

## NOFAT

### Herbal Product for Weight Management

#### Clinical References

##### Ingredients

- 1) Vrakshalam (Garcinia indica)
  - 2) Hydroxy Citric acid
  - 3) Guggulu (Commiphora mukul)
  - 4) Ginger (Zingiber officinale)
  - 5) Piperine (Piper nigrum)
  - 6) Fenugreek (Trigonella foenum-graecum)
  - 7) Madhunashini (Gymnema sylvestre)
- ❖ Medohar Guggulu

#### 1) Vrakshalam (Garcinia indica)

##### 1.1) **Chemistry and biochemistry of (-)-hydroxycitric acid from Garcinia.**

Jena BS, Jayaprakasha GK, Singh RP, Sakariah KK.

##### **Source**

Human Resource Development, Central Food Technological Research Institute, Mysore 570 013, India.

##### **Abstract**

(-)-Hydroxycitric acid [(-)-HCA] is the principal acid of fruit rinds of *Garcinia cambogia*, *Garcinia indica*, and *Garcinia atroviridis*. (-)-HCA was shown to be a potent inhibitor of ATP citrate lyase (EC 4.1.3.8), which catalyzes the extramitochondrial cleavage of citrate to oxaloacetate and acetyl-CoA: citrate + ATP + CoA → acetyl-CoA + ADP + P(i) + oxaloacetate. The inhibition of this reaction limits the availability of acetyl-CoA units required for fatty acid synthesis and lipogenesis during a lipogenic diet, that is, a diet high in carbohydrates. Extensive animal studies indicated that (-)-HCA suppresses the fatty acid synthesis, lipogenesis, food intake, and induced weight loss. In vitro studies revealed the inhibitions of fatty acid synthesis and lipogenesis from various precursors. However, a few clinical studies have shown controversial findings. This review explores the literature on a number of topics: the source of (-)-HCA; the discovery of (-)-HCA; the isolation, stereochemistry, properties, methods of estimation, and derivatives of (-)-HCA; and its biochemistry, which includes inhibition of the citrate cleavage enzyme, effects on fatty acid synthesis and lipogenesis, effects on ketogenesis, other biological effects, possible modes of action on the reduction of food intake, promotion of glycogenesis, gluconeogenesis, and lipid oxidation, (-)-HCA as weight-controlling agent, and some possible concerns about (-)-HCA, which provides a coherent presentation of scattered literature on (-)-HCA and its plausible mechanism of action and is provocative of further research.

#### 2) Hydroxy Citric Acid

##### 2.1) **Compromised mitochondrial fatty acid synthesis in transgenic mice results in defective protein lipoylation and energy disequilibrium.**

Smith S, Witkowski A, Moghul A, Yoshinaga Y, Nefedov M, de Jong P, Feng D, Fong L, Tu Y, Hu Y, Young SG, Pham T, Cheung C, Katzman SM, Brand MD, Quinlan CL, Fens M, Kuypers F, Misquitta S, Griffey SM, Tran S, Gharib A, Knudsen J, Hannibal-Bach HK, Wang G, Larkin S, Thweatt J, Pasta S.

**Source**

Children's Hospital Oakland Research Institute, Oakland, California, USA. ssmith@chori.org

**Abstract**

A mouse model with compromised mitochondrial fatty acid synthesis has been engineered in order to assess the role of this pathway in mitochondrial function and overall health. Reduction in the expression of mitochondrial malonyl CoA-acyl carrier protein transacylase, a key enzyme in the pathway encoded by the nuclear Mcat gene, was achieved to varying extents in all examined tissues employing tamoxifen-inducible Cre-lox technology. Although affected mice consumed more food than control animals, they failed to gain weight, were less physically active, suffered from loss of white adipose tissue, reduced muscle strength, kyphosis, alopecia, hypothermia and shortened lifespan. The Mcat-deficient phenotype is attributed primarily to reduced synthesis, in several tissues, of the octanoyl precursors required for the posttranslational lipoylation of pyruvate and  $\alpha$ -ketoglutarate dehydrogenase complexes, resulting in diminished capacity of the citric acid cycle and disruption of energy metabolism. The presence of an alternative lipoylation pathway that utilizes exogenous free lipoate appears restricted to liver and alone is insufficient for preservation of normal energy metabolism. Thus, de novo synthesis of precursors for the protein lipoylation pathway plays a vital role in maintenance of mitochondrial function and overall vigor.

