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Review

Complementary and alternative therapies for obesity

Lucy Dey and Chun-Su Yuan*

Tang Center for Herbal Medicine Research, Committee on Clinical Pharmacology, and Department of Anesthesia & Critical Care, The Pritzker School of Medicine, The University of Chicago, Chicago, IL 60637

SUMMARY

Obesity is a serious medical disorder because it can cause a myriad of health problems, such as heart disease, hypertension, and adult-onset diabetes. While conventional medical treatment for obesity has limitations, there is enormous public enthusiasm for complementary and alternative treatments of obesity. This article reviews currently commonly used complementary and alternative therapies for obesity, such as medicinal herbs, nutritional supplements and acupuncture. Beneficial effects and possible adverse effects associated with these treatment are discussed.

Key words: Obesity; Complementary and alternative therapies

Obesity is defined as body weight 30% over the ideal body weight. Body mass index (BMI) has emerged as an indicator of obesity (Hollander, 2000; Negro, 2000). BMI is defined as weight in kg divided by height in meter squared (i.e., BMI=kg/m^2, or BMI=pound/$inch^2$×705). The American Heart Association (AHA) has adopted BMI as an indicator to measure adiposity. A person who has a BMI of greater than 25 is considered overweight and greater than 27 is considered obese.

Obesity is a chronic condition that affects approximately one-third of the United States population (KucZmarski *et al.*, 1997; Flegal *et al.*, 1998). Obesity is the second leading cause of preventable deaths in this country (Flegal *et al.*, 1998; McGinnis and Forge, 1993), and it causes or exacerbates many health problems, both independently and in association with other diseases. For example, it is associated with the development of coronary heart disease, type 2 diabetes, an increased incidence of several forms of cancer, respiratory complications (obstructive sleep apnoea) and osteoarthritis of large and small joints (Kopelman, 2000).

The economic burden of the condition is substantial. The weight-loss industry accrues about $33 billion each year. The estimated medical costs of treating obesity are about $238 billion per year, of which approximately $100 billion covers the cost of treating comorbid conditions (Negro, 2000).

FACTORS INFLUENCING OBESITY

Obesity is not a single disorder but a heterogeneous group of conditions with multiple causes. Body weight is determined by an interaction between genetic, environmental and psychological factors acting through the physiological mediators of energy intake and expenditure (Kopelman, 2000).

According to the first law of thermodynamics, obesity results from an imbalance between energy intake and energy expenditure. Energy expenditure can be divided into 3 major components. They are thermic effect of food, resting energy expenditure, and physical activity. Sympathetic nervous system controls part of energy expenditure process (de Jonge and Bray, 1997).

Elements of the system that control obesity are also presented as a feedback model (Bray, 1998, 2000): a controlled system that ingests, metabolizes,

*Correspondence: Chun-Su Yuan, MD, PhD. Department of Anesthesia & Critical Care, The University of Chicago Medical Center, 5841 S. Maryland Avenue, MC 4028, Chicago, IL 60637.
Tel: 82-73-702-1916; Fax: 82-73-834-0601; E-mail: cyuan @midway.uchicago.edu.

and stores food; afferent signals (e.g., cholecystokinin and leptin) that tell the brain about the internal and external environment; the central controller in the brain (e.g., serotonin, adrenergic and noradrenergic receptors in the hypothalamus) that transduces messages from the periphery into action; and the efferent or action system (e.g., endocrine and autonomic nervous system).

CONVENTIONAL THERAPIES

Current therapies for obesity include life style modification, pharmacological therapy, and less frequently, bariatric surgery, all which are summarized below.

Life Style Modification

Once weight begins to exceed the ideal body weight, lifestyle modification should be started. In patients with comorbidities, lifestyle modification should begin when the BMI is $\leq$25. Life style modification includes changes in the diet and addition of exercise. Dietary therapies include moderate calorie restriction, very low calorie diets (VLCDs), and alteration of diet composition (Hollander, 2000).

The caloric intake should be below the minimum amount necessary to maintain weight. A diet and exercise plan resulting in a reduction of 300 to 500 calories per day can result in approximately a 10 lb weight loss over 10 to 20 weeks. VLCDs are indicated when caloric restrictions have failed or when rapid weight reduction is required in a short period time. VLCDs limit daily caloric intake to 800 or fewer calories. Mineral nutrients and vitamin supplements are often needed since they are frequently inadequate in the VLCD (Hollander, 2000).

Pharmacological Therapy

When lifestyle modification does not produce adequate weight loss, pharmacological therapy may be initiated. Patients with BMI > 30 are candidates for pharmacological therapy. Patients with a BMI >27 who have concomitant obesity-related risk factors (e.g., cardiac disease, hypertension, and diabetes) should also receive pharmacological therapy.

There are three theoretical sites at which pharmacological therapy can intervene: energy intake, energy storage, and energy expenditure (Hollander, 2000). Antiobesity medication has been successful at modifying energy intake only. Energy intake can be modified by limiting food intake, such as blocking appetite, delaying gastric emptying, or modifying intestinal absorption of some or all nutrients. Two types of pharmacological therapies are currently available: the systematically acting anorectics that limit intake by suppressing appetite, and nonsystemic lipase inhibitor that interferes with fat absorption.

Systemically Acting Anorectics

Anorectics act on the central nervous system and include three classes of drugs: noradrenergic, serotonergics, and combination noradrenergic and serotogenic agents (Hollander, 2000).

Noradrenergic anorectics. Noradrenergic anorectics include phenylpropanolamine and phentermine, which stimulate norepinephrine release. There are few studies as to either short term or long term safety and efficacy of these drugs. In general, when given as monotherapy they appear to be minimally effective.

Serotonergic anorectics. Serotonergic anorectics include dexfenfluramine and fenfluramine. They act by increasing the release of serotonin and decreasing the uptake of serotonin. These two drugs were withdrawn from the market two years ago, when their combination was demonstrated to produce adverse cardiac effects, including valve abnormalities.

