

Reductive effect of body weight in rats fed a high-fat diet by Sense-line

Hyo-Jin An¹, Hwan-Suck Chung¹, Hyun-Ja Jeong¹, Soon-Ah Lee¹, Hyung-Min Kim¹ and Seung-Hwa Baek^{2,*}

¹College of Pharmacy and KI Co., Ltd., Wonkwang University and ²Department of Natural Products, Professional Graduate School of Oriental Medicine, Wonkwang University, Iksan, Jeonbuk 570-749, Republic of Korea

SUMMARY

Sense-line (SL), a dietary functional food, is our invention for weight loss. To evaluate such an effect of SL, we analyzed the plasma levels of total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and weight changes after rats were fed on high fat diet with SL for 20 days. Plasma total cholesterol level and LDL-cholesterol level was decreased by 52% and 91.89% in 5% SL treated group and by 13% and 51.45% in 10% SL treated group, respectively. But HDL-cholesterol was not changed. In addition, the weight was significantly lower in SL group than in high-fat diet group ($P < 0.05$). Our findings indicate that SL may contain compounds with actions, which can treat blood circulatory trouble as well as overweight.

Key Words: Sense-line; High-fat diet; Total cholesterol; Low-density lipoprotein-cholesterol; High-density lipoprotein-cholesterol; Blood circulatory trouble; Overweight

INTRODUCTION

Obesity is a public health dilemma in developed countries and as steadily increased at an alarming rate in recent years. Morbid obesity increases the risk of hypertension, coronary artery disease, diabetes mellitus, cancer, sleep apnea, and osteoarthritis (Balsiger *et al.*, 2000). Among various therapeutic methods modifying fat balance is one of the key therapy for obesity (Flatt *et al.*, 1995). The popularity of herbal medicine has created a ready market for plant-based medications for weight loss.

Although obesity is usually thought to be simply the result of hyperphagia or energy intake/energy expenditure imbalance, there is evidence that obesity may be induced without significant excess energy intake (Oscari *et al.*, 1987). In this regard, several studies in animal models of diet-induced obesity (Oscari *et al.*, 1984, 1987; Barnard *et al.*, 1998) and humans (Miller *et al.*, 1994; Hill and Prentice, 1995) have demonstrated that increased levels of

refined carbohydrates (e.g. sucrose) and/or saturated fat may lead to obesity in the absence of excessive energy intake. Furthermore, mechanisms underlying the development of obesity may include changes in skeletal muscle and adipose tissue enzymatic and/or receptor regulation (lipoprotein lipase (LPL), hormone-sensitive lipase, very-low density lipoprotein receptor (VLDL-R)) and/or hormonal regulation (i.e. insulin, growth hormone, catecholamine), resulting from physical inactivity and/or inappropriate macronutrient intake (i.e. high saturated fat and/or refined carbohydrates).

Sense-line (SL) is a new dietary functional food for weight loss. SL is composed of seven herbs and one dietary fiber. Every components of SL have a lot of fiber and help digestion, absorption and excretion.

In the present study, we investigated the changes of fat accumulation, total cholesterol and LDL-cholesterol in SL group and high-fat diet group. We also measured the weight to determine the effect of SL on the weight loss.

MATERIALS AND METHODS

Preparation of SL

Plantago asiatica L. semen 50%, glucomanan 13%,

*Correspondence: Prof Seung-Hwa Baek, Department of Natural Products, Professional Graduate School of Oriental Medicine, Wonkwang University, Iksan, Jeonbuk 570-749, Republic of Korea. Tel: 82-63-6225; E-mail: shbaek@wonkwang.ac.kr

Laminaria japonica ARESCH leaf 10%, *Aloe arborescens* 2%, *Rhamnus purshiana* De CANDOLL 10%, *Garsinia Canbogia* 5%, glucose 8%, *Crataegus pinnatifida* BUNGE var. typical SCHNEIDER fruit 1%, *Thea chinensis* leaf 1% were mixed with distilled water. The mixed materials were granulated and dried at 60°C during 6 hours.

Animal experiments

Male SD rats weighing 159-168 g at the age of 6 weeks were purchased from Dae-Han Experimental Animal Center (Eumsung, South Korea). The animals were maintained under a 12 h light/dark cycle at a constant temperature of 23±2°C. Four groups of rats were fed for 8 weeks by: (1) a standard laboratory diet (Samyang formula feed, Samyang Oil & Feed Co., Ltd.); (2) a high-fat diet created by mixing corn oil into the standard laboratory diet (high-fat group; 40% of calories as corn oil); (3) the high-fat diet with two different MP rate, 5% and 10%.