**2.2) Efficacy of a novel calcium/potassium salt of (-)-hydroxycitric acid in weight control.**

Preuss HG, Garis RI, Bramble JD, Bagchi D, Bagchi M, Rao CV, Satyanarayana S.

**Source**

Department of Physiology and Biophysics, Georgetown University Medical Center, Basic Science Building, Room 231 B, 4000 Reservoir Rd., N.W., Washington, DC 20057, USA. preusshg@georgetown.edu

**Abstract**

The weight-loss efficacy of a novel, water-soluble, calcium-potassium salt of (-)-hydroxycitric acid (HCA-SX) was re-examined in 90 obese subjects (BMI: 30-50.8 kg/m<sup>2</sup>). We combined data from two previously reported randomized, double-blind, placebo-controlled clinical studies in order to achieve a better statistical evaluation based on a larger population. This re-examination of data also allowed us to reflect more intensely on various aspects of weight loss studies. Subjects were randomly divided into three groups: group A received a daily dose of HCA-SX 4,667 mg (providing 2,800 mg HCA per day); group B was given a daily dose of a combination of HCA-SX 4,667 mg, niacin-bound chromium (NBC) 4 mg (providing 400 microg elemental chromium), and Gymnema sylvestre extract (GSE) 400 mg (providing 100 mg gymnemic acid); and group C received a placebo in three equally divided doses 30-60 min before each meal. All subjects were provided a 2,000 kcal diet/day and participated in a supervised walking program for 30 min/day, 5 days/week. Eighty-two subjects completed the study. At the end of 8 weeks, in group A, both body weight and BMI decreased by 5.4%, low-density lipoprotein and triglycerides levels were reduced by 12.9% and 6.9%, respectively, while high-density lipoprotein levels increased by 8.9%, serum leptin levels decreased by 38%, serotonin levels increased by 44.5% and urinary excretion of fat metabolites increased by 32-109%. Group B demonstrated similar beneficial changes, but generally to a greater extent. No significant adverse effects were observed. The combined results confirm that HCA-SX and, to a greater degree, the combination of HCA-SX plus NBC and GSE reduce bodyweight and BMI, suppress appetite, improve blood lipid profiles, increase serum leptin and serotonin levels and increase fat oxidation more than placebo. We conclude that dosage levels, timing of administration, subject compliance and bioavailability of HCA-SX significantly affect results and that when taken as directed, HCA-SX is a highly effective adjunct to healthy weightcontrol.

**3) Guggulu (Commiphora mukul)**

**3.1) The efficacy and safety of herbal medicines used in the treatment of hyperlipidemia; a systematic review.**

Hasani-Ranjbar S, Nayeji N, Moradi L, Mehri A, Larijani B, Abdollahi M.

**Source**

Endocrinology and Metabolism Research Center, and Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran.

**Abstract**

**OBJECTIVE:**

This review focuses on the efficacy and safety of effective herbal medicines in the management of hyperlipidemia in human.

**METHODS:**

PubMed, Scopus, Google Scholar, Web of Science, and IranMedex databases were searched up to 11th May 2010. The search terms were "hyperlipidemia" and ("herbal medicine" or "medicine traditional", "extract plant") without narrowing or limiting search elements. All of the human studies on the effects of herbs with the key outcome of change in lipid profiles were included.

**RESULTS:**

Fifty three relevant clinical trials were reviewed for efficacy of plants. This study showed significant decrease in total cholesterol and LDL cholesterol after treatment with Daming capsule (DMC), chungyul-dan, Glycyrrhiza glabra, garlic powder (Allicor), black tea, green tea, soy drink enriched with plant sterols, licorice, Satureja khuzestanica, Monascus purpureus Went rice, Fenugreek, Commiphora mukul (guggul), Achillea wilhelmsii C. Koch, Ningzhi capsule (NZC), cherry, compositie salviae dropping pill (CSDP), shanzha xiaozhi capsule, Ba-wei-wan (hachimijogan), rhubarb stalk, Silybum marianum, Rheum Ribes and Jingmingdan granule (primrose oil). Conflicting data exist for red yeast rice, garlic and guggul. No significant adverse effect or mortality were observed except in studies with DMC, guggul, and Terminalia bellerica, Terminalia chebula, Emblica officinalis, ginger, and garlic powder (Allium sativum).

