GlucodOX™ Overview

Health Benefits of GlucodOX™ Proprietary Guggulsterone Extract

GlucodOX™ is a proprietary oleo-gum-resin extract derived from the trunk of the *Commiphora mukul* tree and formulated in a medium-chain triglyceride (MCT) base, which is composed of C8 and C10 fatty acids for improved absorption. The tree grows in northeast Africa, India, and the Arabian Peninsula and supplies a resin collected from the bark of the growing tree. The oleo-gum-resin known also as guggul has been used for thousands of years in Asia as a natural antiseptic and wound-healing agent and to treat hypercholesterolemia, atherosclerosis, rheumatism, and obesity. The natural product utilizes mukul's rich aromatic compounds, including volatile oil, resin, and gums. GlucodOX™ is standardized by high-performance liquid chromatography to 2.0% of the active compound guggulsterones, which have beneficial effects for supporting normal lipid metabolism, glucose metabolism, and cellular energy. GlucodOX™ is made from a unique optimized supercritical CO_2 extraction using a co-solvent of ethanol that recovers active constituents that are then dissolved in MCT oil for enhanced efficacy and bioavailability.

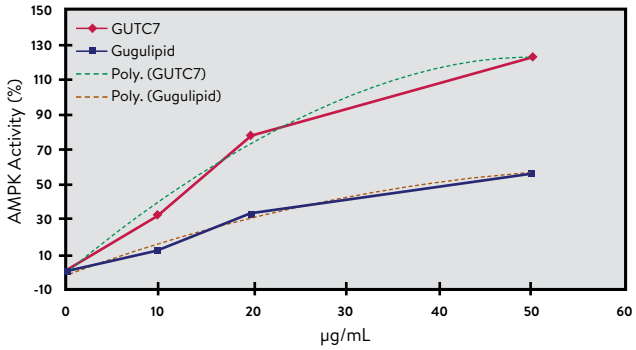
Multiple mechanisms of action

The mechanisms of action of GlucodOX™ vary for its different bioactive effects. For glucose control, GlucodOX™ increases cellular glucose, a measure of improved insulin sensitivity (Claudel, 2005). For supporting cholesterol levels already within the normal range, GlucodOX™ works to inhibit the natural production of cholesterol through the enzyme HMG-CoA reductase, a mechanism that highly effective statin drugs are based on (Izzat, 2000; Urizar, 2002). For healthy weight control and fat metabolism, it reduces transformation of preadipocytes to adipocytes (fat cells) and storage of triglycerides (fats) (Yang, 2008; Rizzo, 2006).

Energizing effects

In addition, GlucodOX™ may have other beneficial health effects. Energizing action was found by its ability to stimulate AMPK, (5' adenosine monophosphate-activated protein kinase) the master energy sensor and regulator in the body that has been described as a nutrient/energy sensor involved in supporting energy levels in cells throughout the body, and in helping with formation of new mitochondria (cellular-energy-producing units) (Lage 2008, Long 2006, Steinberg 2009). AMPK is directly or indirectly involved in the regulation of many other fundamental processes including lipid, carbohydrate, and protein metabolism, cell growth and apoptosis (programmed cell death), and stress response pathways. A comparison between GlucodOX™ and a leading competitor's guggulsterone extract, Gugulipid®, found that GlucodOX™ had significantly better effects on modulation of AMPK activity than Gugulipid® at every dose. GlucodOX™ enhanced AMPK activity by 123% compared with 56.5% by Gugulipid® at 50 µg/mL (see Fig. 1).

Fig. 1: Enhancement of AMPK Activity by GUTC7 (GlucodOX) and Gugulipid in HepG2 cell line (with trendline)



GlucodOX™ outperformed Gugulipid® in enhancement of AMPK activity at different doses. Enhanced AMPK activity at 50 µg/mL.

Joint support

An anti-inflammatory effect for osteoarthritis of the knee is another physiological benefit. Preclinical and clinical investigations of guggul have shown reduction of pain, stiffness, and improved function. A study used 500 mg of guggul extract three times a day along with food, measuring the WOMAC total score as a primary outcome measure, with visual analog scale (VAS) and a 6-minute walk test used as secondary measure. There was a significant improvement of the primary and secondary outcome measures. For the WOMAC total score, participants were significantly improved ($p < 0.0001$) after taking the supplement for 1 month and continued into the 2-month period and after follow-up. The secondary measures of pain in the VAS format demonstrated participant improvement ($p < 0.05$) up to the 2-month assessment ($p < 0.001$). (Singh, 2003).

