A New Potential Weapon for Fighting Obesity

Forskolin—the Active Diterpene in Coleus

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Despite the popularity of many diets today, according to the Centers for Disease Control and Prevention, one third of Americans are obese and another one third are overweight. This may be because low-carbohydrate–high-protein (LCHP) Atkins and Atkins-type diets are not more effective for promoting loss of weight and body fat compared to other types of diets and the dropout rate in most diet-related studies is quite high.

Research on Diets

A pretest/post-test study, with a randomized group design and three cohorts, was utilized to test three types of diets: (1) an LCHP ketogenic diet; (2) the Zone diet; and (3) a conventional hypocaloric diabetic exchange diet that supplied <10 percent, <40 percent, or <50 percent of calories from carbohydrates, respectively.

Each subject's body composition was measured before and after the intervention treatment period via dual energy X-ray absorptiometry (DEXA). The subjects' mean weight loss was 11.24 pounds for those who completed the 12-week program. There were no significant differences in total weight, fat, or lean body mass loss among the diet groups. Attrition was substantial for all diet types at 43 percent, 60 percent, and 36 percent for the LCHP, Zone, and conventional diets, respectively.[1]

Another study compared the weight-loss effects of four commercial programs that use differing approaches.[2] These were the Slim-Fast Plan (a meal replacement approach), the WeightWatchers Pure Points Programme (an energy controlled diet with weekly group meetings), Dr. Atkins' New Diet Revolution (a self-monitored low-carbohydrate eating plan), and Rosemary Conley's "Eat Yourself Slim" Diet & Fitness Plan (a low-fat diet and weekly group exercise class).

The primary outcome measure was percentage of fat loss over 24 weeks, measured via DEXA. A total of 293 healthy people were randomized to either a control group or one of the diet groups. The subjects were 79 (27 percent) men and 214 (73 percent) women, with an average body–mass index (BMI) of 31.7 kg/m^2 (range 27–38) and an average age of 40.3 years old. All of the diets tested were effective and produced significant weight and body-fat losses compared to what occurred in the control group. On average, men lost 9.12 kg (23 percent of initial body fat) and women lost 5.2 kg (16 percent of initial body fat).

However, there was considerable variation in body-fat loss within each diet group. This led to the average differences between the diets being quite small and not significant. This study demonstrated that loss of body fat is possible with a variety of commercial strategies, including the Atkins diet. However, the range of fat loss indicated that some subjects actually lost very little fat and some lost a great deal of fat.

Numerous studies on weight-loss diets indicate that low glycemic index diets are superior to LCHP diets in terms of compliance and overall weight loss. [3] This type of diet is much closer to what our ancestors ate and what more primitive cultures continue to consume today.[4]

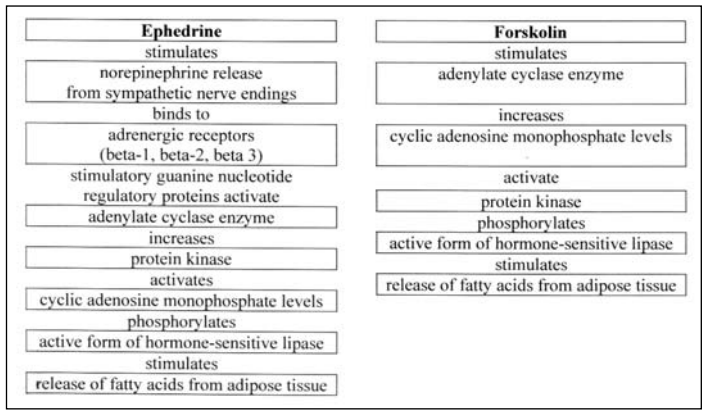
However, based on clinical experience, the weight loss for many individuals is still too slow on any weight-loss plan despite the inclusion of exercise and lifestyle modifications. This situation often leads to attrition and frustration on the part of dieters. Another compounding factor that may slow weight loss is the occasional "cheating" that occurs at parties and social functions.

It appears that very high body fat—in particular, high intra-abdominal fat—is associated with slower metabolism, metabolic syndrome, and slower fat and weight loss.[5] This is often a consequence of constant dieting, which results in greater muscle-to-fat loss and regaining of weight as body fat over time. This constant alteration of body composition in the direction of higher body fat and lower lean-muscle mass can cause decreased metabolism, thermogenesis, and oxidation of adipose tissue.

Safe and effective weight-loss accelerators are important for enhancing weight-loss efforts via diet, exercise, and other forms of lifestyle modification, including stress reduction.[3] Studies have shown that natural products, such as green tea (*Camellia sinensis*) catechins, 5-hydroxytryptophan, and chromium can be excellent adjuncts to a comprehensive weight-loss program. Forskolin, an active plant compound in coleus (*Coleus forskohlii*), is another weight-loss accelerator that can improve body composition; this article focuses on forskolin's history, research, and potentials.