Combination noradrenergic serotonergic anoretics. Sibutramine is b-phenethylamine that selectively inhibits the reuptake of noradrenaline, serotonin and, to a lesser extent, dopamine. Data from a controlled clinical trial showed a dose related reduction in body weight up to 9.4% of their weight after sibutramine administration (Bray, 1999). Side effects of sibutramine include dry mouth, insomnia, headache, constipation, and gastrointestinal upset. Sibutramine may also increase blood pressure and heart rate (Hollander, 2000).

Nonsystemic Lipase Inhibitor

Orlistat is produced under the registered trademark Xenical. Also known as tetrahydrolipstatin, it is a

chemically synthesized derivative of lipstatin, which is naturally produced by *Streptomyces toxytricini* (Hadvary et al.,1988; Borgstrom, 1988). It blocks pancreatic lipase, thereby preventing the degradation of ingested triglycerides into fatty acids and monoglycerides. Thus, nondigested triglycerides are not absorbed and are excreted in the stool (Hollander, 2000). The most frequent side effects of orlistat are GI symptons, such as oily spotting, flatus with discharge, fecal urgency, fatty/oily stool, oily evacuation, increased defecation or fecal incontinence. Orlistat also reduces absorption of fat-soluble vitamins.

Others

Leptin. Leptin, an investigational compound, is a peptide hormone that appears to play a role in affecting fat metabolism. It has produced substantial weight loss in animals (Zhang *et al.*, 1994; Yuan *et al.*, 2000). A recent study of subcutaneous recombinant methionyl human leptin in lean and obese individuals showed that it produced a mean weight loss at 6 months of 5.4 kg (Heymsfield *et al.*, 1999). Although there were no clinically significant adverse effects, there was significant discomfort at the injection site. Leptin has also been shown to be clinically effective in those rare individuals who lack leptin (Farooqi *et al.*, 1999).

Bariatric Surgery

The purpose of bariatric surgery is to impede food intake. There are a number of surgical approaches involving either gastric stapling or gastric bypass. Surgical procedures are currently unsatisfactory in weight reduction because of their serious side effects (Blake *et al.*, 1991; Pi-Sunyer, 1992).

The ideal anti-obesity medication would induce loss of body fat without significant loss of lean body mass, would maintain the weight loss with long-term use, would be non-toxic with few or no side effects, would have no abuse potential or dependency issues, and be cost effective. None of the available therapies meets all of these criteria. Current available treatments, including medications, are palliative and are effective only while the treatment is being actively used. The limited long term effectiveness of conventional weight management is the impetus of major efforts aimed at searching alternative therapies. Among these therapies, medicinal herbs, nutritional supplementation, and acupuncture are commonly used.

ALTERNATIVE THERAPIES

Medicinal Herbs

Ma huang (Ephedra)

Ma haung (Chinese name), also known as desert herb contains ephedra, a compound that is similar to ephidrine. Dietary supplements that contain ephedra alkaloids (Ma haung) are widely promoted and used in the United States as a mean of losing weight and increasing energy. Ephedra has been shown to increase heart rate, affect blood pressure variably and increase 24 hour energy expenditure in humans (White *et al.*, 1997). These effects are probably associated with the thermogenic effect of direct β_1 and β_2 agonism (Shannon *et al.*, 1999).

Cardiovascular symptoms, such as hypertension, followed by palpitation, tachycardia, or both, and central nervous system side effects, such as stroke and seizures, were reported. Death and permanent disability were also noticed. The Food and Drug Administration (FDA) has proposed to establish the limits on the dose and duration of the use of ephedra, due to the recently reported adverse effects. The FDA also requested an independent review of reports of adverse events related to the use of supplements that contained ephedra alkaloids to assess causation and to estimate the level of risk the use of these supplements poses to the consumers (Haller and Benowitz, 2000). Haller and Benowitz (2000) reviewed 140 reports of adverse events related to the use of dietary supplements. Their report indicated that the use of dietary supplements that contain ephedra alkaloids may pose a health risk to some persons. These findings indicate the need for a better understanding of individual susceptibility to the adverse effects of such dietary supplements.

Ma huang is usually available in dried branchlets and tablet form, in combination with Guarana (see below). Some commercial weight

reduction products (e.g., Metabolife) contain a combination of Ma huang and guarana. The usual dosage for Ma haung is 20 mg ephedrine equivalent, and for guarana is 200 mg caffeine equivalent, 3 times daily (Morelli and Zoorob, 2000).

Guarana

Guarana is derived from the seeds of *Paullinia cupana*, and also known as brazilian cocoa. It contains the chief alkaloid caffeine, in addition to small amounts of theophylline and theobromine. Guarana is used by Brazilian Indians in a stimulating beverage similar to coffee or tea. Several studies showed that Guarana may be effective in treating obesity when it used with Ma huang.

A controlled study of 180 obese patients showed significantly greater weight loss using guarana, in combination with Ma huang, over a 24-week (Astrup *et al.*, 1992). However, Breum *et al.* (1994) reported that 54 percent of patients treated with guarana and Ma huang combination experienced central nervous system side effects, especially agitation, but noted that these side effects declined markedly after the first month of the treatment. In another study, the hemodynamic side effects, such as increased systolic, but not diastolic, blood pressure and increased heart rate, were transient while the thermogenic effects on energy expenditure were persistent (Astrup and Toubro, 1993). As mentioned above, the usual dosage is for guarana is 200 mg caffeine equivalent 3 times daily.

Garcinia cambogia and garcinia indica

Garcinia cambogia and garcinia indica which is also known as Brindleberry is isolated from the fruit of Malabar tamarind. It is native to southern India where it is dried and used extensively in curries.

