

Could nutraceuticals be a further weapon in the battle for weight loss?

Nutraceuticals are a growing sector of the supplements market. Several that have been the subject of scientific and medical research are currently being marketed as aids to weight loss. In this article, **Georgina Boon** and **Brian Lockwood** examine the issue



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In the UK, as in many other developed countries, we are experiencing a growing obesity epidemic. Between 1993 and 2003 the number of clinically obese individuals almost doubled. Numbers of clinically obese men rose from 13 per cent to 23 per cent, and women from 16 per cent to 23 per cent.¹ A further 44 per cent of men and 33 per cent of women in the UK are classed as being clinically overweight.¹

Childhood obesity has also become a major issue, with the Government aiming new policies at curbing the increase of unhealthy children,² and the recent Channel 4 television series, "Jamie's School Dinners", highlighted the role of convenience food in the growing childhood obesity epidemic.³

Not only is obesity a major health problem, it worries individuals for cosmetic reasons, and the enormous variety of dieting supplements and popularity of slimming clubs indicate how weight loss has become a multimillion pound industry.

In the US, the number one health issue (as reported by 40 per cent of Americans) is the need to lose weight for reasons of appearance.⁴ Two thirds of Americans (representing 138 million American adults) also report that they have used some method to maintain or manage their weight in the past year.⁴

Methods of weight loss

Low carbohydrate diets are just one example from the seemingly endless list of weight loss diets on offer. The popularity of the Atkins diet, the glycaemic index diet and meal replacement diets, such as Slimfast, are examples of the many routes people are willing to try in order to achieve weight loss.

Clubs and organisations where group support and encouragement are available alongside a diet regimen are also popular. Weight

Watchers is an international slimming organisation that has 6,000 classes weekly in the UK and claims to have helped around 30 million dieters to lose weight.⁵ Slimming World, which has joined forces with NHS primary care trusts to aid dieters,⁶ is another example.

Supplements for weight loss are numerous. People generally prefer to seek a shortcut to weight loss, so the market for such supplements, which often claim to give fast results, is large. Coupled with the fact that many of these products can be marketed as food supplements, with relatively little regulatory control, the market is rapidly expanding.⁷

The universally acknowledged way to weight loss is a calorie-controlled diet with increased physical activity, as most health care professionals advise.⁸ Diet alone is useful, but for long-term maintenance of body weight, exercise is critical, helping prevent the "yo-yo effect" of rapid weight gain after a period of dieting.⁹ Self-monitoring and other behavioural interventions can also enhance weight loss.⁸

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Conventional pharmaceutical treatments, such as orlistat, are also available for weight loss, but only on prescription. Orlistat works by blocking fat absorption but has unpleasant and common side effects of faecal incontinence and flatulence.¹⁰

Nutraceuticals for weight loss?

Nutraceuticals are a growing sector of the supplements market, and encompass a wide variety of products that can be formulated into capsules or tablets, or even incorporated into foods or convenience foods such as snack bars. There are several nutraceuticals currently being marketed as aids to weight loss that have been the subject of scientific and medical research. The major examples include L-carnitine and acetyl-L-carnitine, dehydroepiandrosterone (DHEA), green tea and conjugated linoleic acid (CLA).

L-Carnitine and acetyl-L-carnitine L-Carnitine is an endogenous product found in the kidneys and liver produced from the amino acids methionine and lysine. It can be found in dairy products and red meat.

L-Carnitine is a co-factor in the process of fat oxidation for cellular energy production.¹¹ Fat oxidation in muscle tissue is reduced in obesity due to a reduction of L-carnitine-mediated enzyme activity.¹² It is for the above reasons that carnitine is purported to be of benefit in obese people by increasing fat oxidation,¹³ and why it is often promoted as a “fat burner”. However, it has not been tested for its effectiveness or safety over prolonged periods.

One study in rats found that L-carnitine supplementation in combination with an energy-restricted diet had no effect on weight loss and body composition in comparison with rats fed an energy-restricted diet alone.¹⁴ Results showed both groups lost considerable amounts of weight and had a marked reduction in body fat, but there were no significant differences between the control group and the treated group.

L-Carnitine was shown to reduce body fat drastically in a study of basketball players, although it did not cause a significant fall in overall body mass.¹⁵ The study was investigating L-carnitine as an ergogenic aid for reducing body fat in already lean athletes. A relatively small group of basketball players (n=12) were supplemented with L-carnitine for eight weeks and compared with a control group (n=12). In the supplemented group there were significant improvements in speed, jumping ability and VO₂ max (maximal oxygen uptake), and an average 21 per cent fall in body fat. However, there was no significant difference in overall reduction of body mass between the two groups.