**CONCLUSION:**

Amongst reviewed studies, 22 natural products were found effective in the treatment of hyperlipidemia that deserve further works to isolate and characterization of their constituents to reach novel therapeutic and more effective agents.

**3.2) The hypolipidemic natural product Commiphora mukul and its component guggulsterone inhibit oxidative modification of LDL.**

Wang X, Greilberger J, Ledinski G, Kager G, Paigen B, Jürgens G.

**Source**

The Jackson Laboratory, Bar Harbor, ME 04609, USA. xw@jax.org

**Abstract**

There is accumulating evidence that LDL oxidation is essential for atherogenesis, and that antioxidants that prevent this oxidation may either slow down or prevent atherogenesis. In the present study, we found that Commiphora mukul and its cholesterol-lowering component, guggulsterone, effectively inhibited LDL oxidation mediated by either catalytic copper ions, free radicals generated with the azo compound 2,2'-azobis-(2-amidinopropane)dihydrochloride (AAPH), soybean lipoxygenase enzymatically, or mouse peritoneal macrophages. This inhibition was assessed by the decrease in the following parameters describing LDL oxidation: conjugated dienes, relative electrophoretic mobility (REM), thiobarbituric acid reactive substances, lipid hydroperoxides, oxidation-specific immune epitopes as detected with a monoclonal antibody against oxidized LDL, and the accumulation of LDL derived cholesterol esters in mouse peritoneal macrophages. We concluded that C. mukul and its lipid-lowering component, guggulsterone, significantly inhibit LDL oxidation. The combination of antioxidant and lipid-lowering properties of C. mukul and guggulsterone makes them especially beneficial against atherogenesis.

**3.3) GUGULIPID: a natural cholesterol-lowering agent.**

Urizar NL, Moore DD.

**Source**

Department of Molecular and Cellular Biology, Baylor College of Medicine, Houston, Texas 77030, USA. nurizar@bcm.tmc.edu

## **Abstract**

The resin of the Commiphora mukul tree has been used in Ayurvedic medicine for more than 2000 years to treat a variety of ailments. Studies in both animal models and humans have shown that this resin, termed gum guggul, can decrease elevated lipid levels. The stereoisomers E- and Z-guggulsterone have been identified as the active agents in this resin. Recent studies have shown that these compounds are antagonist ligands for the bile acid receptor farnesoid X receptor (FXR), which is an important regulator of cholesterol homeostasis. It is likely that this effect accounts for the hypolipidemic activity of these phytosteroids.

## **4) Ginger (Zingiber officinale)**

### **4.1) Comparative evaluation of the efficacy of ginger and orlistat on obesity management, pancreatic lipase and liver peroxisomal catalase enzyme in male albino rats.**

Mahmoud RH, Elnour WA.

#### **Source**

Biochemistry and Nutrition Department, Women College, Ain Shams University Cairo, Egypt. dr.rasha.asu@gmail.com.

#### **Abstract**

##### **BACKGROUND:**

Obesity is a disease involving body weight gain. Several synthetic drugs of better efficacy are being introduced in the modern system of medicine. Orlistat is a pharmacological agent promoting weight loss in obese subjects via inhibiting of gastric and pancreatic lipase. Ginger (*Zingiber officinale* Roscoe, Zingiberaceae) is one of the most commonly used spices around the world; it has long been used in traditional medicine as a cure for some diseases.

##### **OBJECTIVE:**

To evaluate the effect of ginger and orlistat on rats fed high fat diet.

##### **MATERIALS AND METHODS:**

Forty male Albino rats were either not treated (control), or fed high fat diet, or fed high fat diet with dietary orlistat supplementation (200 mg/kg diet), or fed high fat diet supplemented with 5% ginger powder. After four weeks of treatment, final body weight and food intake were determined. Blood samples were collected, lipid parameters, total bilirubin, pancreatic lipase were determined. Liver peroxisomes were isolated from rat livers and peroxisomal catalase activity was determined.

##### **RESULTS:**

Treatment with both ginger and orlistat had significant effect in reducing body weight, besides, supplementing diet with orlistat increase food intake. Both ginger and orlistat had the ability to reduce lipid profile, ginger had great effect in increasing HDL-cholesterol than orlistat. When compared to the control group, ginger treatment did not alter either total bilirubin or pancreatic lipase activity while orlistat clearly reduced their concentration. Orlistat supplementation induced a significant reduction in peroxisomal catalase level, while ginger has been reported to interfere with enzyme activity increasing its level.

