

Chios Mastic Gum, the natural “tears” with lipid-lowering and anti-atherosclerotic properties: A new drug candidate?

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Abstract

Chios Mastic Gum (CMG) has been extensively studied for its anti-oxidant and anti-inflammatory properties, while novel data suggest its potent hypolipidemic and anti-atherosclerotic activity. This editorial is an annotation on the current perspectives on the utilization of CMG as potent atherosclerosis-suppressing agent. The existing knowledge derived from clinical and basic research studies is comprehensively summarized.

Key words: Chios Mastic Gum; atherosclerosis; inflammation

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Editorial

Chios Mastic Gum (CMG), is a natural resin exclusively cultivated and extracted from *Pistacia Lentiscus* var *Chia* trees at the Greek island of Chios. It is consisted of an insoluble polymer (poly- β -myrcene) and two different fractions, an acidic and a neutral, including numerous other compounds that synergistically attribute to its beneficial effects [1]. Since antiquity, CMG has been extensively used in the tra-

ditional medicine as an anti-inflammatory agent for the treatment of gastrointestinal disorders and for wound healing. In the modern era, CMG has been officially recognized by the European Medicines Agency (EMA) as a herbal medicinal product with strong anti-ulcer and anti-inflammatory activity against *Helicobacter Pylori* [2]. During the last decades, the scientific interest has shed light on considerable hypolipidemic, hypoglycemic and anti-ath-

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erosclerotic effects of CMG [3-5]. However, do we currently have enough evidence from both in vitro and in vitro studies in order to suggest and establish a novel green drug candidate for cardiovascular protection?

Dedoussis et al [6], were the first to introduce a potent anti-atherosclerotic effect of CMG on peripheral blood mononuclear cells exposed to oxidized low density lipoprotein(oxLDL), a highly cytotoxic agent. Total CMG extract diminished cell senescence by glutathione (GSH) levels restoration and CD36 expression upregulation, both indicating a strong anti-oxidant effect. Remarkably, while High-Performance Liquid Chromatography analysis in the total CMG extract was also performed, the triterpenoid fraction was found as the most drastic anti-atherogenic compound among the others. Subsequently, another study by Loizou et al. [7], confirmed the above results by elucidating the anti-inflammatory effect of CMG on human aortic endothelial cells. Both CMG total extract and tirucallol, an isolated phytosterol from the neutral extract, directly inhibited the phosphorylation of NFkB-p65 and the expression of adhesion molecules dependent to TNF- α stimulation. Since monocyte recruitment and adhesion to endothelial cells in response to low grade inflammation and oxidative stress is a crucial step in the pathogenesis of atherosclerosis, the above stated data suggested strong anti-atherosclerotic and anti-inflammatory properties of CMG and its major compounds [7].

The cardioprotective and atheroprotective effect of CMG has also been related to its antioxidant and hypocholesterolemic effects, observed in animal studies[5,8]. The administration of total CMG without polymer and of neutral fraction in hypercholesterolemic rabbits led to a significant decrease of total cholesterol levels by 47 and 88% respectively, while the administration of Chios mastic gum oil (MGO) in hyperlipidemic rats resulted in a dose-dependent reduction in the constitutive synthesis and plasma levels of serum cholesterol and triglycerides [2]. Notably, camphene, a minor constituent that represents less than 1% of total MGO, was found to exert a strong lipid-lowering effect independently of HMG-CoA reductase activity [3]. Reactivation of lipolytic

enzymes by camphene for early clearance of lipids from circulation in detergent induced hyperlipidemia was considered as an alternative metabolic process that could explain its hypolipidemic effect. It should be highlighted that as camphene acts independently of HMG-CoA reductase, implying thus a possible hepatoprotective effect, that would allow its use not only as a single agent, but also in combination with low dose statins, that occasionally result to liver injury [3]. Additionally, the study of Georgiadis et al. [8], in diabetic mice, not only established the protective effects of low and high dose CMG on liver steatosis and inflammation, but also enlightened a rather new hypoglycemic effect. CMG administration in streptozotocin-induced diabetic mice resulted in a significant decrease of glucose levels, apart from lipid-lowering effects. Interestingly, the low-dose group presented significantly lower serum levels of total cholesterol, LDL and triglycerides and significantly higher levels of high density lipoprotein (HDL), providing evidence of potent therapeutic implications of CMG in patients with metabolic syndrome [8].

As far as human studies are concerned, total mastic extract administration in the form of powder to healthy humans over the age of 50 for 18 months resulted in a decrease in serum lipid and apolipoprotein -A and -B levels [9]. Additionally, CHIOS-MASTIHA was the first prospective, randomized, placebo-controlled, pilot study in healthy volunteers with total cholesterol levels above 200 mg/dl that examined the effect of different CMG constituents and concentrations on lipid levels[9]. The effect was stronger in the group receiving a daily a total dose of 1 g of crude CMG (330 mg capsules) with regards to total cholesterol levels. As the above stated dose is considered low to moderate, the failure to reduce further serum LDL cholesterol and triglycerides levels could be attributed to this relatively low dose. It should be noted that CMG did not present any adverse or toxic effects even in a dose of 28g/person/day [9].

In compliance with the previous data, a recent study in rabbits undergoing myocardial ischemia-reperfusion injury, confirmed the anti-atherosclerotic activity of CMG [4]. Both total CMG

and neutral CMG extract reduced the infarct size and the oxidation of LDL in normal fed rabbits. The reduction in infarct size by CMG can be achieved by several mechanisms such as the elimination of reperfusion injury or by activation of intracellular mediators that are crucial to protect the heart against lethal reperfusion injury. However, this beneficial effect was not observed in cholesterol fed rabbits, that can be attributed to an impaired endothelial function in present of hyperlipidemia and atherosclerosis [4].

In conclusion, Chios Mastic Gum exerts potent lipid lowering and anti-atherosclerotic effects, in parallel to its strong antioxidant capacity in the endothelium. It can be suggested that CMG could be used as a natural agent or combination drug in terms of

cardiovascular prevention and treatment. Summarizing recent studies, it can be hypothesized that CMG could possess antiatherogenic effects by modulating the nuclear peroxisome proliferator-activated receptors (PPAR), especially the PPAR- α isoforms, that orchestrate a transcriptional regulation of the endothelium. However, further pharmacokinetic and in vitro studies are necessary in order to specify the optimal dosage of CMG in cardiovascular protection and its exact mechanisms of action. ▣

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Περίληψη

Μαστίχα Χίου, τα φυσικά "δάκρυα" με υπολιπιδαιμικές και αντιαθηρωματικές ιδιότητες: Νέος φαρμακευτικός παράγων;

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Η Μαστίχα Χίου έχει μελετηθεί εκτενώς για τις αντιοξειδωτικές και αντιφλεγμονώδεις ιδιότητές της, ενώ νεότερα δεδομένα προτείνουν μία ισχυρή υπολιπιδαιμική και αντιαθηρωματική δράση της. Η παρούσα ανασκόπηση αποτελεί έναν σύντομο σχολιασμό στις τρέχουσες προοπτικές χρήσης της Μαστίχας Χίου ως ισχυρό παράγοντα πρόληψης και θεραπείας της αθηροσκλήρωσης και των επιπλοκών της. Οι υπάρχουσες γνώσεις που προκύπτουν από κλινικές μελέτες και πρωτόκολλα βασικής έρευνας συνοψίζονται παρακάτω.

Λέξεις ευρετηρίου: Μαστίχα Χίου, αθηροσκλήρωση, φλεγμονή

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