History of Coleus and Forskolin

Coleus grows on the mountain slopes of Nepal, India, and Thailand. In traditional Ayurvedic medicine, this plant was used to treat skin rashes, asthma, bronchitis, insomnia, epilepsy, and angina pectoris. Coleus was also used as a spice.[6] Scientific studies have focused on forskolin, a diterpene active plant compound that has only been found in coleus. There are more than 5000 studies on the medicinal properties of forskolin.[6] It is a potent stimulator of cyclic adenosine monophosphate (cAMP), which produces a wide variety of effects. Animal studies have shown that forskolin has anticancer and anti-inflammatory effects and human studies have shown that this compound may be effective, in the form of eye drops, for treating glaucoma.[7]



Mechanism of thermogenic action, comparing ephedrine and forskolin-stimulated lipolysis.

Forskolin and Weight Loss

Six (6) overweight, but otherwise healthy, women were selected to receive a 250-mg capsule of a standardized extract of coleus (ForsLean®; Sabinsa Corporation, Piscataway, New Jersey) providing 10 percent forskolin (25 mg).[8] The participants were instructed to take 1 capsule in the morning and 1 in the evening, 30 minutes before a meal. They continued their usual exercise and dietary habits and were monitored by a physician specializing in bariatric medicine. Baseline measurements were taken before the start of the study and at 4 and 8 weeks. Body composition was measured using bioelectric impedance.

During the 8-week trial, the mean values for body weight and fat content were significantly decreased and lean body mass was significantly increased compared to baseline (Wilcoxon matched pairs test). Weight loss was statistically significant ($p<0.05$), with a mean of 4.3 pounds and 9.17 pounds lost, respectively, after 4 and 8 weeks.

Percent of body-fat values were 33.63 ± 3.02 at baseline, 30.10 ± 4.34 at 4 weeks, and 25.88 ± 4.77 at 8 weeks, which was statistically significant ($p<0.05$). Percent of lean body mass values were 67.07 ± 3.02 at baseline, 69.90 ± 4.34 at 4 weeks, and 74.13 ± 4.77 at 8 weeks ($p<0.05$), which was statistically significant.

Treatment did not have any adverse effects on systolic/diastolic blood pressure or pulse rate. Instead, the trend was toward lower systolic/diastolic pressure in the course of treatment. This preliminary study indicated that 50 mg of forskolin can safely and significantly lower body weight and body fat, and increase lean body mass without any changes in diet or exercise regimen.

A 12-week open field study evaluated a lower dose of forskolin on weight loss.[9] Thirteen (13) overweight females and one male received 125 mg of ForsLean, providing 10 percent forskolin (12.5 mg), twice daily. The baseline average weight of participants was 74.1 ± 11.98 kg with an average BMI of 29.9 ± 4.31 and an average body fat percentage of 38.2 ± 4.87. Each patient was examined in a physician's office and body composition was measured with a Futurex 6200 infrared analyzer at baseline, 4 weeks, 8 weeks, and, at the 12-week conclusion of the study.

At 12 weeks, total body weight significantly decreased to an average of 73.5 kg ($p< 0.05$), BMI significantly improved to an average of 29.49 ($p< 0.05$), and body-fat percent significantly improved to an average of 37.1 ($p< 0.01$). Lean body mass had no significant change and was preserved throughout the study. The 12-week treatment with 25 mg of forskolin did not significantly change diastolic and systolic blood pressure and was shown to be effective for inducing weight and body fat loss and preserving lean body mass in overweight volunteers.

In a 12-week, double-blinded, placebo-controlled randomized study, 60 obese male and female volunteers (25–45 years old, with BMIs between 28 and 40, and/or a body-fat percentage above 30 in males and 40 in females) received 250 mg of ForsLean, supplying 25 mg of forskolin, twice daily or placebo.[10] Body composition was measured with bioelectric impedance.

The subjects who took ForsLean lost an average of 3.81 pounds or 4.02 percent of their total body weights while the placebo group gained an average of one half pound or 0.29 percent (250 g) of body weight. These differences were statistically significant ($p = 0.05$). The ForsLean-treated group lost an average of 0.46 percent of body fat while the placebo group gained 0.68 percent of body fat; the difference was statistically significant ($p = 0.05$). There was an increase in lean body mass in subjects who took ForsLean and a decrease in lean body mass in those who took the placebo, with a statistically significant ($p = 0.05$) difference.

Numerous laboratory tests were performed at baseline and at completion of the study including: T_3, T_4, thyroid-stimulating hormone (TSH), triglycerides, total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein LDL, and very–low-density lipoprotein. There were no significant changes in laboratory values in the active or placebo groups except for in HDL. Volunteers who took ForsLean had a significant rise in HDL levels at the end of the study. No subjective or objective side-effects were reported for ForsLean or the placebo.