Twenty-eight male SD rats were divided into four groups of seven rats each. The animals were given free access to food and tap water for twenty days. Body weight was recorded about 5 days. At the end of this period, the animals were kept for overnight fasting. They were thereafter anaesthetized with chloroform and blood samples taken by cardiac puncture. The animals were then sacrificed and the livers were harvested for weight and lipids estimation.

Lipid analysis

Plasma was separated immediately by centrifugation at 10,000 rpm for 10 min. Levels of total cholesterol, HDL-cholesterol and LDL-cholesterol were determined by the colorimetric enzymatic method of Allain *et al.* (Allain *et al.*, 1974) with the modifications of Badham and Trinder (Badham and Trinder, 1972), using an autoanalyzer (Hitachi 747, Hitachi, Japan). Plasma concentrations of total cholesterol and HDL-cholesterol were determined using automated enzymatic methods (Pitt *et al.*, 1995), and LDL-cholesterol was calculated using the Friedewald formula (Friedewald *et al.*, 1972). Decrement ratio of cholesterol was calculated as follows;

Decrement ratio of cholesterol (%) = $\frac{[B - C(\text{or } D)]}{(BA)} \times 100$

where, A is control, B is high-fat diet, C is SL 5% diet, D is SL 10% diet.

Statistical analysis

A statistical analysis was performed using SPSS computer software (SPSS Inc., Chicago, IL). Results were expressed as the mean ± S.E.M. of independent experiments, and statistical analysis was performed by Paired Samples *t*-test to express the difference between two groups.

RESULTS

Effects of SL on the increase

SD rats fed the high-fat diet gained significantly higher weight than normal diet rats rapidly ($P < 0.05$). On the other hand, the 5% or 10% SL group increased significantly less weight than the high-fat diet group ($P < 0.05$). The 10% SL group increased less weight than the 5% SL group (Fig. 1).

Effects on total cholesterol levels

The values of the total cholesterol obtained from the high-fat diet fed rats are compared with those of the normal group, while the values for the SL group is compared with those of the high-fat

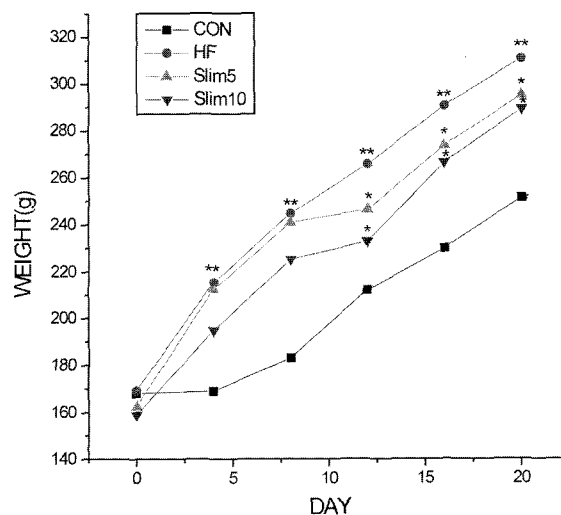


Fig. 1. Effects of SL on weight in the SD rats fed a high-fat diet for 20 days. Significantly different from the high-fat diet-treated group; the values are represented as mean±S.E.M. of four rats. * $P < 0.05$ compared to HF, ** $P < 0.05$ compared to CON. CON, normal diet group; HF, high-fat diet-treated group; SL5, high-fat plus 5% SL treated group; SL10, high-fat plus 10% SL treated group.

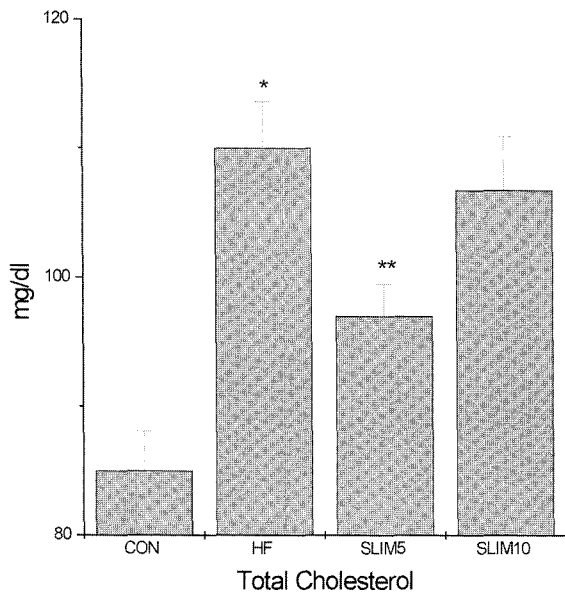


Fig. 2. Effects of SL on total cholesterol levels in the SD rats fed diet as described in materials and methods for 20 days. HF, high-fat diet-treated group; SL5, high-fat plus 5% SL treated group; SL10, high-fat plus 10% SL treated group. The values are represented as mean \pm S.E.M of four rats. * P <0.05 compared to HF, ** P <0.05 compared to CON.