Cholesterol lowering and other cardio benefits

Clinical studies prove the efficacy of the guggulsterone active compounds in GlucodOX™. The effects of a 50-mg dose of guggulipid twice daily for 24 weeks were evaluated for the management of hypercholesterolemia in 61 patients in a randomized, double-blind study. Guggulipid decreased the total cholesterol level by 11.7%, the low-density lipoprotein cholesterol (LDL) by 12.5%, triglycerides by 12.0%, and the total cholesterol/high-density lipoprotein (HDL) cholesterol ratio by 11.1% compared with placebo group. Lipid peroxides, which are related to vascular damage from free radicals and progression of cardiovascular disease, declined 33.3% in the guggulipid group compared with the placebo group (Singh, 1994).

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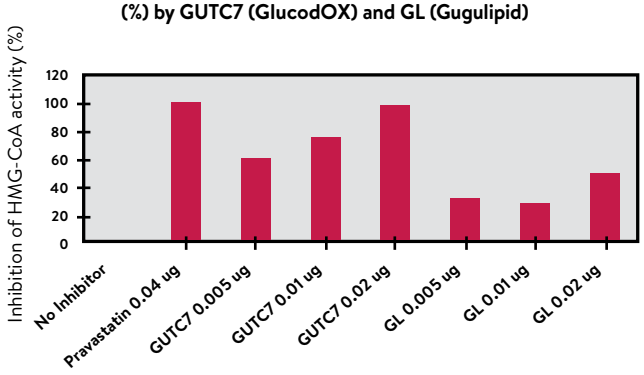
Cardio health physiology

There are multiple mechanisms of action for the cardiovascular benefits of guggulsterone. It has been established as an antagonist at farnesoid x receptor, a key transcriptional regulator for the maintenance of cholesterol and bile acid homeostasis, which have hypolipidemic effects. Guggulsterone upregulates the bile salt export pump, an efflux transporter responsible for removal of cholesterol metabolites through excretion of bile acids from the liver. Guggulsterone has been found to potently inhibit the activation of nuclear factor-κB, an important regulator of inflammatory responses, explaining its anti-inflammatory effect (Deng, 2007). GlucodOX™ also inhibits a principle enzyme involved in cholesterol biosynthesis known as HMG-CoA reductase, the same mechanism by which statin drugs work, though guggul is not known to have the adverse effects of statins such as muscle and liver damage. GlucodOX™ inhibited HMG-CoA reductase as potently as Pravastatin, a leading statin drug, at only 0.02 mcg, half the concentration of 0.04 mcg of the latter (see Fig. 2).

Fig. 2: Inhibition of HMG-Co A reductase activity (%) by GUTC7 (GlucodOX) and GL (Gugulipid)

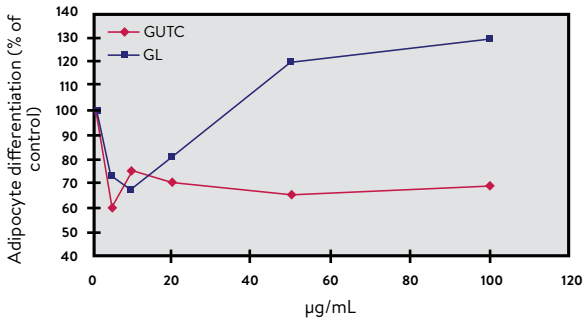


GlucodOX™ is about twice as potent an inhibitor of HMG-CoA reductase as Gugulipid®

Anti-obesity effect

A form of guggul known as guggulsterone phosphate salt compound was tested on body composition and mood states in overweight adults. In a double-masked, randomized, placebo-controlled study, 20 overweight subjects received guggulsterones (750 mg) and phosphate (1,650 mg) daily and were instructed to follow the American Heart Association Step One diet and a 3-day-per-week circuit exercise program. Body weight significantly decreased 3.2%, ($p < 0.05$) in the experimental group, and fat mass significantly decreased 20.6% in the experimental compared with 8.6% in the control groups ($p < 0.01$). In addition, mood and fatigue indices improved significantly in the experimental group (63.7%, $p < 0.01$) (Antonio, 1999).

Fig. 3: Inhibition of adipocyte differentiation by GUTC7 (GlucodOX) and GL (Gugulipid) in 3T3-L1 adipocytes



Inhibiting adipocyte differentiation helps reduce fat cell synthesis and subsequent storage and growth of fat tissue. GlucodOX™ inhibited adipocyte differentiation almost twice as effectively as a regular guggulsterone extract over a wide range of concentrations, from 60 µg/mL to 100 µg/mL.

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