A review of common dietary supplements for weight loss concluded that there was insufficient or conflicting evidence for L-carnitine, and that despite proven quality and safety, no trials demonstrated L-carnitine's effectiveness as a supplement for weight loss. The review suggested doctors

should advise patients that L-carnitine has so far not been proven useful for weight loss, but if a patient wanted to use the supplement, then doctors should monitor them for any positive or negative effects.¹⁶

Acetyl-L-carnitine has similar roles to L-carnitine, and it is used by athletes as a metabolic source of L-carnitine. It is synthesised by mitochondria and found in the brain, kidney and liver. Claims have been made that it can increase energy and help weight loss.¹⁷ Acetyl-L-carnitine is capable of restoring mitochondrial energy production, so it is believed to increase general metabolic activity as well. It is for these reasons that acetyl-L-carnitine is purported to increase ambulatory activity and increase metabolism, although animal studies show mixed results, with one study showing an improvement in metabolic function of rats supplemented with acetyl-L-carnitine,¹⁷ and another study showing that acetyl-L-carnitine prevented weight loss in rats.¹⁸ There has been no scientific evidence for weight loss in humans with acetyl-L-carnitine.

Dehydroepiandrosterone DHEA is an adrenal hormone, found naturally in the body. Blood levels of DHEA in humans peak at around 20 years of age, and then decrease rapidly after 25 years of age. DHEA plays a role in receptor and enzyme adaptations that are thought to favour increased fat oxidation and decreased fat deposition.¹⁹ Administration of DHEA to rats leads to a decrease in their visceral fat accumulation, and also results in a smaller increase of body fat with advancing age.¹⁹ DHEA is only available on prescription in the UK but is widely available for sale on the internet. DHEA is marketed as a “thermogenic” compound with the ability to burn fat and also to help maintain fat loss.¹⁸

One study concluded that insufficient energy utilisation and obesity in rats was corrected with DHEA treatment.²⁰ DHEA was administered to rats for a 17-day period, in which the rats sustained significant weight loss. This weight loss was partly attributed to enhanced use of energy ingested. It suggested that DHEA corrected the decrease in expression levels of uncoupling protein-1 in brown adipose tissue, which contributed to more efficient energy use and weight loss in the rats.

A study of the effects of DHEA in humans concluded that, compared with a placebo, DHEA induced significant decreases in abdominal fat in elderly men and women.¹⁹ In a randomised, double blind, placebo-controlled six-month trial of men and women over 65 years, a daily dose of 50mg DHEA reduced visceral and subcutaneous fat significantly. The volunteers in this study were included if their weight had been stable for the previous year. During the study volunteers were asked not to alter their usual diet or activity levels. No significant adverse effects were reported with the DHEA supplements. The suggested mechanism of action for DHEA from this study was that DHEA is a peroxisome proliferator-activated receptor α (PPAR α)

agonist, and that previously PPAR α agonists have been shown to reduce fat stores in muscle, and reduce obesity. DHEA also increased the concentration of circulating insulin-like growth factor 1 (IGF-1) within the body, and that increased IGF-1 levels have been shown to reduce abdominal fat.

More research is needed to assess the side effect profile of DHEA, and there are inherent dangers involved in unsupervised use of steroids. Long-term studies are also needed with DHEA to assess the effects of increased IGF-1 levels, and the effect of changes in oestradiol and testosterone levels on the body, since this supplement may be taken for long periods, if found to be efficacious.

Green tea The claimed benefits of drinking green tea and taking green tea supplements are becoming more widely disseminated, with websites dedicated to their available health benefits. Green tea contains catechin polyphenols (including epigallocatechin gallate [EGCG]), which have been shown to inhibit catechol ortho-methyltransferase (COMT), an enzyme responsible for the degradation of noradrenaline (which has an important role in the control of thermogenesis and fat metabolism).²¹

Tea catechins have been shown to cause loss of appetite, which might involve neuropeptides other than leptins, since EGCG is effective in reducing body weight of both lean and obese (leptin receptor-negative) rats. However, body weight loss is reversible, animals regain body weight when EGCG administration is stopped. The *in vitro* thermogenic effect of green tea extract on adipose tissue could be mimicked by EGCG, giving credence to the belief that EGCG is the important component of green tea.²²