Garcinia cambogia and garcinia indica is now incorporated into many commercial weight loss products. Hydroxycitric acid is the active ingredient and it competitively inhibits the extramitochondrial enzyme adenosine triphosphate-citrate (pro-3S)-lyase. In many *in vitro* and *in vivo* studies, investigators demonstrated that hydroxycitric acid not only inhibited the actions of citrate cleavage enzyme and suppressed fatty acid synthesis (Lowenstein, 1971), but also increased rates of hepatic glycogen synthesis (Sullivan *et al.*, 1974), suppressed food intake (Sullivan *et al.*, 1973), and decreased body weight gain (Nageswara *et al.*, 1988).

Six published human studies have examined hydroxycitric acid in weight loss. Of these studies, five some reported positive results, but all had experimental inadequacies (Heymsfield *et al.*, 1998). A randomized controlled study over a 12 week period found no differences in weight loss between a group of obese individuals given 3,000 mg of Garcinia cambogia (50% hydroxycitric acid) daily and a control group given placebo (Heymsfield *et al.*, 1998). However, this study did not measure either the appetite suppressant effect or the plasma concentration of hydroxycitric acid. Opponents of this study have postulated that the high fiber diet used in the study may have limited the bioavailability, thus rendering the study ineffective and leading to the disappointing results (Firenzuoli *et al.*, 1999). It appears that hydroxycitrate may offer a safe, natural aid for weight loss when taken at 500mg three times daily (Murray and Pizzorno, 1999).

Green Tea

Green tea has been widely consumed in China and Japan for many centuries. Using *in vitro* intercapsular brown adipose tissue system, Dulloo et al. (2000) showed that the effect of green tea on the thermogenesis and fat oxidation may be attributed to an interaction between its high content in catechin-polyphenols and caffiene on sympathetic activity (Dulloo *et al.*, 2000). In *in vivio* animal experiments, Kao *et al.* (2000) demonstrated that green tea epigallocatechin gallate reduced food intake. Human studies by Dulloo *et al.* (1999) observed that administration of capsules containing the green tea extract resulted in a significant increase in 24 hour energy expenditure, thermogenesis, fat oxidation and urinary noradrenalin relative to placebo. These findings could be of value in assisting the management of obesity. The dosage used in the clinical study is green tea extract (50 mg caffiene and 90 mg epigallocatechin gallate). No adverse effects have been reported.

Gymnema sylvestre (Gurmar)

The leaves of *Gymnema sylvestre* have been highly valued as folk medicine for diabetes in India for more than 2,000 years (Nadkarni, 1982). Gymnemic acid, a mixture of triterpene glycosides extracted from the leaves of *Gymnema sylvestre*, can improve glucose tolerance and decrease the blood glucose level in diabetic patients (Baskaran *et al.*, 1990; Shanmugasundaram *et al.*, 1990). On the basis of this effect, gymnemic acid has been suggested as a useful agent in therapy for obesity (Terasawa *et al.*, 1994), since over ingestion of carbohydrates is a well documented cause of obesity. Wang *et al.* (1998) observed that gymnemic acid also potently inhibits the oleic acid absorption in the rat intestine which was dose dependent and reversible. To date, no controlled studies have been conducted to evaluate the efficacy of Gymnema extract on obesity.

The recommended dose of Gymnema extract is 400 mg/day. An undesirable effect of this agent is that it reduces or abolishes the taste sensation of sweetness and bitterness (Mozersky *et al.*, 1999).

Ginseng

There are over a dozen articles reporting the effects of ginseng on animal body weight changes. However, in most cases, the report on ginsengs body weight effects was based on one of the measurements in the study, rather than being the primary goal of the project. Interestingly, these results are highly variable: six articles showed an increase in body weight effect, three showed a decreased effect, and another four showed no effect.

Several studies reported an increase in body weight after treatment with *Panax ginseng* root. Rats fed a diet containing purified ginseng saponin extract (Rhee *et al.*, 1982; Rim *et al.*, 1997), and ginseng root extract (Hong, 1972; Eui *et al.*, 1978) showed an increase in body weight. In addition, some studies reported that treatment with *Panax ginseng* extract or ginsenosides prevented stress-associated weight loss (Fujimoto *et al.*, 1989; Zierer, 1991). Other studies reported that *Panax ginseng* root had a body weight reducing effect. Park et al. (1998) observed that red ginseng total saponins caused a significant drop in the body weight of rats. A single high dose of red ginseng total saponins significantly reduced the weight of rats and mice (Kim *et al.*, 1998). Administration of panaxatriol (isolated from *Panax ginseng* root) to healthy mice suppressed their maturity-associated increase in body weight (Kim *et al.*, 1990). Results of other studies failed to show an association between ginseng and body weight (Hong *et al.*, 1976; Hess, 1982, 1983; Murphy *et al.*, 1998). It is important to point out that these studies used different ginseng preparations and components in different animal species and models.

A clinical trial (Sotaniemi *et al.*, 1995) that investigated anti-diabetic effects of ginseng root reported that in addition to an improvement in fasting blood glucose levels, the subjects experienced a reduction in body weight. In this study of patients with type 2 diabetes, patients in both the control and ginseng-treated group were encouraged to reduce body weight by exercise and food intake control. Thus, patients in the ginseng-treated group as well as the placebo group loss weight. It appears that anti-obese effect of ginseng is inconclusive.

The recommended daily ginseng dosage is 1-2 g of the crude root, or 200-600 mg of standardized extracts (Schulz et al., 1998). As the possibility of hormone-like or hormone-inducing effects cannot be ruled out, some authors suggest limiting treatment to 3 months (Schulz *et al.*, 1998).

Kelp

Kelp generically refers to seaweed species including Laminaria, Macrocystitis, Nereocystis, and Fucus. It has been used as anti-obesity agent presumably by supplying iodine, hence increasing thyroid hormone production with consequent increased metabolism and removal of fat. Iodine content is different in kelp products. Hyperthyroidism is reported after using kelp product (Foster and Tyler, 1999). Potassium iodide content may result in hypersensitivity reactions in sensitive patients. Concomitant use of kelp with levothyroxine could result in excessive replacement resulting in typical symptoms of hyperthyroidism (Miller, 1998). Since kelp and related seaweed products contain sodium, they should consequently be avoided by those who must restrict their salt intake. In addition, using any thyroid hormone-related

product to control body weight is inadvisable and should be discouraged.

