Complementary and Alternative Medicine for the Treatment of Obesity: A Critical Review

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Context: Obesity and its associated morbidities pose a major health hazard to the public. Despite a multiplex of available diet and exercise programs for losing and maintaining weight, over the past years, interest in the use of complementary and alternative medicine (CAM) for obesity treatment has greatly increased.

Evidence Acquisition: We searched PubMed, Google scholar and the Cochrane databases for systemic reviews, review articles, meta-analysis and randomized clinical trials up to December 2013.

Results: In this review, the efficacy and safety of the more commonly used CAM methods for the treatment of obesity, namely herbal supplements, acupuncture, and non-invasive body-contouring, are briefly discussed. The evidence supporting the effectiveness and safety of these methods is either lacking or point to a negligible clinical benefit, barely surpassing that of the placebo. Furthermore, several limitations are observed in the available scientific literature. These shortcomings include, without being limited to, uncontrolled trial designs, non-random allocation of subjects to treatment arms, small number of patients enrolled, short durations of follow-up, and ambiguous clinical and laboratory endpoints.

Conclusions: Further investigations are necessary to accurately determine the efficacy, safety, standard dosage/procedure, and potential side effects of the various CAM methods currently in use.

Keywords: Weight Loss; Obesity; Biliopancreatic Diversion; Complementary Therapies; Dietary Supplements; Acupuncture Therapy; Laser Therapy; Treatment Outcome

1. Context

According to the World Health Organization (WHO) 2010 global report on non-communicable diseases, overweight/obesity is claiming 2.8 million lives annually (1). The plague of obesity has reached epidemic proportions and is spreading at an unprecedented pace, particularly in urban areas of low and middle income countries (2, 3). However, this global calamity is not only confined to the developing world (3, 4), as about 60% of the adults in the United States are currently either obese or overweight (5).

Obesity, defined by WHO as body mass index (BMI) equal to or greater than 30 kg/m\(^2\), has been linked to a wide array of illnesses and disabilities, including type 2 diabetes, cardiovascular diseases, chronic kidney disease, sleep apnea and its resultant chronic fatigue and poor attention, arthritis, lung disease, and several forms of cancer (e.g. breast and prostate) (6-10). Obese individuals are also at increased risk of premature death (9, 11).

Overweight/obesity is assumed to be a product of imbalanced caloric intake and expenditure. Therefore, increased physical activity, coupled with a calorie-restricted diet, remains the mainstay of treatment in obese/overweight individuals. Physical activity lowers the risk of diabetes, hypertension, stroke, ischemic heart disease and several types of cancers (12-14). The prevalence of insufficient physical activity is rising globally. According to a WHO report, 48% of women and 41% of men have insufficient physical activity in high-income countries and almost 3.2 million deaths each year are attributed to physical inactivity (1). Adherence to unhealthy diets, high in simple carbohydrates and saturated fatty acids, has also been rising, especially in low- and middle-income countries. Collectively, approximately 80% of coronary heart disease and cerebrovascular disease are attributable to behavioral risk factors, such as inadequate physical activity, and adherence to unhealthy dietary patterns (15).

Busy schedules, sedentary lifestyle, increased automation of work, and decreased transport-related physical activity in modern societies, all contribute to the increasing physical inactivity trend. It is suggested that, as long as culture and environment support unhealthy lifestyle patterns, especially through media, modifying lifestyle would be unattainable (16). Consequently, alternative methods, with little or no scientific evidence supporting them, have attracted the interest of individuals at risk for obesity.
and have replaced the standard weight-lowering methods, with proven efficacy.

Complementary and alternative medicine (CAM) is defined by the National Center for Complementary and Alternative Medicine (NCCAM) as "a group of varied medical and healthcare systems, practices, and products that are not considered to be part of any current Western health care system" (17).

Increased public awareness regarding obesity-related health problems, along with the social pressure concerning the body image and a desire to have a slim body, has enormously given way to CAM during the recent years. However, up to present, there are insufficient researches regarding the effectiveness of CAM therapies for weight loss and much of the existing literature have fundamental methodological problems (18). The present review provides a summary of the more commonly used CAM methods for the treatment of overweight/obesity. In each section, after a brief introductory passage, the body of evidence endorsing or disapproving the method, as a weight-lowering strategy, is discussed.

2. Evidence Acquisition

We searched PubMed, Google scholar and the Cochrane review database for related publications written in English language (Abstract and/or full-text). Systematic reviews, review articles, meta-analyses and randomized clinical trials, conducted and published up to December 1st, 2013, were considered. Studies published from 2000 and afterwards were given a high priority. The combination of keywords used for our research was as follows: obesity treatment, weight loss, herbal supplements, Chinese herbal medicine, *Garcinia cambogia* (*G. cambogia*), *Camellia sinensis* (*C. sinensis*), chromium picolinate, conjugated linoleic acid (CLA), *Hoodia gordonii* (*H. gordonii*), *Cynanchum auriculatum* (*C. auriculatum*), chitosan, acupuncture, non-invasive body contouring, including high intensity focused ultrasound (HIFU), laser therapy, cryolipolysis and radiofrequency (RF). A list of keywords was derived initially. Authors then performed independent literature reviews and the findings were shared in a designated article database. To increase the inclusiveness of our search strategy, authors also reviewed the texts to find other relevant manuscripts cited that were not retrieved in the initial search. Given the narrative nature of the review, no formal quality assessment was performed.

3. Results

Available evidence on the CAM methods used for the treatment of obesity are summarized in Table 1.