It has been recommended that patients who use green tea for weight loss should be cautioned and closely monitored, because product quality and efficacy is uncertain, although it is considered likely to be safe to use if the equivalent of five cups daily is not exceeded.¹⁶

A small study (n=10) of male adults indicated that green tea extract significantly increased 24-hour energy expenditure.²¹ This was a crossover study in which the 10 volunteers were assigned one of three treatments (a placebo, green tea extract or the equivalent amount of caffeine to that in the green tea extract) on three occasions. Treatment with the placebo, and also caffeine, did not have any significant effects on energy expenditure. These results rule out the hypothesis that caffeine alone is responsible for the effect seen on increased energy expenditure. The major limitation of this study, aside from its small sample size, is that it did not actually measure body weight as a parameter, since it was only carried out for a period of 24 hours at any one time. However, the authors do suggest that green tea extract has the potential to influence body weight and body composition due to its promotion of fat oxidation and thermogenic properties. An important obser-



Green tea is a source of the polyphenol epigallocatechin gallate, a nutraceutical taken for weight loss, but its use should be monitored

vation of the study was that there was no increase in the volunteers' heart rates, as there is with other substances that increase energy expenditure, eg, ephedrine and other sympathomimetic drugs, which means that the risk of adverse cardiovascular effects is greatly reduced.

Another study, on the effects of green tea for weight maintenance after weight loss, showed that weight maintenance over a 13-week period, after a 7.5 per cent body weight loss, was not affected by green tea consumption.²³ The randomised, parallel and placebo-controlled trial (n=104) was undertaken over a four-week weight loss period, followed by a 13-week weight maintenance period. Overweight and moderately obese men and women volunteers were recruited. This study attempted to try to find a solution to the common problem of "yo-yo" weight loss, and the issue of long-term weight maintenance that is clearly required if patients are to maintain the benefits of their initial weight loss. Overall results showed that the body weight regained (as a percentage of body weight lost)

by the green tea and placebo groups was not significantly different. Hunger and satiety were also the same in the two groups, and there were no metabolic differences. The same study²³ showed that the high habitual caffeine consumers had higher weight gain in the 13 weeks compared with low habitual caffeine consumers. Habitual caffeine consumption did not differ between the green tea and the placebo group. This result could indicate that the green tea supplement was only effective when habitual caffeine intake was low (or that a much increased dose was needed if caffeine intake was high). The authors suggested that saturation of the ability of green tea to stimulate further noradrenaline-related mechanisms of weight loss may be important, as caffeine and green tea both produce some of their effects through this mechanism. This seems to contradict the previous study²¹ that claimed that it was the catechins, not the caffeine, exerting the effect on fat metabolism and thermogenesis. However, caffeine may be exerting its effect via a different mechanism.

No side effects were reported in any of the studies. Since green tea is consumed by a large number of people worldwide with few reported adverse effects, it would appear to be relatively safe.

Green tea could be incorporated into an everyday lifestyle without the trouble of buying and taking tablets and capsules. However, some people may be unable to palate the astringent taste of green tea, in which case supplements may be preferred.

Conjugated linoleic acid CLA is a collective term used to describe a mixture of positional and geometric dienoic linoleic acid isomers with conjugated double bonds. In dietary supplements, various combinations of the different isomers are found. CLA isomers are found in dairy and meat products.

A review of 13 randomised, placebo-controlled trials in humans concluded that there was little evidence to support the proposition that CLA reduced body weight or promoted repartitioning of body fat in humans.²⁴ It only reviewed trials that had lasted for longer than four weeks, and concluded that the CLA *trans*-10, *cis*-12 isomer may produce liver hypertrophy and insulin resistance. Due to these potentially adverse effects it recommended that CLA supplementation should be cautioned before studies with further data to clarify this situation were published.

Studies in rodents have shown that CLA can significantly reduce body fat and lower body weight.²⁴⁻²⁷ However, in human studies, results have been mixed. One review article found that of all the studies reviewed (n=13), none showed any evidence for significant reduction in body weight and only two showed significant fat lowering effects.²⁵ It has been noted that the body fat lowering effect of CLA is due to the *trans*-10, *cis*-12 isomer^{25,26} (but that over 90 per cent of human CLA intake from food is from the *cis*-9, *trans*-11 isomer²⁵).