Capsaicin

Capsaicin is the major pungent principle in various species of capsaicin fruits such as hot chilli peppers and has long been globally used as an ingredient of spices, preservatives and medicines (Suzuki and Iwai, 1984).

Dietary supplementation of capsaicin in high fat diets lowered the peripheral adipose tissue weight and serum triglyceride concentration in rats due to enhancement of energy metabolism (Kawada et al., 1986a; 1986b). Watanabe *et al.*, (1987; 1988) have investigated neurophysiolgical functions of capsaicin and have demonstrated that capsaicin increases energy metabolism by catecholamine secretion from the adrenal medulla through sympathetic activation via the central nervous system. In a human study, Yoshioka *et al.*, (1995) observed that energy expenditure increased immediately after the meal containing red pepper, where as this enhancement of energy metabolism by a red pepper diet was inhibited after the administration of b-adrenergic blocker, propranolol. In a recent human study, Matsumoto *et al.*, (2000) have investigated the effect of capsaicin on the sympathetic nervous system activity and energy metabolism in 16 lean and obese young women, age and height matched. Their observation supported previous investigations and reinforce the finding that the altered specific sympathetic function related to thermogenic capacity may be a significant sign reflecting the autonomic state in human obesity. However, data from their study also indicated that the reduced sympathetic responsiveness to thermogenic perturbation such as that found in capsaicin diet, which may cause impaired diet-induced thermogenesis and further weight gain, could be an important etiological factor leading to obesity in young women. The dose in the study was 3 mg of capsaicin in spicy yellow curry sauce.

Guggul gum (Gugulipid)

This resin from the myrrh species, in addition to being used as a cholesterol lowering agent, is found in some over-the-counter diet products. Gugulipid has been shown to stimulate the release of endogenous thyroid hormone in rats (Tripathi *et al.*, 1984), although there are no additional animal or human studies supporting this claim. Gugulipid is available in the extract form, powdered resin and concentrated tablets.

Nutritional supplements

Chromium

Chromium has lately gained a great deal of public attention as an aid to weight loss. One of the key goals for enhancing weight loss is to increase insulin sensitivity of cells throughout the body, based on the fact that chromium plays an important role in cellular sensitivity to insulin (Anderson, 1998).

Preliminary studies with chromium demonstrated that chromium picolinate promoted an increase in lean body weight percentage and a decrease in percentage of body fat, which may lead to weight loss (Evans, 1993; Anderson, 1998). Greater muscle mass means greater fat burning potential. Chromium supplementation also improves blood sugar control and lowers cholesterol and triglyceride levels (Press *et al.*, 1993).

Several forms of chromium are available, such as chromium picolinate, chromium polynicotinate, chromium chloride, and chromium-enriched yeast. The recommended chromium dose is 200-400 μg daily (Murray and Pizzorno, 1999). There have been reports of possible tissue accumulation and damage to DNA and renal damage following long-term ingestion of large doses of chromium (Sterns *et al.*, 1995; Cerulli *et al.*, 1998).

5-Hydroxytryptophan (Serotonin)

There are 3 clinical studies with 5-Hydroxytryptophan or 5-HT in overweight women (Ceci *et al.*, 1989; Cangiano *et al.*, 1991; 1992) and these studies showed that 5-HT appeared to promote weight loss by promoting satiety, leading to fewer calories being consumed at meals. Besides mild nausea, no other side effects were reported.

The recommended dosage to begin at is 5-HT at 50-100 mg 20 minutes before meals for 2 weeks, and then double the dosage to a maximum of 300 mg if weight loss is less than 1 pound per week.

Higher dosage of 5-HT is associated with nausea, but this symptom disappears after 6 weeks of use (Murray and Pizzorno, 1999).

L-Carnitine

L-Carnitine is an amino acid found in meat and dairy products, made from the amino acids, lysine and methionine, in the liver and kidney. The proposed action is it increases the fat metabolism. Two studies have shown no changes in the rate of fat oxidation following L-Carnitine supplementation (Sulkers *et al.*, 1990; Vukovich *et al.*, 1994). Control studies examining the effects of L-Carnitine on weight loss have not been published. Oral supplementation may cause diarrhea, but no other major adverse effects have been noted.

Medium-chain triglycerides

Medium-chain triglycerides (MCTs) are saturated fats (extracted from coconut oil) that range in length from 6 to 12 carbon chains. Unlike regular fats and long-chain triglycerides (LCTs), MCTs appear to promote weight loss rather than weight gain. MCTs may promote weight loss by increasing thermogenesis (Baba *et al.*, 1982). A study demonstrated that MCT oil given over a 6 day period can increase diet induced thermogenesis by 50% (Hill *et al.*, 1986). In order to gain the benefit from MCTs, a diet must remain low in LCTs. MCTs can be used as an oil for salad dressing, a bread spread, or simply taken as a supplement. Dosage recommendation for MCTs is 1-2 tablespoons per day. Diabetics and individuals with liver disease should be monitored very closely when using MCTs as they may develop ketoacidosis.

Coenzyme Q_{10}

Coenzyme Q_{10} is an essential compound required in the transport and breakdown of fatty acids into energy. In one study, Coenzyme Q_{10} levels were found to be low in 52% of overweight subjects tested. In the study, nine subjects (five with low Co Q_{10} levels and four with normal levels) were given 100 mg/day of Co Q_{10} along with low calorie diet. After 9 weeks, mean weight loss in the Co Q_{10} deficient group was 29.7 pounds, compared with 12.8 pounds in those with initially normal levels of Co Q_{10} (Van Gaal L *et al.*, 1984). The recommended dosage is 100-300 mg/day.