Table 1. Summary of the Available Evidence on Complementary and Alternative Medicine Methods Used for the Treatment of Overweight/Obesity

| Methods Name                  | Main Mechanism of Action                                                                 | Strength of Publication | Effect Size           | Possible Side Effects                           |
|-------------------------------|------------------------------------------------------------------------------------------|-------------------------|-----------------------|------------------------------------------------|
| Herbal Supplements            |                                                                                         |                         |                       |                                                 |
| *Garcinia cambogia*           | Inhibition of citrate lyase enzyme, inducing satiety                                     | a                       | 95% CI: 0.00 – 1.75 kg| Minor (e.g. rhinitis, joint pain)               |
| *Camellia sinensis*          | 1. Stimulation of sympathetic nervous system, leading to increase in energy consumption 2. Fat oxidation | a                       |                       |                                                 |
| Chromium picolinate          | Stimulation of neurotransmitters responsible for eating behaviors                         | a                       |                       | Non-specific and well tolerated (e.g. nausea, watery stools, weakness, dizziness) |
| Conjugated linoleic acid      | Not fully understood                                                                      | a                       | 95% CI: 0.86 – 1.79 kg| Mild gastrointestinal complaints               |
| *Hoodia gordonii*            | Inhibiting appetite by altering the neuropeptide pathways of the central nervous system  | a                       |                       |                                                 |
| *Cynanchum auriculatum*      | Appetite inhibiting effects, similar to *Hoodia gordonii*                                | a                       |                       |                                                 |
| Chitosan                     | Reducing nutritional fat absorption                                                      | a                       | 95% CI: 2.10 – 3.30 kg| Mild gastrointestinal complaints (e.g. nausea, bloating, indigestion, abdominal pain), comparable to placebo |
### 3.1. Herbal Supplements

Welcomed by the public at large, one of the fastest burgeoning methods for weight loss is the use of medicinal plant extracts. Despite the long history of their traditional use for purposes of chronic disease prevention and cure, the effectiveness of these products, which consist of dietary phytochemical constituents, remains to be ascertained (19). The recent interest in how suitable these natural supplements are in treating obesity, on a long-term basis, has led to a raft of research. Nonetheless, there is a need for further investigation into their efficacy, long-term safety, optimum dosage, possible side-effects, and mechanisms of action. Two other aspects of these weight loss aids, which pose a significant problem to the dietary supplement industry, are their overhype, despite inadequate supporting proof and incompetent quality control, resulting, at times, in incorrect label information (20). There is a flurry of herbal plants marketed over the counter, claiming anti-obesity effects. The most frequently mentioned ones are reviewed next.

### 3.1.1. Garcinia Cambogia

Extracted from the dehydrated fruit rind of *G. cambogia*, hydroxycitric acid is one such dietary supplement, which is a popular cooking ingredient in Southern India. Its mechanism of action consists of preventing the activity of the ATP-dependent citrate lyase enzyme, which stimulates the breakdown of citrate into oxaloacetic acid and acetyl-CoA, thus either inducing a sense of satiety or lessening the appetite (21, 22). Consumed for centuries on a regular or supplemental basis, *G. cambogia* is claimed to be free of adverse or side effects (22). Experiments on rats and humans indicate that administering hydroxyocitric acid indeed contributes to a feeling of satiety and subsequent weight reduction (23). Conversely, a number of human trials have produced unconvincing evidence, supporting that no significant difference was found between the effects of this supplement and those of the placebo (24-27). The results of a meta-analysis, which pooled the data from nine clinical trials, evaluating the effectiveness of hydroxycitric acid in weight reduction, indicated that hydroxycitric acid is relatively more effective than the placebo (mean difference: -0.88 kg; 95% confidence interval (CI): 0.00-1.75 kg). Collectively, research trials point to the fact that *G. cambogia* extracts can positively act as weight loss agents, on a short-term basis. Nonetheless, their effect is limited and their clinical relevance is yet to be determined (28). In conclusion, given the fact that most human trials have been conducted on a short-term basis and on small patient samples, there is no proof supporting the effectiveness of *G. cambogia* for a length of time longer than 12 weeks of administration.

### 3.1.2. Camellia Sinensis

Used for a variety of reasons over centuries, the green tea produced from the leaves of *C. sinensis* is another popular remedy for obesity (19). Commonly referred to as catechins, the most bioactive constituent of green tea are the polyphenols (29). The mechanism of action of green tea can be outlined as influencing the sympathetic nervous system, thereby increasing energy consumption and triggering the oxidation of fat. Reduced nutrient absorption, appetite prevention, and up-regulation of enzymes responsible for hepatic fat oxidation may also be enumerated as alternative mechanisms (30).
According to a recent review of three studies on weight maintenance and fifteen weight loss trials, which involved 1945 human subjects, consumption of green tea, over a minimum period of 12 weeks, was unlikely to be clinically effective (30). A further conclusion was that the maintenance of weight loss is not considerably affected by green tea, either. No information concerning costs, patient satisfaction or illnesses, as a consequence of green tea preparation, was included in these studies (31).

Several studies have attempted, although they ultimately failed, to validate the curative effect of *C. sinensis* on appetite reduction or energy consumption, as observed in and compared between the experimental and the placebo group (32-35). Overall, although there is scant proof, which can substantiate the role of *C. sinensis*, as an appetite inhibitor, most studies conclude that *C. sinensis* functions through mechanisms other than appetite suppression (e.g. increased energy expenditure), which may indeed help reduce body weight (32, 34, 36, 37).