A further review concluded that although CLA reduced weight gain and fat deposition in rodents, the effects in humans are less significant and often inconsistent.²⁶ The different mechanisms thought to be responsible for the activity of CLA, are increasing energy expenditure, reduced fat cell size, increasing apoptosis of fat cells, and the inhibition of lipogenesis in the liver or increasing fat oxidation. Side effects of CLA that have been found are the negative effect on insulin sensitivity and glycaemic control, and the development of fatty liver and spleen. However, these side effects have so far only been shown in rodents.²⁷ This indicates that further reliable data are required before a clear judgement can be made on the use of CLA for weight management in humans. The safety of CLA was investigated in this trial, in which the equivalent of 30 times the human dose was used, and no adverse effects were observed.²⁷ Several human trials have been reported in which no adverse effects occurred when high-quality CLA was taken at doses of 3-6g per day.

A year-long study into the effects of CLA on body fat mass concluded that long-term supplementation of CLA in healthy overweight adults significantly reduced body fat mass.²⁸ It was a randomised, double blind, placebo-controlled study, with no diet or lifestyle restrictions placed on the volunteers. A slight reduction in body mass index and body weight was seen in the CLA group, whereas there was no change in the placebo group. Adverse effects were mainly gastrointestinal, and classed as just "mild" or "moderate". A high compliance and low drop-out rate of volunteers also showed CLA was well tolerated.

A further review found that there were insufficient data to support the use of CLA for weight loss in humans, and that overall quality, safety and efficacy of CLA are uncertain.¹⁶ It recommended that doctors should caution patients about the use of CLA, and closely monitor those who take the supplement, because efficacy and safety have not been proven.

A recent study concluded that the metabolic effects of CLA are complex and still not well understood.²⁹ This is partly due to the lack of knowledge regarding the mechanisms of CLA at a molecular level, and the lack of controlled studies on the different isomers of CLA. Another study found that there was no effect on body weight and body mass index in volunteers taking CLA for a 12-week period, but that CLA in a dose of 3.4g per day was found to be safe.³⁰ Further studies are required in order to make a clear judgement on the efficacy of CLA as a weight loss aid.

Conclusion

Of the nutraceuticals reviewed, DHEA seems the most likely candidate for producing actual weight loss, as opposed to alteration of body composition. It has shown weight loss effects in both animal and human studies. L-Carnitine has demonstrated potential as an ergogenic aid, but there is little firm evidence to support its use for weight loss. Green tea has also shown little evidence of an ability to cause weight loss, although studies have shown it can increase energy expenditure, so further long-term trials may be valuable to assess whether it can have effects on body weight over an increased period. Green tea also seems to have a better safety profile than the other nutraceuticals reviewed. CLA has been shown to have variable ability to reduce body fat in humans. However, although it has shown weight loss effects in rodents, it has not yet been shown to cause weight loss in humans.

So far, the studies that have been published do not go far enough in establishing the safety that is critically important for supplements that are likely to be taken in the long term, or the efficacy of these nutraceuticals in large studies in humans with actual body weight loss as a parameter, as opposed to energy expenditure or body fat loss with no overall weight loss.

Despite the promise and lure of nutraceutical supplements and crash diets, consumers can never expect dramatic weight loss and long-term maintenance of a lower body weight unless they reduce their calorie intake and undertake some form of exercise. For those individuals with a body mass index indicative of clinical obesity (30kg/m² and above), medical intervention for weight loss must be considered to reduce the risk of weight-related health problems such as type 2 diabetes and cardiovascular disease.

Even if taking a nutraceutical is only a psychological prop or placebo to aid weight loss, alongside diet or lifestyle changes, it may be helpful because if there is an overall weight loss then that will be beneficial to the patient's health. One argument frequently claimed for use of supplements is that when patients have tried and failed on other weight loss programmes and various diets, their weight may have become a serious health threat, so that any possible aid to weight loss

becomes worth trying. The risks of any dieting aids must be balanced against the benefits of weight loss and the reduction of the health risks of remaining overweight.

With the huge range of products available, pharmacists are at the front line when it comes to explaining and justifying the relative merits of the various weight loss supplements available, alongside offering basic diet and lifestyle advice to customers, and knowing when to direct them to their GP if medical intervention is required. The ability of pharmacists to analyse and evaluate the clinical evidence of different products will allow them to offer good quality advice, as opposed to the possibility of inaccurate and often unreliable information supplied by the media and on the internet. However, a lack of quality data clearly impacts on the ability of the pharmacist to offer good quality advice. Further trials are needed for these nutraceuticals to establish a greater degree of knowledge on their potential contribution to weight loss.

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