Chitosan

Chitosan is an amino polysaccharide derived from the powdered shells of marine crustaceans such as prawns and crabs. Some clinical studies have shown lipid lowering effects (Ventura, 1996), as well as weight loss (Maezaki *et al.*, 1993; Abelin and Lassus, 1994; Veneroni *et al.*, 1996). The proposed action of chitosan is it binds to dietary fat, preventing digestion and storage. However, in a recent controlled trial in 17 people, weight reduction effect of chitosan was not confirmed (Pittler *et al.*, 1999). Risks such as steatorrhoea and malabsorption of essential nutrients are possible.

Fiber supplements

Increasing the amount of dietary fiber promotes weight loss. The best fiber sources for weight loss are psyllium, chitin, guar gum, glucumannan, gum karaya and pectin, which are rich in water-soluble fibers. When taken with water before meals, these fiber sources bind to water in the stomach to form a gelatinous mass, which induces a sense of satiety (Murray and Pizzorno, 1999). Fiber supplements have been shown to enhance blood sugar control, decrease insulin levels, and reduce the number of calories absorbed by the body (Spiller, 1994). The most impressive results in weight loss studies have been achieved with guar gum, a water soluble fiber obtained from the Indian cluster bean (*Cyamopsis tetragonoloba*).

The starting dose should be between 1 and 2 g before meals and at bed time and gradually increase the dosage to 5 g (Murray and Pizzorno, 1999). Water soluble fibers are fermented by intestinal bacteria; therefore, a great deal of gas can be produced, leading to increased flatulence and abdominal discomfort.

Acupuncture

One indication for acupuncture is obesity (Cassell and Larocca, 1994). Ernst (1997) reviewed the results of sham/placebo-controlled clinical trials of acupuncture/acupressure for obesity. His goal was to determine whether or not these therapies have specific effects on appetite and body weight reduction. Two studies suggested a positive effect

of acupuncture on appetite and body weight (Giller, 1975; Shafshak, 1995), whereas two other trials showed no effect of acupuncture or acupressure (Mok *et al.*, 1976; Allison *et al.*, 1995). Richards and Marley (1998) studied the effectiveness of transcutaneous electrical nerve stimulation of specific auricular acupuncture points on appetite suppression. They observed that frequent stimulation of specific auricular acupuncture point is an effective method of appetite suppression which leads to weight loss. It has been postulated that acupuncture stimulation of certain parts of the ear can reduce appetite by activating the satiety center within the hypothalamus (Huang *et al.*, 1996), or control stress and depression via endorphin and dopamin production (Richards and Marley, 1998).

CONCLUSIONS

Alternative therapies, especially herbal medicines, are increasingly used by obese people and some non-obese people who want to lose weight. Ephedra (Ma huang) and ephedra-containing products are often effective, especially at high doses of ephedra alkaloids. However, ephedra may cause significant cardiovascular and central nervous system adverse effects, particularly in individuals with increased susceptibility to these effects. Most herbs and nutritional supplements are used in conjunction with prescription anti-obese drugs. Thus, potential adverse herb-drug interactions should also be kept in mind for patients who are receiving conventional pharmacological agents. In addition, since a single herb (e.g., ephedra) may be used in different commercial anti-obese dietary preparations, consumers should not take more than one product simultaneously to avoid any undesirable additive effects.

REFERENCES

Abelin J, Lassus AL. (1994) 112 Bipolymar-Fat [binder] as a weight reducer in patients with moderate obesity. Medical Research report. A study performed at Ars Medicinar, Heisinki, August-October.

Allison DB, Krie K, Heshka S, Heymsfield SB. (1995) A randomised placebo-controlled clinical trial of an acupressure device for weight loss. *Int. J. Obesity* **19**, 653-658.

Anderson RA. (1998) Effects of chromium on bodycomposition and weight loss. *Nutr. Rev.* **56**(9), 266-270.

Astrup A, Breum L, Toubro S, Hein P, Quadde F. (1992) The effect and safety of an ephedrine/caffeine compound compare to ephidrine, caffeine and placebo in obese subjects on an energy restricted diet. A double blind trial. *Int. J. Obes. Relat. Metab. Disord.* **16**, 269-277.

Astrup A, Toubro S. (1993) Thermogenic, metabolic and cardiovascular responses to ephedrine and caffeine in man. *Int. J. Obes. Relat. Metab. Disord.* 17 (suppl 1): S41-S43.

Baba N, Bracco EF, Hashim SA. (1982) Enhanced thermogenesis and diminished deposition of fat in response to overfeeding with diet containing medium chain triglyceride. *Am. J. Clin. Nutr.* **35**, 678-682.

Baskaran, K, Kizar AB, Radha SK, Shanmugasundaram ER. (1990) Antidiabetic effect of a leaf extract from *Gymnema sylvestre* in non-insulindependent diabetesmellitus patients. *J. Ethnopharmacol.* **30**, 295-300.

Blake M, Fazio V, Brien PO. (1991) Assessment of nutrient intake in association with weight loss after gastric restrictive procedures for morbid obesity. *Aust. N. Z. J. Surg.* **61**, 195-199.

Borgstrom B. (1988) Mode of action of tetrahydrolipstatin, a derivative of the naturally occuring lipase inhibitor lipstatin. *Biochem. Biophys. Acta* **962**, 308-316.

Bray GA. (2000) *Diabetes and Endocrinology Clin Mgmt* Vol. 3 - Physiology and Consequences of obesity, Medscape, Inc.

Bray GA. (1998) Drug treatment of obesity: Don't throw the baby out with the bath water. *Am. J. Clin. Nutr.* **67**, 1-4.

Bray GA, Blackburn GL, Ferguson JM, Greenway FL, Jain AK, Mendel CM, Mendels J, Ryan DH, Schwartz SL, Scheinbaum ML, Seaton TB. (1999) Sibutramine produces dose-related weight loss. *Obes. Res.* **7**, 189-198.