### 3.1.3. Chromium Picolinate

Sold as over-the-counter slimming aid throughout the USA and Europe, (ii) chromium picolinate stimulates the neurotransmitters responsible for the regulation of food cravings, mood and eating behavior (38). Chromium supplementation also boosts glucose metabolism, body composition, and insulin sensitivity, to a modest extent, in human trials (39). A systematic review of nine trials accounting for 622 subjects (experimental group = 346; control group = 276) was conducted on the use of chromium picolinate for weight loss. The subjects in the experimental group, who were given four different doses of chromium picolinate (200 µg, 400 µg, 500 µg, 1,000 µg) were reported to have lost 1 kg more than those receiving placebo (Mean Difference: 1.1 kg, 95% CI: 0.4-1.7; P = 0.001). Furthermore, the safety and long-term effects of chromium picolinate could not be determined due to the relatively short length (maximum of 24 weeks) of the studies reviewed. This paucity of evidence, therefore, prevented the reviewers from reaching any conclusions regarding the effectiveness and safety of this dietary supplementation in overweight and obese adults (40).

### 3.1.4. Conjugated Linoleic Acid

Conjugated linoleic acid refers to a set of isomers in the cis-9, trans-11 form or the cis-12, trans-10 form (41). It is hypothesized that certain doses of CLA (1.7-6.8 g/day) can help increase the fat-free mass and reduce fat mass (42, 43). Currently, a number of dietary supplements, with CLA content for the purposes of weight loss, are being advertised, even though not all studies have reported positive results (44, 45).

According to a meta-analysis from 2012, four out of seven clinical trials were methodologically flawed (46). Overall, the CLA was favored over the placebo due to a small difference in the amount of fat loss (mean kg: 1.33 kg; 95%CI: 0.86-1.79; I² = 54%; the I² statistics were used to evaluate statistical heterogeneity between studies, demonstrating low, medium, and high statistical heterogeneity, with values of 25, 50, and 75%, respectively). However, since the magnitude of the positive effects was small and no p values were documented, the evidence was concluded to be unconvincing and therefore, the long-term effects of the CLA on body composition cannot be decisively considered of clinical importance (46).

### 3.1.5. Hoodia Gordonii

Widely consumed for its alleged weight loss effect (47), *H. gordonii*, which is a member of the Asclepiadaceae (the milkweed family), has been traditionally used as an appetite (both food and water) suppressant during hunting expeditions by the Khoi-San tribe, in South America (48). Although little is known about its mechanism of action, it seems that its bioactive element, steroidal glycosides P57, which is associated with appetite inhibition, alters the neuropeptide-mediated pathways of the central nervous system (47). Based on animal studies, the injection of P57 into the central nervous system of mice leads to reduced food intake over the following 24 hours (49). Human trials have displayed positive results as well. According to a press release from Phytopharm (Huntingdon, UK), reporting a phase I/II randomized trial, after 15 days, a statistically significant reduction was documented in the average calorie consumption and body fat content of the group receiving P57, compared to the placebo group (P = 0.014 and P = 0.035, respectively).

According to a review of the commercial importance of *H. gordonii*, there are very few scientifically-based studies on chief features (bioactivity of its chemical ingredients, clinical relevance, in vivo biopharmaceutics, and safety) of this anti-obesity plant. Obviously, this has brought about considerable concern, as *H. gordonii* is among the most popular organic anti-obesity products (48).

### 3.1.6. Cynanchum Auriculatum

Native to China, *C. auriculatum* (Royle ex Wight) is a plant species of which the roots, according to Chinese traditional medicine, enhance immunity and espouse longevity (50). Pregnane glycosides and baishouwubenzenophenone have been found to exist in *C. auriculatum* (51). The similarity in the structure of pregnane and that of P57 (found in *H. gordonii*) shows that *C. auriculatum* could be an alternative to *H. gordonii* in developing anti-obesity dietary supplementation (51). Wilfoside KN is the most widely known pregnane glycoside, which bears great structural resemblance to P57 (51). An animal trial, involving rats, has demonstrated that Wilfoside KN can produce a considerable appetite-inhibiting effect (51). The efficacy and safety of pregnane glycosides need to be further investigated, especially because, unlike *H. gordonii*, which may soon become an endangered species, *C. auriculatum* is an abundant plant source (50, 52).
3.1.7. Chitosan

Chitosan is a polysaccharide extractable through the partial deacetylation of chitin (53). A non-toxic dietary supplement, Chitosan has been shown to bring about anti-obesity effects (54, 55) and is widely believed to be a safe compound (56). Its anti-obesity effects have been generally attributed to its fat-binding quality, which restricts the absorption of nutritional fat from the gastrointestinal tract (57). In vivo studies on mice indicate that the consumption of chitosan can lead to reduced food intake (58, 59). The effect of chitosan on obesity was evaluated through a review of fifteen randomized trials, with a total of 1219 subjects. Although initial analyses ascribed a considerable weight loss to the use of chitosan preparations (mean loss: 1.7 kg; 95%CI: 1.3–2.1 kg, P < 0.00001), high-quality trials, conducted later, revealed that the anti-obesity effect of chitosan was not nearly as large as the previous subliminal trials claimed. In fact, the anti-obesity effect of chitosan was deemed minimal at best and therefore clinically irrelevant (60).

3.1.8. Gambisan

Gambisan is a newly developed extract formula which was designated as HH911G at Kyung Hee University and Korean Medicine Hospital, Seoul, South Korea (60). In spite of the fact that its mechanism of action is yet to be understood, Gambisan has been clinically used as a popular supplement, with over 2800000 prescribed doses from 2010 to 2013. Indeed, Gambisan may be able to offer an effective method of weight loss, though more in vivo investigations and clinical trials are required before any indisputable conclusions are to be drawn, concerning the safety, effectiveness, and the mechanisms of action of Gambisan (61–63).

