological flaws such as small sample size, unbalanced gender ratio, short-term duration and the lack of safety evaluations required attention. In fact, study respondents were mostly women, making this review more biased toward their dietary habits and preference. This might increase possible bias by the authors such as underreporting or overreporting of the interventions. Therefore, more well-designed study protocols are recommended for future studies.

Conclusions

In conclusion, this review suggests that hypnotherapy, spirulina, chitosan, probiotic, EPA + DHA, vitamin D, fiber, and herbal extract supplementation have shown some promising results for body weight reduction. However, an increased risk of adverse events after supplementation was found in chitosan and fiber. Some methodological weaknesses such as small sample sizes, safety evaluation and varied doses or duration of

CATs supplementation have restricted a more definitive conclusions, thus warranting further replication. Well-designed studies with an ample and longer duration of follow-up should be performed to offer proof of CATs' positive effects in reducing body weight.

Authors' Note

All authors attended multiple collaborative meetings to determine the review protocol (inclusion/exclusion) and discuss the structure of the results and discussion. Nurul Afiedia Roslim, Aryati Ahmad and Farahdilla Hamzah conducted the review process, reviewed all articles and wrote all sections of the manuscript. Pei Lin Lua critically revised, provided feedback and suggestion on multiple drafts of the manuscript and corrected the manuscript before submission. All authors have checked and approved the final version of the manuscript. Pei Lin Lua was the corresponding author. This research has been approved by the UniSZA Human Research Ethics Committee (UHREC) with a study protocol code: UniSZA/UHREC/2019/116. Participation in this study was voluntary and the participants were verbally briefed and have clarified their doubts regarding this study. Written consent was obtained from participants prior to their enrolment.

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