Breum L, Pedersen JK, Ahlstrom F, Frimodt-Moller J. (1994) Comparison of an ephedrine/caffeine combination and dexfluramine in the treatment of obesity. A double-blind multi-center trial in general practice. *Int. J. Obes. Relat. Metab. Disord.* **18**, 99-103.

Cangiano C, Ceci F, Cairella M, Cascino A, Del Ben M, Laviano A, Muscaritoli M, Rossi-Fanelli F. (1991) Effectts of 5-hydroxytryptophan on eating behavior and adherence to dietary prescriptions in obese adult subjects. *Adv. Exp. Med. Biol.* **294**, 591-593.

Cangiano C, Ceci F, Cascino A, Del Ben M, Laviano A, Muscaritoli M, Antonucci F, Rossi-Fanelli F. (1992) Eating behavior and adherence to dietary prescriptions in obese adult subjects treated with 5-hydroxytryptophan. *Am. J. Clin. Nutr.* **56**, 863-867.

Cassell DK, Larocca FE. (1994) The encyclopedia of obesity and eating disorders. Fact on File, Inc. New York.

Ceci F, Cangiano C, Cairella M, Cascino A, Del Ben M, Muscaritoli M, Sibilia L, Rossi Fanelli F. (1989) The effects of oral 5-hydroxytryptophan administration on feeding behavior in obese adult female subjects. *J. Neural. Transm.* **76**, 109-117.

Cerulli J, Grabe DW, Gauthier l, Malone M, McGoldrick MD. (1998) Chromium picolinate toxicity. *Ann. Pharmacother.* **32**, 428-431.

de Jonge L, Bray GA. (1997) The thermic effect of food and obesity: a critical review. *Obes. Res.* **5**, 622-631.

Dulloo AG, Duret C, Rohrer D, Girardier L, Mensi N, Fathi M, Chantre P, Vandermander J. (1990) Efficacy of a green tea extract rich in catechin polyphenols and caffiene in increasing 24-h energy expenditure and fat oxidation in humans. *Am. J. Clin. Nutr.* **70**, 1040-1045.

Dulloo AG, Seydoux J, Girardier L, Chantre P, Vandermander J. (2000) Green tea and thermogenesis: interactions between catechin-polyphenols, caffeine and sympathetic activity. *Int. J. Obes.* **24**, 252-258.

Ernst E. (1997) Acupuncture/Acupressure for weight reduction? Asystemic review. *Wien. Klin. Wochenschr.* **109**(2), 60-62.

Eui S, Kim BY, Paik TH, Joo CN. (1978) The effect of ginseng on alcohol metabolism. *Hanguk Saenghwa Hakhoe Chi.* **11**, 1-15.

Evans GW. (1993) Chromium picolinate is an efficacious and safe supplement. *Int. J. Sport. Nutr.* **3**, 117-122.

Farooqi IS, Jebb SA, Langmack G, Lawrence E, Cheetham CH, Prantice AM, Hughes IA, McCamish MA, ORahilly S. (1999) Effects of recombinant leptin therapy in a child with congenital leptin deficiency. *N. Engl. J. Med.* **341**, 879-884.

Firenzuoli F, Gori L. (1999) Garcinia cambogia for weight loss. *JAMA.* **282**, 234.

Flegal KM, Carroll MD, Kuczmarski RJ, Johnson CL. (1998) Overweight and obesity in the United States: prevalence and trends, 1960-1994. *Int. J. Obes.* **22**, 39-47.

Foster S, Tyler VE. (1999) *Tylers honest herbal.* A sensible guide to the use of herbs and related remedies. Foster S, Tyler VE , eds. Fourth edition Haworth Press, Inc Binghamton, NewYork. 233-239.

Fujimoto K, Sakata T, Ishimaru T, Etou H, Ookuma K, Mamoru K, Machidori H. (1989) Attenuation of anorexia induced by heat or surgery during sustained administration of ginsenoside Rg_1 into rat third ventricle. *Psychopharmacol.* **99**, 257-260.

Giller RM. (1975) Auricular acupuncture and weight reduction. A controlled study. *Am. J. Acupuncture* **3**, 151-153.

Hadvary P, Lengsfeld H, Wolfer H. (1988) Inhibition of pancreatic lipase in vitro by the covalent inhibitor tetrahydrolipstatin. *Biochem. J.* **256**, 357-361.

Haller CA, Benowitz NL. (2000) Adverse cardiovascular and central nervous system events associated with dietary supplements containing ephedra alkaloids. *N. Engl. J. Med.* **343**, 1833-8.

Hess FG Jr, Parent RA, Stevens KR, Cox GE, Becci PJ. (1983) Effects of subchronic feeding of ginseng extract G115 in beagle dogs. *Food Chem. Toxicol.* **21**, 95-97.

Hess FG Jr., Parent RA, Cox GE, Stevens KR, Beci PJ. (1982) Reproduction study in rats of ginseng extract G115. *Food Chem. Toxicol.* **20**, 189-192.

Heymsfield SB, Allison DB, Vasselli JR, Pietrobelli A, Greenfield D, Nunez C. (1998) Garcinia cambogia (hydroxycitric acid) as a potential antiobesity agent: a randomized controlled trial. *JAMA.* **280**, 1596-1600.

Heymsfield S, Greenberg A, Fujioka K, Dixon RM, Kushner R, Hunt T, Lubina JA Patane J, Self B, Hunt P, McCamish M. (1999) Recombinant leptin for weight loss in obese and lean adults: a randomized, controlled, dose-escalation trial. Recombinant leptin for weight loss in obese and lean adults. *JAMA.* **282**, 1568-1575.

Hill JO, Peters JC, Yang D, Sharp T, Kaler M, Abumrad NN, Greene HL. (1986) Thermogenesis in humans during over feeding with medium-chain triglycerides in man. *Am. J. Clin. Nutr.* **44**, 630-634.

Hollander P. (2000) Strategies for reducing weight to increase insulin sensitivity. *Drug Benefit Trends* Cliggott Publishing Co., Division of SCP/ Cliggott Communications, Inc. **12**, (Suppl A): 57-65.