In conclusion, herbal supplements are widely marketed and commercialized, yet the evidence in support of their effectiveness is either non-existent or point to a negligible effect. This should be viewed in light of their possible side effects and lack of proof of their long-term safety.

3.2. Acupuncture

A longstanding oriental practice, acupuncture consists of the insertion of needles into certain points on the skin, called acupoints (64). Over the recent years, this technique has come to be increasingly regarded as an alternative treatment for obesity. Although there is evidence favoring electroacupuncture over its manual variations, in terms of effectiveness, there is less consensus over the optimal frequency for the procedure (65).

Studies on animals and humans indicate a number of possible mechanisms, by which acupuncture contributes to weight reduction. First, it is suggested that acupuncture can regulate obesity-related neuropeptides in the central nervous system, as well as fat depot derived adipokines (66, 67). Second, acupuncture may be involved in the regulation of hypothalamus-pituitary-adrenal cortex and sympathetic-adrenal cortex axis (68). Third, a number of studies have observed a reduction in triglycerides (69, 70), LDL (70, 71), and total cholesterol (69, 70) with acupuncture and thereby might exert lipid lowering effects. Fourth, since high levels of bacteroides have been observed in obese patients (72), one of the weight loss mechanisms of abdominal acupuncture may involve the reduction of bacteroides.

According to a systematic review and meta-analysis including 29 randomized controlled trials, acupuncture was illustrated to be more effective than conventional medication both in terms of body weight reduction (mean reduction = 1.90 kg; 95%CI: 1.66–2.13 kg) and obesity treatment (relative risk = 1.13; 1.04–1.22) (73). Despite these promising results, because of the poor methodological quality of the trials reviewed, the reviewers concluded that to determine the efficacy of acupuncture in treating obesity, it was urgent that more organized and long-term studies need to be conducted (73).

Another systematic review of eight clinical trials, including 1017 participants, that evaluated the effectiveness of acupuncture, revealed that acupuncture was a safe complementary treatment for simple obesity, defined as an imbalance between caloric intake and energy expenditure. Yet, owing to the limited quantity of conducted randomized trials and their poor methodological quality, further investigations are necessary before acupuncture can be conclusively certified as an effective solution to obesity (74).

In a more recent systematic review of Chinese medicine and acupuncture, a total of 44 randomized clinical trials were examined (75). According to the pooled analysis, lifestyle modification and placebo were found to be less effective than acupuncture in terms of weight and BMI reduction (75). Compared to anti-obesity drugs (Orlistat and Sibutramine), moreover, acupuncture displayed equally positive results, with a reduced number of side effects and relapses (75). Nonetheless, the small size of the sample and substandard methodological rigor limits the validity of the conclusions (75).

In summary, the shortcomings observed in the available literature on acupuncture are manifold. To begin, several studies draw their conclusions from uncontrolled trials. Additionally, studies with controlled trial designs are riddled with flaws, as they suffer from methodological weaknesses, such as limited durations of follow up, absence of placebo control groups, loosely observed protocols, and arbitrary selection of acupoints, in terms of the precise location, as well as the correct depth, angle and direction of insertion (71, 73, 74). If a conclusive result is to be achieved, concerning the effectiveness of acupuncture, future studies need to map the acupuncture site on the body and determine factors, such as depth and angle, as well (75).

3.3. Non-invasive Body Contouring

Invasive body-contouring refers to the surgical removal of localized areas of adiposity from under the skin (76).
Liposuction is the most common cosmetic plastic surgery procedure used around the world (77). However, this popular method still raises serious concerns about the safety of its invasive nature. Possible complications, resulting from the invasive procedure, range in severity from prolonged swelling, bruising, and numbness, to thrombophlebitis and pulmonary embolism (78). A pressing need for safer procedures, with faster recovery time, as well as smaller number of side effects, therefore, makes non-invasive body contouring techniques perhaps several of the most appealing and fastest growing extents of esthetic surgery today (77, 79). Focused ultrasound, cryolipolysis and low level laser therapy are among these non-invasive methods, which have gained popularity over the last decade.

3.3.1. High Intensity Focused Ultrasound

High Intensity Focused Ultrasound is a non-invasive technique used for the ablation of subcutaneous fat tissue. Mechanisms by which HIFU affects the fat depot include (1) hyperthermia, whereby a coagulative necrosis of certain areas is brought about with no harm to adjacent areas (80, 81), and cavitation formation (2), which exerts high degrees of heat and pressure in the microenvironment, therefore subjecting the adipose tissue to mechanical damage (82). Available evidence suggests patients with a BMI lower than 30 kg/m² show the optimal results to HIFU (83).

A 12-week study of 137 participants, analyzing the effects of focused ultrasound treatment, revealed positive results. Within 2 weeks of treatment, the mean reduction in the circumference of the treatment area and the skin fat thickness were reported to be approximately 2 cm and 2.9 mm, respectively (84).

3.3.2. Low Level Laser Therapy

Developed and popularized over the past decade, Low Level Laser Therapy (LLLT) is another non-invasive body contouring method, which has yielded successful results in fat reduction of localized areas, such as the hips, waist, thighs, and upper arms (85, 86). The mechanism of action of LLLT is open to investigation. According to one narrative, by forming temporary pores in the adipocytes’ membrane, LLLT triggers the release of intracellular lipid for additional metabolismization (87). In a double-blind study of 67 randomized subjects, aged 18-65 years old, with BMI 25-30 kg/m², LLLT resulted in a reduction of total circumference of the waists, hips and bilateral thighs (88). Despite these preliminary findings, suggestive of the efficacy of the method, further research into LLLT is required to fully appreciate its cellular and systemic effects, and to ascertain treatment protocols, which allow the highest degree of safety and effectiveness possible.