##### **CONCLUSIONS:**

Ginger has a great ability to reduce body weight without inhibiting pancreatic lipase level, or affecting bilirubin concentration, with positive effect on increasing peroxisomal catalase level and HDL-cholesterol.

### **4.2) The safety and efficacy of a dietary herbal supplement and gallic acid for weight loss.**

Roberts AT, Martin CK, Liu Z, Amen RJ, Woltering EA, Rood JC, Caruso MK, Yu Y, Xie H, Greenway FL.

#### **Source**

Pennington Biomedical Research Center, Baton Rouge, Louisiana 70808, USA.

#### **Abstract**

The objective of this study was to test the safety and efficacy of NT, a dietary herbal supplement made from rhubarb, ginger, astragalus, red sage, and turmeric, combined with gallic acid (GA) to reduce food intake and cause weight loss. A total of 105 healthy subjects, 18-60 years old with a body mass index of 25-35 kg/m<sup>2</sup> and on no chronic medication, were randomized to a 300 mg/1.2 g NT-GA combination, a 600 mg/2.4 g NT-GA combination, or placebo in three divided doses daily for 24 weeks. Food intake was

measured at baseline and 2 weeks, and safety parameters were followed regularly. Pharmacokinetic studies of a 200 mg/800 g NT-GA combination and 800 mg GA alone were performed with and without food. There was no dose-related weight loss or reduction in food intake at the 8-week analysis, and the study was terminated early. Pharmacokinetic studies showed plasma levels of GA did not increase above 10 microM and were not dose-related. The NT-GA at all concentrations was well tolerated, but was ineffective in causing weight loss or in suppressing food intake. Pharmacokinetics suggested that GA plasma levels were limited by oral absorption, and may be the reason for lack of efficacy.

## 5) Maricha (*Piper nigrum*)

### 5.1) Molecular target of piperine in the inhibition of lipid droplet accumulation in macrophages.

Matsuda D, Ohte S, Ohshiro T, Jiang W, Rudel L, Hong B, Si S, Tomoda H.

#### Source

Graduate School of Pharmacy, Kitasato University, Shirokane, Tokyo, Japan.

#### Abstract

An alkaloid piperine isolated from the *Piper Nigrum* was found to inhibit lipid droplet accumulation in mouse macrophages, and especially inhibited cholesteryl ester (CE) synthesis (IC<sub>50</sub>: 25 microM). The metabolism of cholesterol from lysosome to lipiddroplet was inhibited with a similar IC<sub>50</sub> (18 microM), indicating that the site of inhibition is one of the steps between the lysosomes and the endoplasmic reticulum. Therefore, effects of piperine on acyl-CoA:cholesterol acyltransferase (ACAT) activity in the microsomes prepared from mouse macrophage and liver were studied, to show that the compounds inhibited the activity in both cases (IC<sub>50</sub>: 9.1, 7.0 microM, respectively). Furthermore, piperine was found to inhibit both ACAT1 and ACAT2 isozymes to a similar extent (IC<sub>50</sub>: 16, 18 microM, respectively) in cell-based assays using ACAT1- or ACAT2-expressing cells. Thus, it was suggested that piperine inhibited macrophage ACAT to decrease CE synthesis, leading to a reduction of lipid droplets.

### 5.2) Improvement in insulin resistance and favourable changes in plasma inflammatory adipokines after weight loss associated with two months' consumption of a combination of bioactive food ingredients in overweight subjects.

Rondanelli M, Opizzi A, Perna S, Faliva M, Solerte SB, Fioravanti M, Klersy C, Edda C, Maddalena P, Luciano S, Paola C, Emanuela C, Claudia S, Donini LM.

#### Source

Department of Applied Health Sciences, Section of Human Nutrition and Dietetics, Faculty of Medicine, University of Pavia, Azienda di Servizi alla Persona di Pavia, Servizio Endocrino Nutrizionale, Istituto di Riabilitazione "Santa Margherita", Via Emilia 12, Pavia, Italy, mariangela.rondanelli@unipv.it.