group. Keeping the rats on high-fat diet increased the total cholesterol levels by 29.4% in plasma compared to normal diet rats. When high-fat diet was co-administered with 5% or 10% of SL, the total cholesterol-increasing effect of high-fat diet was decreased by 52% or 13%, respectively (Fig. 2). The cholesterol-lowering action of SL was found to be significant in 5% SL than 10% SL (P <0.05).

Effects on LDL-cholesterol levels

The values of the LDL-cholesterol obtained from the high-fat diet fed rats are compared with those of the SL group. The LDL-cholesterol levels were decreased by 91.89% and 51.45% in 5% and 10% SL group, respectively (Fig. 3). However, the HDL-cholesterol levels were similar with each group (Data not shown).

DISCUSSION

We demonstrated that SL decreased total cholesterol level and LDL-cholesterol level. In addition, we have found that SL reduced weight in rats following high-fat diet. These results indicate that SL is good

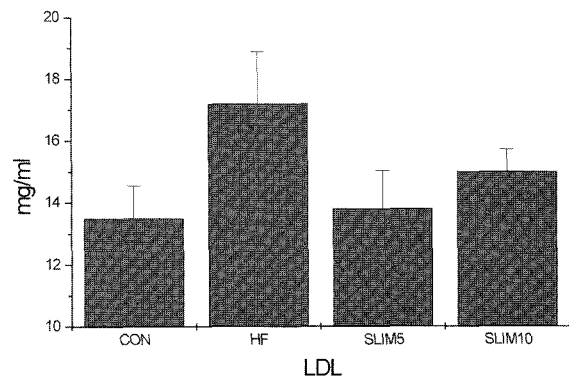


Fig. 3. Effects of SL on LDL-cholesterol levels in the SD rats fed diet as described in materials and methods for 20 days. HF, high-fat diet-treated group; SL5, high-fat plus 5% SL treated group; SL10, high-fat plus 10% SL treated group.

candidate for treatment on high-fat diet-induced blood circulatory trouble and obesity.

SL is composed of glucose, glucomannan and seven herbs (*Plantago asiatica* L. semen, *Laminaria japonica* ARESCH leaf, *Aloe arborescens*, *Rhamnus purshiana* De CANDOLL, *Garsinia Canbogia*, *Crataegus pinnatifita* BUNGE var. typical SCHNEIDER fruit, *Thea chinensis* leaf). Most all of these herbs have anti-obesity and lipid metabolism related effects. Glucomannan was reported that it decreased plasma cholesterol and increased cholesterol excretion in overweight normocholesterolemic humans (Gallaher *et al.*, 2002). *Plantago asiatica* L. semen containing product which is already taken by many people world-wide control bowel function, may be a useful supplement in weight control diets as it affects fat intake, and may have some effect in the subjective feeling of fullness (Turnbull *et al.*, 1995). *Aloe arborescens* contains a hypoglycaemic agent which lowers the blood glucose (Ghannam *et al.*, 1986). *Rhamnus purshiana* De CANDOLL has emodin as a effective component. The effects of emodin on 3T3-L1 cell's proliferation and differentiation are dose dependent. Emodin inhibits the activity of FAS. Therefore *Rhamnus purshiana* De CANDOLL has a fat-reducing effect (Zhang *et al.*, 2002). *Garsinia Canbogia* is that extract of dry-pell from South Asia Tree. It is consist of HCA (Hydroxy Citric Acid). HCA inhibits metabolism in the body and makes energy from glycogen synthesis. *Crataegus pinnatifita* BUNGE var. typical SCHNEIDER fruit is often used in patients with heart failure because of its positive

inotropic effect. Additionally, crataegus acts as an antiarrhythmic substance by prolonging refractory period of the action potential (Zbinben *et al.*, 2002). *Thea chinensis* leaf extract has been reported that it increases 24-h energy expenditure and fat oxidation in humans (Dulloo *et al.*, 2000). Even though those herbs are frequently used to treat the various diseases, these effects are never the same as SL. This prescription was also composed on the basis of the theory of oriental medicine to maximize its efficacy.