3.3.3. Cryolipolysis

Regarded as an efficacious method for subcutaneous fat reduction, cryolipolysis is an emergent technology which targets fat selectively through controlled cooling. A number of studies have assessed the safety and effectiveness of cryolipolysis. According to a retrospective study on 518 participants, the abdomen, back and flank areas were most effectively treated by means of cryolipolysis. Three months follow-up of the patients, moreover, displayed no significant adverse events or side effects (88). Appraising the findings of preclinical and clinical studies on the use of cryolipolysis for animals and humans, a 2009 review of four clinical studies concluded that there was sufficient evidence to support the efficacy and safety of cryolipolysis, as a noninvasive fat reduction procedure, even though its mechanism of action is yet to be explained (89).

3.3.4. Radiofrequency

Radiofrequency is yet another non-invasive technique used for body contouring (90). The mechanism of action of RF is based on thermal alteration of the dermal/hypodermal layers. Increasing tissue temperature raises vascular perfusion, resulting in lipid turnover secondary to the increased oxygen content. Increased lipid turnover eventually leads to fat cell shrinkage, and circumferential reduction (79). Brightman and colleagues (91) evaluated nineteen participants who underwent five weekly treatments of the upper arms and 10 patients received four weekly treatments of abdomen and flank, with Vela Shape (Syneron Medical Ltd., Irvine, CA, USA) a RF energy device that has a FDA approval for both circumferencereduction and cellulitis. Reductions of both arm and abdomen circumference were statistically significant, with a mean loss off 0.597 cm and 1.82 cm, respectively at 3 months of follow up. At present, the non-invasive reduction of fat is the most common use of RF-based devices and there are many articles to support the clinical efficacy and safety of using RF (79, 91, 92).

Non-invasive body contouring techniques are generally regarded as safe. By far, the most critical issue concerning these methods is patient dissatisfaction. Non-invasive body contouring only results in moderate reductions of 2 to 4 cm in limb or waist circumference. Therefore, their efficacy in morbidly obese patients is fairly limited (79).

At present, there are no systematic evaluations of the non-invasive methods used in body contouring or subcutaneous fat reduction, in terms of efficacy, safety, and patient satisfaction. Carrying out more sophisticated outcome studies, in the form of systematic reviews and meta-analyses, is essential to offer proof of the value of non-invasive body contouring.

4. Conclusions

Complementary and alternative medicine is an umbrella term used to describe a wide array of treatment strategies that, by definition, do not conform to the principles and ideas of western medicine. This alleged marginaliza-
tion, by no means has affected their popularity. Today, more than ever, patients are seeking alternative ways to lose weight and get lean and this vogue has been welcomed by the industry, as well as media outlets, and a sizable proportion of healthcare practitioners. Despite their widespread commercialization and an ever increasing demand from the public, scientific evidence supporting their efficacy and safety is strikingly limited and in a sense, ‘non-existent’.

Herbal supplements are widely marketed. However, at present, available data supporting their long-term usage and safety for obesity treatment is scarce and, at best, conflicting. Clinical studies have often reported negligible effects for herbal supplements barely exceeding that of the placebo. Studies investigating the putative role of acupuncture in weight loss and management have been positive, yet, given the low quality of the studies conducted and extreme diversity in site, depth, and angle of needle insertion, caution should be practiced in interpreting the findings. Preliminary studies, investigating treatment outcomes, with non-invasive body contouring methods, have been promising. However, since these techniques only cause a mild to moderate amount of weight loss in patients with a reasonable BMI range, their widespread application in other patient groups remains to be elucidated.

Although promising results have been obtained by bariatric surgery techniques, the procedure is invasive, costly, and is associated with long-term morbidity and complications and thus, is only reserved for a select population of obese patients, with very high BMI, who do not respond well to lifestyle interventions (93).

To the present moment, pharmacotherapy for obesity has not yielded satisfactory results due to its numerous shortcomings. Most of anti-obesity drugs have been withdrawn from the market, as a result of their substantial side effects. Orlistat (Roche Holding AG, Basel, Switzerland), the FDA approved anti-obesity drug, cannot be well tolerated because of its gastrointestinal adverse effects (94). The most lately approved anti-obesity drugs, including lorcaserin, and topiramate/phentermine are definitely requiring post approval clinical trials to carefully assess their long-term efficacy and safety (95). Considerable adverse effects, limited efficacy and alarms over the safety of medications, along with utilizing anti-obesity drugs in combination with a low calorie diet in clinical trials (95), remind the fact that the key to effective weight reduction is still a low-calorie diet, accompanied by physical exercise.

Putting together larger, more carefully designed clinical trials, with long duration of follow up and strict protocols, for registering side effects and adverse events, is mandatory to offer proof of the value of herbal supplements, acupuncture and non-invasive body contouring in overweight/obese individuals. Until concrete evidence, with regard to effectiveness and long-term safety of CAM weight loss techniques, is available, a combination of healthy nutrition and physical activity should be the treatment strategy offered to overweight and obese individuals.

Authors’ Contributions

Literature review: Tina Mazaheri, Mona Vahidi Rad; Drafting the manuscript: Alireza Esteghamati, Tina Mazaheri, Mona Vahidi Rad, Sina Noshad; Critical revision of the manuscript for important intellectual content: Alireza Esteghamati, Sina Noshad; Study supervision: Alireza Esteghamati.