#### Abstract

This randomized, double blind, placebo-controlled, 8 week trial assessed the efficacy on metabolic changes produced by a consumption of a combination of bioactive food ingredients (epigallocatechin gallate, capsaicins, piperine and L-carnitine) versus a placebo, as part of a therapeutic 'lifestyle change' diet, in 86 overweight subjects. Forty-one patients (2/14 F/M; age 43.7 ± 8.5; BMI 30.3 ± 3.5 kg/m<sup>2</sup>) were randomized to the supplemented group and 45 (29/16; age 40.7 ± 10.2; BMI 30.0 ± 2.7) to the control group. We observed that consumption of the dietary supplement was associated with a significantly greater decrease in insulin resistance, assessed by homostasis model assessment ( $p < 0.001$ ), leptin/adiponectin ratio ( $p < 0.04$ ), respiratory quotient ( $p < 0.008$ ). LDL-cholesterol levels ( $p < 0.01$ ). Moreover, statistically significant differences were recorded between the two groups in relation to urinary norepinephrine levels ( $p < 0.001$ ). Leptin, ghrelin, C-reactive protein decreased and resting energy expenditure increased significantly in the supplemented group ( $p < 0.05$ , 0.03, 0.02 and 0.02 respectively), but not in the placebo group; adiponectin decreased significantly in the placebo group (0.001) but not in the supplemented group, although no statistical significance between the groups was elicited. BMI, fat mass (assessed by DXA) and vascular endothelial growth factor significantly decreased, whilst the resting energy expenditure/free fat mass significantly increased in both groups. In general, a greater change was recorded in the supplemented group compared to the placebo, although no

statistically significant difference between the two groups was recorded. These results suggest that the combination of bioactive food ingredients studied might be useful for the treatment of obesity-related inflammatory metabolic dysfunctions.

### **5.3) Piperine, an active principle from Piper nigrum, modulates hormonal and apo lipoprotein profiles in hyperlipidemic rats.**

Vijayakumar RS, Nalini N.

#### **Source**

Department of Biochemistry and Biotechnology, Annamalai University, Annamalainagar-608 002, Tamilnadu, India.

#### **Abstract**

##### **PURPOSE:**

To study the effect of piperine, an alkaloid, on thyroid hormones and apolipoproteins in high-fat-diet (HFD) and antithyroid drug-induced hyperlipidemic rats.

##### **EXPERIMENTAL:**

Male Wistar rats were first divided into two groups, control diet and high-fat diet (HFD) and then subdivided into four subgroups of ten animals each. The animals were treated with the following regimens for 10 weeks: 1% carboxymethyl cellulose; 10 mg carbimazole (CM)/kg body weight; 10 mg CM + 40 mg piperine/kg body weight, and 10 mg CM + 2 mg atorvastatin /ATV//kg body weight. Lipid profiles, hormone levels, and apolipoprotein levels were studied in all groups.

##### **RESULTS:**

HFD and/or CM administration significantly elevated the plasma levels of total cholesterol, VLDL, LDL, triglycerides, free fatty acids, and phospholipids, but significantly reduced the HDL levels. Moreover, CM administration significantly reduced apo A-I levels and T3, T4 and testosterone levels while significantly elevating plasma apo B, thyroid stimulating hormone (TSH) and insulin levels. The simultaneous administration of piperine and HFD significantly reduced plasma lipids and lipoproteins levels, except for HDL, which was significantly elevated. Piperine supplementation also improved the plasma levels of apo A-I, T3, T4, testosterone, and I and significantly reduced apo B, TSH, and insulin to near normal levels.

##### **CONCLUSIONS:**

The data presented here provide evidence that piperine possesses thyrogenic activity, thus modulating apolipoprotein levels and insulin resistance in HFD-fed rats, opening a new view in the management of dyslipidemia by dietary supplementation with nutrients.

### **5.4) Piperine-mediated changes in the permeability of rat intestinal epithelial cells. The status of gamma-glutamyl transpeptidase activity, uptake of amino acids and lipid peroxidation.**

Johri RK, Thusu N, Khajuria A, Zutshi U.

#### **Source**

Regional Research Laboratory (CSIR), Jammu-Tawi, India.