Hong BJ, Kim CI, Kim UH, Rhee YC. (1976) Effect of feeding ginseng crude saponin on body weight gain and reproductive function in chicken. *Hanguk Chuksan Hakhoe Chi.* **18**, 355-361.

Hong SA. (1972) Effects of panax ginseng on the general behavioral activity and survival time of food deprivation in rats. *Choesin Uihak.* **15**, 87-91.

Huang MH, Yang RC, Hu SH. (1996) Preliminary results of triple therapy for obesity. *Int. J. obes.* **20**, 830-836.

Kao YH, Hiipakka RA, Liao S. (2000) Modulation of endocrine systems and food intake by green tea epigallocatechin gallate. *Endocrinology* **141**, 980-987.

Kawada T, Hagiharaa K, Iwai K. (1986a) Effects of capsaicin on lipid metabolism in rats fed a high fat diet. *J. Nutr.* **116**, 1272-1278.

Kawada T, Watanabe T, Takaishi T, Tanaka T, Iwai K. (1986b) Capsaicin-induced b-adrenergic action on energy metabolism in rats: Influence of capsaicin on oxygen consumption, the respiratory quotient, and substrate utilization. *Proc. Soc. Exp. Biol. Med.* **183**, 250-256.

Kim JG, Park CW, Lee YS, Kim JG, Kim KS, Cho DH.

(1998) Acute toxicity study of red ginseng total saponin in rats and mice. *J. Toxicol. Public Health* **14**, 69-75.

Kim YS, Kang KS, Kim S, II. (1990) Effects of a cytotoxic substance, panaxytriol from Panax Ginseng C.A. Meyer on the immune responses in normal mice. *Korean J. Toxicol.* **6**, 13-19.

Kopelman PG. (2000) Obesity as a medical problem. *Nature* **404**, 635-651.

Kuczmarski RJ, Carroll MD, Flegal KM, Troiano RP. (1997) Varying body mass index cutoff points to describe overweight prevalence among U.S. adults: NHANES III (1988-1994). *Obes. Res.* **5**, 542-548.

Lowenstein JM. (1971) Effect of (-0-hydroxycitrate on fatty acid synthesis by rat liver in vivo. *J. Biol. Chem.* **246**, 629-632.

Maezaki Y, Tsuji K. (1993) Hypochlosterolaemic effect of chitosan in adult males. *Biosc. Biochem. Biotech.* **57**, 1439-1444.

Matsumoto T, Miyawaki C, Ue H, Yuasa T, Miyasuji A, Moritani T. (2000) Effects of Capsaicin- containing yellow curry sauce on sympathetic nervous system activity and diet-induced thermogenesis in lean and obese young women. *J. Nutr. Sci. Vitaminol.* **46**, 309-315.

McGinnis JM, Forge WH. (1993) Actual causes of death in the United States. *JAMA.* **270**, 2207-2212.

Miller LG. (1998) Herbal Medications, Nutraceuticals, and Diabetes. In: Miller LG, Murray WJ, eds. *Herbal Medicinals, A Clinicians Guide*, Binghamton, NewYork, Pharmaceutical Products Press, Imprint of the Haworth Press, Inc. 115-133.

Mok MS, Parker LN, Voina S, Bray GA. (1976) Treatment of obesity by acupuncture. *Am. J. Clin. Nutr.* **29**, 832-835.

Morelli V, Zoorob RJ. (2000) Alternative therapies: Part 1. Depression, diabetes, obesity. *Am. Fam. Phys.* **62**(5), 1051-1060.

Mozersky RP. (1999) Herbal products and supplemental nutrients used in the management of diabetes. *JAOA.* **99**(12), S4-S9.

Murphy LL, Cadena RS, Chavez D, Ferraro JS. (1998) Effect of American ginseng (*Panax quinquefolium*) on male copulatory behavior in the rat. *Physiol. Behav.* **64**, 445-450.

Murray MT, Pizzorno Jr JE. (1999) Obesity. In: Pizzorno Jr JE , Murray MT, eds. *Textbook of Natural Medicine.* 2nd Edition, Churchill Livingstone publishing, 1429-1439.

Nadkarni KM. (1982) *Gymnema sylvestre*, R.Br. or Asclepias geminata. In : Indian Materia Medica. Nadkarni KM, ed. Popular Prakashan Pvt. Ltd., Bombay. **1**, 596-599.

Nageswara Rao R, Sakeriak KK. (1988) Lipid-lowering and antiobesity effect of (-) hydroxycitric acid. *Nutr. Res.* **8**, 209-212.

Negro AD. (2000) Its time to treat Obesity. American Heart Association Scientific Sessions.

Park CW, Kim JG, Lee YS, Kim GJ, Kim KS, Cho DH. (1998) Subacute toxicity study of red ginseng total saponin in rats. *J. Toxicol. Public Health* **14**, 77-82.

Pi-Sunyer FX. (1992) Obesity. In: Cecil Textbook of Medicine. Wyngaarden JB, Smith LH and Bennett JC, eds. Saunders, Philadelphia, 1162-1170.

Pittler MH, Abbot NC, Harkness EF, Ernst E. (1999) Randomized, double-blind trial of chitosan for body weight reduction. *Eur. J. Clin. Nutr.* **53**, 379-381.

Press RI, Gellaer J, Evans GW. (1993) The effect of chromium picolinate on serum cholesterol and apolipoprotein fractions in human subjects. *Western J. Med.* **152**, 41-45.

Rhee DK, Lim CJ, Kim DH, Hong SK, Park EH, Han YN. (1982) Studies on the acute and subacute toxicity of ginseng saponin. *Yakhak Hoe Chi.* **26**, 209-214.

Richards D, Marley J. (1998) Stimulation of auricular acupuncture points in weight loss. *Aust Fam Physician* 27 Suppl **2**, 73-77.