References

1. Alwan A. Global status report on noncommunicable diseases 2010.Geneva: World Health Organization; 2011.
2. Mokdad AH, Bowman BA, Ford ES, Vinicor F, Marks JS, Koplan JP. The continuing epidemics of obesity and diabetes in the United States. Jama. 2001;286(10).
3. Chandrasekaran C, Vijayalakshmi M, Prakash K, Ransal V, Meenakshi J, Amit A. Review Article: Herbal Approach for Obesity Management. Am J Plant Sci. 2013.
4. Obesity: The Prevention, Identification, Assessment and Management of Overweight and Obesity in Adults and Children.London: National Institute for Health and Clinical Excellence: Guidance; 2006.
5. Hurt RT, Kulisek C, Buchanan IA, Clavence SA. The obesity epi demic: challenges, health initiatives, and implications for gas troenterologists. Gastroenterol Hepatol (NY). 2010;6(2):780–92.
6. Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ. Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. N Engl J Med. 2003;348(17):1625–38.
7. Field AE, Coakley EH, Must A, Spadano J, Laird N, Dietz WH, et al. Impact of overweight on the risk of developing common chronic diseases during a 10-year period. Arch Intern Med. 2001;161(13):1588–6.
8. Kannel WB, Adrienne Cupples L, Ramaswami R, Stokes III J, Kreger BE, Higgins M. Regional obesity and risk of cardiovascular disease: the Framingham Study. Clinical Epidemiology. J. 1991;44(2):283–90.
9. Knower WC, Barrett-Connon E, Fowler SE, Hamman RF, Lachin JM, Walker EA, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med. 2002;346(6):393–401.
10. Marmot M, Atimmo T, Byers T, Chen J, Hirohata T, Jackson A, et al. Food, nutrition, physical activity, and the prevention of cancer: a global perspective. UCL Discovery. 2007.
11. Sui Y, Zhao HI, Wong VC, Brown N, Li XL, Kwan AK, et al. A systematic review on use of Chinese medicine and acupuncture for treatment of obesity. Obes Rev. 2012;13(5):409–30.
12. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med. 2006;3(11).
13. Organization WH . Switzerland: 2010. Global health risks: morbidity and burden of disease attributable to selected major risks.
14. Organization WH . Switzerland: 2010. Global recommendations on physical activity for health.
15. Ezzati M, Organization WH . Comparative Quantification of Health Risks: Global and Regional Burden of Disease Attributable to Selected Major Risk Factors.Geneva: World Health Organization.
16. Mitchell NS, Catenacci VA, Wyatt HR, Hill JO. Obesity: overview of an epidemic. Psychiatr Clin North Am. 2011;34(4):771–32.
17. Health NIO Health NIO. Complementary, Alternative, or Integrative Health: What’s In a Name? 2014
18. Sharpe PA, Blanck HM, Williams JR, Ainsworth BE, Conway JM. Use of complementary and alternative medicine for weight control in the United States. J Altern Complement Med. 2007;13(2):217–22.
19. Astell KJ, Mathai ML, Su XQ. A Review on Botanical Species and Chemical Compounds with Appetite Suppressing Properties for Body Weight Control. Plant Foods for Human Nutrition. 2013;68(3):213–21.
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20. Haller CA, Duan M, Benowitz NL, Jacob P3. Concentrations of ephedra alkaloids and caffeine in commercial dietary supplements. J Anal Toxicol. 2004;28(3):345–51.

21. Triscari J, Sullivan AC. Anti-obesity activity of a novel lipid synthesis inhibitor. Int J Obes. 1984;8(4 Suppl):227–39.

22. Marquez F, Baho N, Bullo M, Salas-Salvado J. Evaluation of the safety and efficacy of hydroxyecitrin or Garcinia cambogia extracts in humans. Crit Rev Food Sci Nutr. 2012;52(7):585–94.

23. Preuss HG, Rao CV, Garis R, Bramble JD, Ohia SE, Bagchi M, et al. An overview of the safety and efficacy of a novel, natural-\(\text{\textregistered}\)hydroxyecitrin extract (HCA-SX) for weight management. J Med. 2004;15(1):13–48.

24. Heymsfield SB, Allison DB, Vasselli JR, Pietrobelli A, Greenfield D, Nunez C. Garcinia cambogia (hydroxyecitrin) as a potential antiobesity agent: a randomized controlled trial. JAMA. 1998;280(18):1596–600.

25. Kovaes EM, Westerterp-Plantenga MS, de Vries M, Bouws F, Saris WH. Effects of 2-week ingestion of \(\text{-}\)-hydroxyecitrin and \(\text{-}\)-hydroxyecitrin combined with medium-chain triglycerides on satiety and food intake. Physiol Behav. 2001;74(4-5):534–9.

26. Mattes RD, Bormann L. Effects of \(\text{-}\)-hydroxyecitrin on appetite variables. Physiol Behav. 2000;70(1-2):67–94.

27. Vasques CA, Rossetto S, Halmenschlager G, Linden R, Heckler E, Fernandez MS, et al. Evaluation of the pharmacotherapeutic efficacy of Garcinia cambogia plus Amorphophallus konjac for the treatment of obesity. Phytother Res. 2010;24(2):231–40.

28. Onakpoya I, Hung SK, Perry R, Wider B, Ernst E. The Use of Garcinia Extract (Hydroxycitric Acid) as a Weight Loss Supplement: A Systematic Review and Meta-Analysis of Randomised Clinical Trials. J Obes. 2018;2018:90938.

29. Wolfram S, Wang Y, Thielecke F. Anti-obesity effects of green tea: from bedside to bench. Mol Nutr Food Res. 2008;52(2):176–87.

30. Rainier L, Heiss CJ. Conjugated linoleic acid: health implications and effects on body composition. J Am Diet Assoc. 2004;104(6):963–8.

31. Pariza MW, Park Y, Cook ME. The biologically active isomers of conjugated linoleic acid. Prog Lipid Res. 2001;40(4):283–98.