#### **Abstract**

The effect of piperine (1-[5-(1,3-benzodioxol-5-yl)-1-oxo-2,4-pentadienyl]piperidine), (from Piper nigrum) on the absorptive function of the intestine was studied. In vitro experiments showed that piperine (25-100 microM) significantly stimulated gamma-glutamyl transpeptidase (gamma-GT, EC 2.3.2.2.) activity, enhanced the uptake of radiolabelled L-leucine, L-isoleucine and L-valine, and increased lipid peroxidation in freshly isolated epithelial cells of rat jejunum. The kinetic behaviour of gamma-GT towards substrate and acceptor altered in the presence of piperine. In the presence of benzyl alcohol, an enhanced gamma-GT activity due to piperine was maintained. These results suggested that piperine may interact with the lipid environment to produce effects which lead to increased permeability of the intestinal cells.

## **6) Fenugreek (Trigonella foenum-graecum)**

### **6.1) Antihyperglycemic and protective effects of Trigonella foenum graecum seed powder on biochemical alterations in alloxan diabetic rats.**

Kumar P, Kale RK, Baquer NZ.

**Source**

School of Life Sciences, Jawaharlal Nehru University, New Delhi, India.

**Abstract**

**BACKGROUND:**

Trigonella foenum-graecum, an annual herb belonging to the family Leguminosae, commonly known as fenugreek, has been reported to have hypoglycemic, hypocholesterolemic, hyperinsulinemic and antidiabetic properties. In the present study, the effect of oral feeding of Trigonella foenum-graecum seed powder (TSP) has been studied on blood glucose, monoamine oxidase (MAO), membrane fluidity, neurolipofuscin content, DNA degradation and glucose transporter-4 (GLUT4) accumulation in the alloxan-induced diabetic rat brain.

**METHODS:**

Diabetes was induced by administration of alloxan monohydrate (15 mg/100 g body weight) and diabetic rats were treated with 2 IU insulin, per day and 5% TSP in the diet for 21 days.

**RESULTS:**

Diabetic rats showed hyperglycemia with almost four fold high blood glucose levels. Increased MAO activity with correlated increase in genomic DNA degradation in the diabetic brain supports the hypothesis that catecholamine oxidation is an important source of oxidative stress, causing loss of membrane fluidity, increased neurolipofuscin and decreased of GLUT4 expression with diabetes in the brain. The present study showed that TSP treatment reversal the changes to near normal levels in diabetic rat brain.

**CONCLUSIONS:**

The present findings indicate that the TSP exerts its anti-diabetic and neuroprotective effects, probably mediated through a decrease in hyperglycemia and oxidative stress thereby ameliorating the control and management of diabetic complications.

**6.2) Dose-dependent effects, safety and tolerability of fenugreek in diet-induced metabolic disorders in rats.**

Muraki E, Hayashi Y, Chiba H, Tsunoda N, Kasono K.

**Source**

Department of Clinical Dietetics & Human Nutrition, Josai University, Saitama, Japan. e-muraki@josai.ac.jp

**Abstract**

**BACKGROUND:**

We previously reported that fenugreek (*Trigonella foenum-graecum* L.) improved diet-induced metabolic disorders in rats. The purpose of the present study was to examine the dose-dependent effects, safety and tolerability of fenugreek.

**METHODS:**

The diets used in this study were the high-fat high-sucrose diet (HFS; lard 50%kcal, sucrose 25%kcal) as a control (Ctrl group) or the HFS containing 0.25% (VL group), 1.25% (L group), 2.50% (M group), 5.00% (H group) or 12.30% (VH group) fenugreek based on the modified version of the AIN-93G purified diet.

**RESULTS:**

Fenugreek dose-dependently reduced the hepatic triglyceride and total cholesterol levels. Fenugreek also dose-dependently increased the excretion of cholesterol and total bile acids into the feces. However, the glucose tolerance showed no significant change by fenugreek administration. The VL and L groups did not significantly change triglyceride or total cholesterol levels in the liver. The VL group showed no increase in excretion of triglyceride, total cholesterol or bile acids in the feces. The VH group showed appetite reduction and diarrhea, while no adverse effect or symptoms were observed in the M group.

## **CONCLUSION:**

These results suggest that fenugreek inhibited lipid accumulation in the liver by increasing the lipid excretion in the feces. The effective, safe and tolerable dose of fenugreek was found to be around 2.50% (w/w).

### **6.3) A fenugreek seed extract selectively reduces spontaneous fat consumption in healthy volunteers.**

Chevassus H, Molinier N, Costa F, Galtier F, Renard E, Petit P.