Compelling evidences link overweight and obesity with serious disorders including the cardiovascular diseases, diabetes, musculoskeletal problems, and cancer (Garrow, 1988). Overweight and obesity are a major public health concern. Figures for the United States, using the World Health Organization classification of obesity indicate that more than 1 in 5 of the general adult population can be classified as obese (Flegal *et al.*, 1998). Obesity has become one of the most important avoidable risk factors for morbidity (Garrow, 1992), with considerable costs directly attributable to this condition. These considerations and the notoriously poor compliance with conventional weight management programs based on diet and regular physical exercise render the identification of safe and effective options to reduce body weight a matter of high relevance to health care services in industrialized countries. Rats that are fed a high fat diet are a useful model of the metabolic syndrome being among other things, insulin resistance and obese (Wojcicki *et al.*, 1985).

In the relationship between weight loss and plasma lipid, Weight loss was shown significantly to reduce total cholesterol, LDL-cholesterol and to increase HDL-cholesterol at stabilized weight. However, when individuals were actively losing weight, the HDL-cholesterol levels were decreased (Dattilo *et al.*, 1992). So, it is important to consider the timing of lipid analysis in the interpretation of the plasma lipid response to weight loss (Noakes *et al.*, 2000). The present study showed that SL in a high fat diet tends to reduce total cholesterol and LDL-cholesterol. But HDL-cholesterol levels in SL treated group were similar as that in the high fat diet group. We supposed that when we evaluated the lipid levels, SL treated rats were actively losing

weight, so the HDLcholesterol levels were not changed. The level of LDL-cholesterol in plasma is the major determinant of the risk of vascular disease and lowering the level of LDL diminishes that risk, both in those with and those without symptomatic vascular disease (Shepherd *et al.*, 1995; Sacks *et al.*, 1996; Downs *et al.*, 1998). Fully understanding the factors that govern the concentration of plasma LDL-cholesterol is, therefore, one of our most important challenges. Reduced plasma LDL-cholesterol levels have been recognized as a very potent independent risk factor for atherosclerotic cardiovascular disease (ACVD) (Gordon *et al.*, 1977; Miller *et al.*, 1977; Gordon and Rifkind, 1989). We supposed that the reason why SL induced weight loss and reduced total cholesterol, LDL-cholesterol is rich fiber in SL. A fiber-rich diet is lower in energy, often has a lower fat content, is larger volume, and is richer in micronutrients, all of which have beneficial health effects. By encouraging people to eat fiber-rich plant foods, the dietetics professional can have a significant impact on the prevention and treatment of obesity, cardiovascular disease, as well as constipation (Judith *et al.*, 2002).

In conclusion, the observed cholesterol and weight reducing action of the SL indicates that the product possesses some potential medicinal value on obese patient. However, further work needs to investigate whether fiber in SL affect lipid cholesterol and weight.

REFERENCES

- Allain CC, Poon LS, Chan CSG, Richmond W, Fu PC. (1974) Enzymatic determination of total plasma cholesterol. *Clin. Chem.* **10**, 470-475.
- Badham D, Trinder P. (1972) An improved color reagent for the determination of blood glucose by the oxidase system. *Analyst.* **97**, 142-145.
- Balsiger BM, Murr MM, Poggio JL, Sarr MG. (2000) Surgery for weight control in patients with morbid obesity. *Med. Clin. North Am.* **84**, 477.
- Dattilo AM, Kris-Etherton PM. (1992) Effects of weight reduction on blood lipids and lipoproteins: a meta-analysis. *Am. J. Clin. Nutr.* **56**, 320-328.
- Downs JR, Clearfield M, Weis S, Whitney E, Shapiro DR, Beere PA, Langendorfer A, Stein EA, Krueyer W, Gotto AM. (1998) For the AFCAPS/TexCAPS Research Group. Primary prevention of acute