It appears that ForsLean is safe and effective for reducing body weight and body fat, and may preserve lean body mass. This product significantly increased HDL serum levels and significantly decreased the ratio of total cholesterol to HDL suggesting that ForsLean may improve specific aspects of patients' lipid profiles.

Safety Review

In December 2000, a toxicologic study was performed on ForsLean by MB Research Laboratories (Spinnerstown, Pennsylvania), a specialized independent laboratory. The oral LD_{50} (lethal dose) was above 2000 mg/kg. This extremely high dose did not result in any animal deaths. The Ames test for bacterial mutagenicity was performed, in November 2000, by BioReliance Corporation (Rockville, Maryland); no mutagenicity was associated with ForsLean.

Weight loss remains one of the most challenging health issues in clinical practice.

An earlier study on forskolin also showed that it was extremely safe with an oral LD_{50} of 3100 mg/kg.[11] In a double-blinded, randomized, placebo-controlled trial, 19 sedentary overweight females supplemented their usual diets with 250 mg of ForsLean (n = 7) or placebo (n = 12), twice daily, for 12 weeks. Body composition was analyzed, using DEXA, and body weight and psychometric instruments were obtained at baseline and at 4, 8, and, 12 weeks. Fasting blood samples and dietary records were obtained at baseline and at 12 weeks. Data were analyzed by repeated measures and analysis of variance, and were presented as mean changes from baseline for the active and placebo groups.

ForsLean tended to mitigate gains in body mass ($p = 0.10$) and scanned mass ($p = 0.08$) but this did not achieve statistical significance. There were no significant changes in fat mass, fat-free mass, or body fat. However, subjects who took ForsLean tended to report less fatigue ($p = 0.07$) and hunger ($p = 0.02$), and more fullness ($p = 0.04$). More importantly, there were no significant interactions among metabolic markers, blood lipids, muscle and liver enzymes, electrolytes, red cells, white cells, insulin, TSH, T_3, T_4, heart rate, or blood pressure, nor were there reports of side-effects. These results suggested that ForsLean may help mitigate weight gain with no clinically significant side-effects that are apparent.

Discussion

These preliminary studies have provided evidence that ForsLean, a proprietary extract of coleus, supplying 10 percent forskolin, may induce weight loss and changes in body composition without additional diet or exercise interventions. All available data on forskolin and weight loss came from studies that were sponsored by the Sabinsa Corporation. It appears that 50 mg of forskolin per day yields greater changes in body composition and weight loss compared to a 25-mg dose[8–10] but both doses seem to effective.

The weight loss achieved with ForsLean was greater than the weight loss achieved in numerous studies that only controlled diet[1–3] and the effect was produced in a shorter amount of time (12 weeks versus 12 months).

In addition, it seems that ForsLean may impart some cardiovascular benefit by raising HDL cholesterol levels.[10] Forskolin exerts a very specific effect by activating and raising levels of cAMP. cAMP is essential for lipolysis via the mechanism of thermogenesis. It also increases circulation of anabolic hormones.

Unlike ephedrine alkaloids, which also stimulate cAMP, forskolin does not have a stimulatory effect on the central nervous system and does not result in elevated blood pressure or pulse rate. Instead, there is evidence that forskolin may tend to lower blood pressure.[8,9] Forskolin bypasses the need for hormonal activation of cAMP via norepinephrine and activation of adrenergic receptors (beta-1, beta-2, beta-3), which are responsible for some of the reported adverse effects of ephedrine, such as anxiety, increased blood pressure, and elevated pulse rate.[13,14]

Forskolin has also been reported to have potential therapeutic effects on asthma, glaucoma, skin conditions, hypertension, and angina pectoris.[3,6–10,13] Both human and animal data have shown that that ForsLean is safe with an extremely high LD_{50} and no mutagenicity.

The preliminary data obtained from research sponsored by the Sabinsa Corporation has led to a recently completed, double-blinded, randomized, placebo-controlled trial with 30 very overweight subjects (personal communication with Dr. Vladimir Badmaev, vice president of scientific and medical affairs, Sabinsa Corporation, October 14, 2004). This study has been submitted for publication.

Conclusions

Weight loss remains one of the most challenging health issues in clinical practice. The attrition rate is high when diets are too restrictive and/or weight loss is unreasonably slow (less than 1–2 pounds per week). Based on personal clinical experience and the experience of colleagues, it seems that diet and exercise modification may simply not be enough to induce sustained desirable effects in some individuals. Based on ForsLean's apparent safety and possible efficacy it appears to be another potential weight-loss accelerator that may enhance diet and exercise efforts, in particular, by improving body composition by inducing weight loss predominantly as body fat and preserving lean body mass. □

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