#### **Source**

CHRU Montpellier, Centre d'Investigation Clinique, Montpellier, France. h-chevassus@chru-montpellier.fr

#### **Abstract**

##### **PURPOSE:**

Fenugreek seeds (*Trigonella foenum-graecum* L.) are an old herbal remedy used to treat metabolic and nutritive dysfunctions. They have been shown to modulate feeding behaviour in animals, but strong clinical data are lacking. The aim of this study was to investigate the effects of a repeated administration of a fenugreek seed extract on energy intake and eating behaviour in healthy human volunteers.

##### **METHODS:**

Twelve healthy male volunteers completed a double-blind randomized placebo-controlled three-period cross-over trial of two different doses of a fenugreek seed extract (588 and 1176 mg). The three 14-day treatment periods were separated by a 14-day washout period. The main endpoints were energy intake, assessed in volunteers under normal ambulatory and free-living conditions by a 3-day detailed dietary record and during a meal test, weight, fasting glucose level, insulin and lipid profile, visual analogue scale scores of appetite/satiety and blood glucose and insulin levels measured repeatedly after a standardized breakfast.

##### **RESULTS:**

Daily fat consumption was significantly decreased by the higher dose of fenugreek seed extract [3.73 vs. 4.51 MJ day<sup>-1</sup>], -17.3% vs. placebo, 95% confidence interval (CI) -1.51 to -0.05, n = 12, P = 0.038]. This specific reduction tended to lower the total energy intake (9.97 vs. 11.29 MJ day<sup>-1</sup>), -11.7% vs. placebo, 95% CI -2.91 to 0.26, n = 12, P = 0.094). No significant effect was observed on the other nutrients or other endpoints.

##### **CONCLUSIONS:**

The repeated administration of a fenugreek seed extract specifically decreases dietary fat consumption in humans which, given the traditional use of the plant, constitutes a novel result.

## **7) Madhunashini (*Gymnema sylvestre*)**

### **7.1) Effects of a natural extract of (-)-hydroxycitric acid (HCA-SX) and a combination of HCA-SX plus niacin-bound chromium and *Gymnema sylvestre* extract on weight loss.**

Preuss HG, Bagchi D, Bagchi M, Rao CV, Dey DK, Satyanarayana S.

#### **Source**

Department of Physiology and Biophysics, Georgetown University Medical Center, Georgetown, Washington, DC 20057, USA. preussHG@georgetown.edu

#### **Abstract**

##### **AIM:**

The efficacy of optimal doses of highly bioavailable (-)-hydroxycitric acid (HCA-SX) alone and in combination with niacin-bound chromium (NBC) and a standardized *Gymnema sylvestre* extract (GSE) on weight loss in moderately obese subjects was evaluated by monitoring changes in body weight, body mass index (BMI), appetite, lipid profiles, serum leptin and excretion of urinary fat metabolites. HCA-SX has been shown to reduce appetite, inhibit fat synthesis and decrease bodyweight without stimulating the central nervous system. NBC has demonstrated its ability to maintain healthy insulin levels, while GSE has been shown to regulate weight loss and blood sugar levels.

##### **METHODS:**

A randomized, double-blind, placebo-controlled human study was conducted in Elluru, India for 8 weeks in 60 moderately obese subjects (ages 21-50, BMI >26 kg/m<sup>2</sup>). Subjects were randomly divided into

three groups. Group A was administered HCA-SX 4667 mg, group B was administered a combination of HCA-SX 4667 mg, NBC 4 mg and GSE 400 mg, while group C was given placebo daily in three equally divided doses 30-60 min before meals. All subjects received a 2000 kcal diet/day and participated in supervised walking.

**RESULTS:**

At the end of 8 weeks, body weight and BMI decreased by 5-6% in both groups A and B. Food intake, total cholesterol, low-density lipoproteins, triglycerides and serum leptin levels were significantly reduced in both groups, while high-density lipoprotein levels and excretion of urinary fat metabolites increased in both groups. A marginal or non-significant effect was observed in all parameters in group C.

**CONCLUSION:**

The present study shows that optimal doses of HCA-SX and, to a greater degree, the combination of HCA-SX, NBC and GSE can serve as an effective and safe weight-loss formula that can facilitate a reduction in excess body weight and BMI, while promoting healthy blood lipid levels.

**7.2) Hypoglycemic activity of *Gymnema sylvestre* extracts on oxidative stress and antioxidant status in diabetic rats.**

Kang MH, Lee MS, Choi MK, Min KS, Shibamoto T.