- coronary events with lovastatin in men and women with average cholesterol levels. *JAMA* **279**, 1615-1622.
- Dulloo AG, Duret C, Rohrer D, Girardier L, Mensi N, Fathi M, Chantre P, Vandermander J. (2000) Efficacy of a green tea extract rich in catechin polyphenols and caffeine in increasing 24-h energy expenditure and fat oxidation in humans. *Am. J. Clin. Nutr.* **72**, 1232-1234.
- Flatt JP. (1995) Diet, lifestyle, and weight maintenance. *Am. J. Clin. Nutr.* **62**, 820-836.
- Flegal KM, Carrol MD, Kuczmarski RJ, Johnson CL. (1998) Overweight and obesity in the United States: prevalence and trends, 1960-1994. *Int. J. Obesity.* **22**, 39-47.
- Friedewald WT, Levy RI, Fredrickson DS. (1972) Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin. Chem.* **18**, 499-502.
- Gallaher DD, Gallaher CM, Mahrt GJ, Carr TP, Hollingshead CH, Hesslink R Jr, Wise J. (2002) A glucomannan and chitosan fiber supplement decreases plasma cholesterol and increases cholesterol excretion in overweight normocholesterolemic humans. *J Am Coll Nutr.* **21**, 428-433.
- Garrow JS. (1988) *Obesity and Related Diseases*, Churchill Livingstone, London.
- Garrow JS. (1992) Treatment of obesity. *Lancet.* **340**, 409-413.
- Ghannam N, Kingston M, Al-Meshaal IA, Tariq M, Parman N S, Woodhouse N. (1986) The antidiabetic activity of aloes: preliminary clinical and experimental observation. *Hormone Research.* **24**, 288-294.
- Gordon DJ, Rifkind BM. (1989) high density lipoprotein: the clinical implications of recent studies. *New Engl. J. Med.* **321**, 1311-1316.
- Gordon T, Castelli WP, Hjortland MC, Kannel WB, Dawber TR. (1977) High density lipoprotein as a protective factor against coronary heart disease: the Framingham study. *Am. J. Med.* **62**, 707-714.
- Hill JO, Prentice AM. (1995) Sugar and body weight regulation. *Am. J. Clin. Nutr.* **62**, 264S-273S Discussion 73S-74S.
- Judith A Marlett, Michael I McBurney, Joanne L Slavin. (2002) Position of the American Dietetic Association: Health implications of dietary fiber. *J. Am. Diet. Assoc.* **102**, 993-1000.
- Miller NE, Forde OH, Thelle DS, Mjos OD. (1977) The Tromso Heart Study: high-density lipoprotein as a protective factor against coronary heart disease: a prospective case-control study. *Lancet.* **1**, 965-967.
- Miller WC, Niederpruem MG, Wallace JP, Lindeman AK. (1994) Dietary fat, sugar, and fiber predict body fat content. *J. Am. Diet. Assoc.* **94**, 612-615.
- Noakes, Manny, Clifton, Peter M. (2000) Weight loss and plasma lipids. *Curr Opin Lipidol.* **11**, 65-70.
- Oscari LB, Brown MM, Miller WC. (1984) Effect of dietary fat on food intake, growth and body composition in rats. *Growth* **48**, 415-424.
- Oscari LB, Miller WC, Arnall DA. (1987) Effects of dietary sugar and of dietary fat on food intake and body fat content in rats. *Growth* **51**, 64-73.
- Pitt B, Mancini GBJ, Ellis SG, Rosman HS, Park JS, McGovern ME. (1995) Pravastatin limitation of atherosclerosis in the coronary arteries (PLAC I): reduction in atherosclerosis progression and clinical events. *J. Am. Coll. Cardiol.* **26**, 1133-1139.
- Sacks FM, Pfeffer M, Moye LA, Rouleau JL, Rutherford JD, Cole TG, Brown L, Warnica JW, Arnold JM, Wun CC, Davis BR, Braunwald E. (1996) The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. *New Engl. J. Med.* **335**, 1001-1009.
- Shepherd J, Cobbe SM, Ford I, Isles CG, Lorimer A, MacFarlane PW, McKillop JH, Packard CJ. (1995) For the West of Scotland Coronary Prevention Study Group. Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia. *New Engl. J. Med.* **333**, 1301-1307.
- Turnbull WH, Thomas HG. (1995) The effect of a *Plantago ovata* seed containing preparation on appetite variables, nutrient and energy intake. *Int. J. Obes. Relat. Metab. Disord* **19**, 338-342.
- Wojcicki J, Samochowiec L, Jaworska M, Hinek A. (1985) A research for a model of experimental atherosclerosis; comparative studies in rabbits, guinea pigs and rats. *Pol. J. Pharmacol. and Pharm.* **37**, 11-21.
- Zbinben S, Seiler Ch. (2002) Phytotherapy in cardiovascular medicine *Ther. Umsch.* **59**, 301-306.
- Zhang C, Teng L, Shi Y, Jin J, Xue Y, Shang K, Gu J. (2002) Effect of emodin on proliferation and differentiation of 3T3-L1 preadipocyte and FAS activity. *Chin. Med. J.* **115**, 1035-1038.