32. Gualtieri JM, Halse J, Hoye K, Kristiansen K, Fagerhut H, Vik H, et al. Conjugated linoleic acid supplementation for 1 y reduces body fat mass in healthy overweight humans. Am J Clin Nutr. 2004;79(6):1188–215.

33. Kamphuis MM, Lejeune MP, Saris WH, Westerterp-Plantenga MS. The effect of conjugated linoleic acid supplementation after weight loss on body weight regain, body composition, and resting metabolic rate in overweight subjects. Int J Obes Relat Metab Disord. 2001;27(4):430–7.

34. Zambelli KL, Reim NL, Van Loan MD, Gale B, Benito P, Kelley DS, et al. Conjugated linoleic acid supplementation in humans: effects on body composition and energy expenditure. Lipids. 2000;35(7):777–82.

35. Onakpoya IJ, Posadzki PP, Watson PK, Davies LA, Ernst E. The efficacy of long-term conjugated linoleic acid (CLA) supplementation on body composition in overweight and obese individuals: a systematic review and meta-analysis of randomized controlled trials. Eur J Nutr. 2012;51(2):327–34.

36. Lee RA, Balick MJ. Indigenous use of Hoodia gordoni and appetite suppression. Explore (NY). 2007;3(4):404–6.

37. Vermaak I, Hamman JH, Viljoen AM. Hoodia gordoni: an up-to-date review of a commercially important anti-obesity plant. Pflanze Med. 2011;77(3):1149–60.

38. MacLean DB, Luo LG. Increased ATP content/production in the hypothalamus may be a signal for energy-sensing of satiety: studies of the anorectic mechanism of a plant steroidal glycoside. Brain Res. 2001;880(1-2):12–3.

39. Lu Y, Teng J, Yang ZC, Mei ZN. Three New Steroidal Glycosides from the Roots of Cynanchum auriculatum. Molecules. 2011;16(12):3901–9.

40. Gu XJ, Yao N, Qian SH, Li YB, Li P. Four New C22Steroidal Glycosides from the Roots of Cynanchum auriculatum. Helvetia Chimica Acta. 2009;92(1):158–97.

41. Liu S, Chen Z, Wu J, Wang L, Wang H, Zhao W. Appetite suppression of pregnant glycocides from the Roots of Cynanchum auriculatum. Phytochemistry. 2013;93:344–53.

42. Baldrick P. The safety of chitosan as a pharmaceutical excipient. J Pharm Pharmacol. 2010;62(1):290–9.

43. Han CK, Kimura Y, Okuda H. Reduction in fat storage during chitin-chitosan treatment in mice fed a high-fat diet. Int J Obes Relat Metab Disord. 1999;23(2):374–9.

44. Sumiyoshi M, Kimura Y. Low molecular weight chitosan inhibits obesity induced by feeding a high-fat diet long-term in mice. J Pharm Pharmacol. 2006;58(2):202–7.

45. Thanou M, Verhoef JC, Junginger HE. Oral drug absorption enhancement by chitosan and its derivatives. Adv Drug Deliv Rev. 2003;55(2):187–26.

46. Zhang J, Liu J, Li X, Xia W. Dietary chitosan improves hypercholesterolemia in rats fed high-fat diets. Nutr Res. 2008;28(5):383–90.

47. Kumar SG, Rahman MA, Lee SH, Huang HS, Kim HA, Yun JW. Plasma proteome analysis for anti-obesity and anti-diabetic potencies of chitosan oligosaccharides in ob/ob mice. Proteomics. 2009;9(9):2149–62.

48. Rahman M, Kumar SG, Yun JW. Proteome analysis in adipose tissue of ob/ob mice in response to chitosan oligosaccharides treatment. Biotechnology and Bioprocess Engineering. 2010;15(4):559–71.

49. Ni Mhrurch C, Dunshea-Mooy CAE, Bennett D, Rodgers A, Ni Mhrurch C. Chitosan for overweight or obesity. 2005.

50. Hasani-Ranjbar S, Naebye N, Larijani B, Abdollahi M. A systematic review of the efficacy and safety of herbal medicines used in the treatment of obesity. World J Gastroenterol. 2009;15(25):3073–85.

51. Joyal SV. A perspective on the current strategies for the treatment of obesity. Curr Drug Targets CNS Neurol Disord. 2004;3(4):341–56.

52. Yang JW, Nam D, Kim KH, Huh J, Lee JD. Effect of Gambosin on the Inhibition of Adipogenesis in 3T3-L1 Adipocytes. Evid Based Complement Alternat Med. 2013;2013:579067.

53. NIH Consensus Conference. Acupuncture. JAMA. 1998;280(7):3518–24.

54. Belvani M, Dimitroutula C, Katsiki N, Apostolopoulou M, Cuminings M, Hatzitolios AI. Acupuncture in the treatment of obesity: a narrative review of the literature. Acupuncture Med. 2013;31(1):88–97.