**Source**

Department of Food Science and Nutrition, Graduate School of Venture for BK21, Hoseo University, Asan, South Korea.

**Abstract**

Diabetes mellitus, which is associated with oxidative damage, has a significant impact on health, quality of life, and life expectancy. An ethanol extract of *Gymnema sylvestre* leaf was examined in vitro and in vivo to investigate the role of antioxidants in diabetic rats. The extract exhibited strong antioxidant activity in the assays, including TBA (56%), SOD-like (92%), and ABTS (54%). Blood glucose levels in the diabetic rats fed *G. sylvestre* extract decreased to normal levels. The presence of the antihyperglycemic compounds gymnemagenin and gymnemic acids in *G. sylvestre* extract was detected by LC/MS analysis. Lipid peroxidation levels were decreased by 31.7% in serum, 9.9% in liver, and 9.1% in kidney in the diabetic rats fed the extract. Feeding *G. sylvestre* extract to the diabetic rats decreased the activity of glutathione peroxidase in cytosolic liver and glutamate pyruvate transaminase in serum to normal levels.

**7.3) An open label study on the supplementation of *Gymnema sylvestre* in type 2 diabetics.**

Kumar SN, Mani UV, Mani I.

**Source**

Department of Foods and Nutrition, WHO Collaborating Centre for Research & Training in Promoting Nutrition in Health & Development, The M S University of Baroda, Vadodara, Gujarat 390 020, India. smitz 22@yahoo.co.in

**Abstract**

Diabetes mellitus is a complex metabolic disorder characterized by chronic hyperglycemia, and associated with long-term damage and dysfunction of various organs. Management of diabetes is therefore vital and involves maintaining euglycemia as much as possible by reducing blood glucose and by increasing insulin sensitivity and peripheral glucose uptake. Ayurveda has promoted the management of diabetes by regulating carbohydrate metabolism using several medicinal herbs, one of which is *Gymnema sylvestre* (GS). GS has been used in parts of India as a hypoglycemic agent and the results have been encouraging. Accordingly, we planned a quasi-experimental study to investigate the efficacy of the herb among type 2 diabetics. Patients enrolled from free-living population were purposively assigned to experimental or control groups, based on their willingness to participate in the study. The experimental group was supplemented with 500 mg of the herb per day for a period of 3 months, and the efficacy of the herb was assessed through a battery of clinical and biochemical tests. Supplementation of the diet with GS reduced polyphagia, fatigue, blood glucose (fasting and post-prandial), and glycosylated hemoglobin and there was a favorable shift in lipid profiles and in other clinico-biochemical tests. These findings suggest a beneficial effect of GS in the management of diabetes mellitus.

## Medohar Guggulu

### **Medohar Guggulu (Ayurvedic Weight Loss Formula)**

Medohar Guggulu - Ayurvedic Weight Loss Formula

Medohar Guggulu is a unique classical Ayurvedic Anti Obesity formula which is used to maintain proper cholesterol and weight levels. It removes kapha accumulations from the body gently and effectively. Ayurveda suggests to use Guggulu in the treatment of 'Santarpana' born disorders. This term is used for the lifestyle where in one eats a lot, particularly high calorie diet rich in fats and carbohydrate and leads an physically lazy life and sedentary daily routine.

Obesity as well as other "Civilization born disorders" like diabetes, hypertension are now proved to be facilitated by this life style. One of the Guggul's main action is to help in weight loss. It acts best when it is coupled with dietary and exercise regimen. Remember, it is foolishness to take herbs or other holistic treatment simply to get rid of some disease while adopting the lifestyle that promotes that kind of disorders.

**Suggested Usage:** 2 tabs thrice daily with warm water.

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MORE ENHANCED STUDIES CAN BE REVIEWED BELOW**

- <http://www.ncbi.nlm.nih.gov/pubmed/15640470?dopt=Abstract>

- <http://www.ncbi.nlm.nih.gov/pubmed/17557985>

- <http://www.webmd.com/diet/news/19991128/green-tea-boosts-metabolism-protects-against-diseases>

- <http://www.ncbi.nlm.nih.gov/pubmed/23569867>
- <http://www.webmd.com/vitamins-supplements/ingredientmono-591-GUGGUL.aspx?activeIngredientId=591&activeIngredientName=GUGGUL>
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