Rim KT, Choi JS, Lee SM, Cho KS. (1997) Effect of ginsenosides from red ginseng on the enzymes of cellular signal transduction system (Korean). *Koryo Insam Hakhoechi.* **21**, 19-27.

Schulz V, Hansel R, Tyler VE. (1998) Rational phytotherapy. In: *Agents that Increase Resistance to Diseases.* New York: Springer-Verlag. 269-272.

Shafshak TS. (1995) Electuroacupuncture and exercise in body weight reduction and their application in rehabilitating patients with knee osteoarthritis. *Am. J. Clin. Med.* **13**, 15-25.

Shanmugasundaram ER, Rajeswari G, Baskaran, K, Rajesh KBR, Radha SK, Kizar AB. (1990) Use of *Gymnema sylvestre* leaf extract in the control of blood glucose in insulin dependent diabetesmellitus. *J. Ethnopharmacol.* **30**, 281-294.

Shannon Jr, Gottesdiener K, Jordan J, Chen K, Flattery S, Larson PJ, Candelore MR, Gertz B, Robertson D, Sun M. (1999) Acute effect of ephidrine on 24-h energy balance. *Clin. Sci.* (Colch). **96**, 483-491.

Sotaniemi EA, Haapakoski E, Rautio A. (1995) Ginseng therapy in non-insulin-dependent diabetic patients. *Diabetes Care.* **18**, 1373-1375.

Spiller GA.(1994) Dietary fiber in health and nutrition. Boca Raton, FL: CRC Press.

Stearns DM, Belbruno JJ, Wetterhahn KE. (1995) A prediction of chromium (111) accumulation in humans from chromium dietary supplements. *FASEB J.* **9**, 1650-1657.

Sulkers EJ, Lafeber HN, Degenhart HJ, Przyrembel H, Schlotzer E, Sauer PJ. (1990) Effects of high carnitine supplementation on substrate utilization in low-birth-weight infants receiving total parentral nutrition. *Am. J. Clin. Nutr.* **52**, 889-894.

Sullivan AC, Triscari J, Hamilton JG, Neal Miller O. (1973) Effect of (-)-hydroxycitrate upon the accumulation of lipid in the rat: appetite. *Lipids* **9**, 129-134.

Sullivan AC, Triscari J, Neal Miller O. (1974) The influence of (-)- hydroxycitrate on in vivo rates of hepatic glycogenesis: lipogenesis and cholesterol genesis. *Fed. Proc.* **33**, 656.

Suzuki T, Iwai K. (1984) Constituents of red pepper spices: Chemistry, pharmacology and food science of the pungent principle of Capsicum species. In: The Alkaloids. Bross A. ed. Academic Press. Newyork. **23**, 227-229.

Terasawa H, Miyoshi M, Imoto T. (1994) Effects of long term administration of *Gymnema sylvestre* watery-extract on variations of body weight, plasma glucose, serum triglyceride, total cholesterol and insulin in Wistar fatty rats. *Yonago Acta Med.* **37**, 117-127.

Tripathi YB, Malhotra OP, Tripathi SN. (1984) Thyroid stimulation action of Z-guggulsterone obtained from Commiphora mukul. *Planta Med.* **1**, 78-80.

Van Gaal L. (1984) Exploratory study of coenzyme Q_{10} in obesity. In: Folkers K, Yamamura Y, eds. Biomedical and clinical aspects of coenzyme Q_{10}. Amsterdam: Elsevier Science. **4**, 369-373.

Veneroni G, Veneroni F, Contos S. (1996) Effect of a new chitoson on hyperlipidaemia and overweight in obese patients. In: Muzzarelli RAA, ed. *Chitin enzymology*, Ancona, Italy: Atec Edizioni, **2**, 63-67.

Ventura P. (1996) Lipid lowering activity of chitosan, a new dietary integrator. In: Muzzarelli RAA, ed. *Chitin enzymology*. Ancona, Italy: Atec Edizioni **2**, 55-62.

Vukovich MD, Costill DL, Fink WJ. (1994) Carnitine supplementation: effect on muscle carnitine and glycogen content during exercise. *Med. Sci. Sports Exerc.* **26**, 1122-1129.

Wang LF, Luo H, Imoto T, Hiji Y, Sasaki T. (1998) Inhibitory effect of gymnemic acid on intestinal absorption of oleic acid in rats. *Can. J. Physiol. Pharmacol.* **76**, 1017-1023.

Watanabe T, Kawada T, Iwai K. (1987) Enhancement by capsaicin of energy metabolism in rats through secretion of catecholamine from adrenal medulla. *Agric. Biol. Chem.* **51**, 75-79.

Watanabe T, Kawada T, Kurosawa M, Sato A, Iwai K. (1988) Adrenal sympathetic efferent nerve and catecholamine secretion excitation caused by capsaicin in rats. *Am. J. Physiol.* **255**, E23-E27.

White LM, Gardner SF, Gurley BJ, Marx MA, Wang PI. (1997) Pharmacokinetics and cardiovascular effects of ma-huang (Ephedra sinica) in normotensive adults. *J. Clin. Pharmacol.* **37**, 116-22.

Yoshioka M, Lim K, Kikuzato S, Kionaga A, Tanaka H, Shindo M, Suzuki M. (1995) Effects of red-pepper diet on the energy metabolism in men. *J. Nutr. Sci. Vitaminol.* **41**, 647-656.

Yuan CS, Attele AS, Zhang L, Lynch JP, Xie JT, Shi ZQ. (2000) Leptin reduces body weight gain in neonatal rats. *Pediatr. Res.* **48**, 380-383.

Zhang Y, Proenca R, Maffei M, Barone M, Leopold L, Friedman JM. (1994) Positional cloning of the mouse obese gene and its human homologue. *Nature* **372**, 425-432.

Zierer R. (1991) Prolonged infusion of *Panax ginseng* saponins into the rat does not alter the chemical and kinetic profile of hormones from the posterior pituitary. *J. Ethnopharmacol.* **34**, 269-274.