55. Cabioglu MT, Ergene N. Changes in serum leptin and beta en-
dorphin levels with weight loss by electroacupuncture and diet restriction in obesity treatment. *Am J Chin Med.* 2006;34(3):3-11.
67. Guce F, Bahar B, Demirtas C, Mit S, Cevik C. Influence of acupuncture on leptin, ghrelin, insulin and cholecystokinin in obese women: a randomised, sham-controlled preliminary trial. *Acupunct Med.* 2012;30(3):203-7.
68. Yin S, Lin-shan Z. Therapeutic idea and approaches to obesity with acupuncture. *Journal of Acupuncture and Tuina Science.* 2005;3(4):54-7.
69. Sun Q, Xu Y. Simple obesity and obesity hyperlipemia treated with tooacupoint pellet pressure and body acupuncture. *J Tradit Chin Med.* 1991;11(3):22-6.
70. Tugrul Cabioglu M, Ergene N. Electroacupuncture Therapy for Weight Loss Reduces Serum Total Cholesterol, Triglycerides, and LDL Cholesterol Levels in Obese Women. *The American Journal of Chinese Medicine.* 2005;33(04):525-33.
71. Abdi H, Zhao R, Darbandi M, Ghayour-Mobarhan M, Tavallae S, Rahsepar AA, et al. The effects of body acupuncture on obesity: anthropometric parameters, lipid profile, and inflammatory and immunologic markers. *ScientificWorldJournal.* 2012;2012:603539.
72. Abdallah Ismail N, Ragab SH, Abd Elbaky A, Shorbib AR, Alhosary Y, Fekry D. Frequency of Fimcibutes and Bacteroides in gut microbiota in obese and normal weight Egyptian children and adults. *Arch Med Sci.* 2011;7(3):501-7.
73. Cho SH, Lee JS, Thabane L, Lee J. Acupuncture for obesity: a systematic review and meta-analysis. *Int J Obes (Lond).* 2009;33(2):183-96.
74. Lin XM, Li B, Du YH, Xiong J, Sun F. Systematic evaluation of therapeutic effect of acupuncture for treatment of simple obesity. *Zhongguo Zhen Jiu.* 2009;29(10):856-60.
75. Liang F, Koya D. Acupuncture: is it effective for treatment of insulin resistance? *Diabetes Obes Metab.* 2010;12(7):555-69.
76. Khan R, Ahmed A, Ismail FW, Abid S, Awan S, Shah H, et al. Perception and knowledge about dietary intake in patients with liver cirrhosis and its relationship with the level of education. *J Coll Physicians Surg Pak.* 2012;22(7):435-9.
77. Shaping B, Reduction C. Technology Proliferation Driven by Demand:Aliso Viejo, CA:Medical Insight, Inc; 2009.
78. Bernstein G, Hanke CW. Safety of liposuction: a review of 9478 cases performed by dermatologists. *J Dermatol Surg Oncol.* 1988;14(10):1112-4.
79. Mulholland RS, Paul MD, Chalfoun C. Noninvasive body contouring with radiofrequency, ultrasound, cryolipolysis, and low-level laser therapy. *Clin Plast Surg.* 2013;32(3):501-20.
80. Saed N, Kaminier M. New waves for fat reduction: high-intensity focused ultrasound. *Semin Cutan Med Surg.* 2011;32(1):26-30.
81. Shalom A, Wiser I, Brawer S, Azhari H. Safety and Tolerability of a Focused Ultrasound Device for Treatment of Adipose Tissue in Subjects Undergoing Abdominoplasty: A Placebo-Control Pilot Study. *Dermatologic Surgery.* 2013;39(5):744-51.
82. Zhou YF. High intensity focused ultrasound in clinical tumor ablation. *World J Clin Oncol.* 2012;3(1):8-27.
83. Stephan P, Kenkel M. Updates and advances in liposuction. *Aesthet Surg J.* 2010;30(1):83-97.
84. Teitelbaum SA, Burns J, Kubota J, Matsuda H, Otto MJ, Shirakabe Y, et al. Noninvasive body contouring by focused ultrasound: safety and efficacy of the Contour I device in a multicenter, controlled, clinical study. *Plast Reconstr Surg.* 2007;120(3):779-89.
85. Nestor MS, Newburger J, Zarraga MB. Body contouring using 655-nm low level laser therapy. *Semin Cutan Med Surg.* 2013;32(1):35-40.
86. Jackson RE, Stern FA, Neira R, Ortiz-Neira CL, Maloney J. Application of low-level laser therapy for noninvasive body contouring. *Lasers Surg Med.* 2012;44(3):231-7.
87. Avci P, Nyame TT, Gupta GK, Sadasivam M, Hamblin MR. Low-level laser therapy for fat layer reduction: a comprehensive review. *Lasers Surg Med.* 2013;45(6):349-57.
88. Jackson RE, Dedo DD, Roche GC, Turok DJ, Maloney RJ. Low-level laser therapy as a non-invasive approach for body contouring: a randomized, controlled study. *Lasers Surg Med.* 2009;41(10):799-809.
89. Janik RR, Avram MM. Cryolipolysis: a historical perspective and current clinical practice. *Semin Cutan Med Surg.* 2013;32(1):31-4.
90. Weiss RA. Noninvasive radio frequency for skin tightening and body contouring. *Semin Cutan Med Surg.* 2013;32(1):9-17.
91. Brightman L, Weiss E, Chapas AM, Karen J, Hale E, Bernstein L, et al. Improvement in arm and post-partum abdominal and flank subcutaneous fat deposits and skin laxity using a bipolar radiofrequency, infrared, vacuum and mechanical massage device. *Lasers in Surgery and Medicine.* 2009;41(10):791-8.
92. Winter ML. Post-pregnancy body contouring using a combined radiofrequency, infrared light and tissue manipulation device. *J Cosmet Laser Ther.* 2009;10(4):229-35.
93. Buchwald H, Avidor Y, Braunwald E, Jensen MD, Pories W, Fabrach K, et al. Bariatric surgery: a systematic review and meta-analysis. *JAMA.* 2004;292(4):372-37.
94. Bray GA, Ryan DH. Drug treatment of the overweight patient. *Gastroenterology.* 2007;132(6):2239-52.
95. Cheung BM, Cheung TT, Samaranayake NR. Safety of antiobesity drugs. *Ther Adv Drug Saf.* 2013;4(4):271-81.