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Medicinal properties of Mediterranean plants against glucose and lipid disorders

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Abstract
There are several components isolated from plants grown in Mediterranean environment exhibiting significant beneficial properties against a variety of disorders related to lipid or glucose metabolism. In this context, plant species (e.g. *Salvia officinalis, Rosmarinus officinalis, Lavandula stoechas, Melissa officinalis, Mentha piperita*, *Thymus vulgaris, Origanum majorana, Sideritis raeseri, Ocimum basilicum*, *Pistacia lentiscus*, *Crocus sativus*, *Daucus carota*) may act against lipid or carbohydrate metabolic disorders through their antioxidant, anti-inflammatory or other properties, or due to the beneficial actions of their compounds. New horizons are very promising, since these plant species have been used both in Traditional Medicine and in current clinical practice.

Keywords: Plants, Mediterranean, medicine, glucose, lipid metabolism

Introduction
Nowadays, there is an increased demand for the use of natural products in order to treat different diseases, instead of using synthetic drugs which might have adverse effects. The rich and fertile land of Mediterranean fosters the growth of various species of plants known for their considerable medicinal properties. This review aims to summarize the principal observations regarding the lipid and glucose lowering activities of plants grown in Greece and in other Mediterranean countries with special focus on the possible mechanisms involved.

Methodology
Various scientific search engines such as PubMed, Medline, Science Direct, Scopus, Springer Link were used to retrieve online literature. Human, in vitro and animal studies investigating the favorable effects of medicinal plants grown in Mediterranean countries on lipid or glucose metabolism were included. Studies in languages other than English and also studies which their full text were not available and had no abstract, were excluded. In particular, pre-set searching strings such as "medicinal plants", the classic latin name of the plant species or the species name, "medicinal plants" and "lipid lowering effects'', "medicinal plants" and "Mediterranean", "plants" and "glucose lowering effects", "plants" and "antioxidant properties'', "plants" and "lipid metabolism" were used to collate the relevant studies. The results were then cross-referenced to generate a total number of 69 references cited in this review (mainly during the period 2005–2015). To systematically summarize the lipid lowering effects and the hypoglycemic properties of medicinal plants along with the potential mechanisms involved, a total of 12 plant species belonging to 4 families were included in this review. Table 1 represents a list of these medicinal plants according to their corresponding families. The major medicinal effects of these plants or their compounds on lipid and glucose metabolism are reported. Moreover, the main biological properties of these plant species which may account for their favorable actions on lipid and glucose levels are also discussed.

Table 1: Plant species grown in Greece and other Mediterranean countries

Families	Lamiaceae	Anacardiaceae	Iridaceae	Apiaceae
Common name (Species)	Sage (*Salvia officinalis*) Rosemary (*Rosmarinus officinalis*) Lavender (*Lavandula stoechas*) Lemon balm (*Melissa officinalis*) Peppermint (*Mentha piperita*) Thyme (*Thymus vulgaris*) Marjoram (*Origanum majorana*) Basil (*Ocimum basilicum*) Oregano (*Origanum vulgare*	Mastic Tree (*Pistacia lentiscus*)	Kozani Crocus or Saffron (*Crocus sativus*)	Wild carrot (*Daucus carota*)

Therapeutic properties against disorders on lipid and glucose metabolism

Sage *(Salvia officinalis)* (Figure 1) is described in literature to exhibit significant hypoglycemic and hypolipidemic activity both in experimental studies with animals but also in clinical level [1, 2]. The regulating properties of Rosemary (Rosmarinus *officinalis*) on glucose metabolism have been documented *in vitro* [3] and *in vivo* [4]. Both lavender (*Lavandula stoechas*) and Lemon balm (*Melissa officinalis*) have shown significant lipid lowering effects whereas their impact on leptin and insulin pathways have been also suggested [5, 6, 7, 8]. Animal studies and clinical trials report the protective effects of Peppermint (*Mentha piperita*) against disorders in lipid and glucose homeostasis [9, 10, 11, 12, 13, 14]. Pharmacological studies showed that Wild carrot *(Daucus carota)* also exhibits hypoglycemic and hepatoprotective activity [15]. In recent studies, an improvement in metabolic parameters and serum glucose levels of diabetic mice were observed following administration of a marjoram *(Origanum majorana)* extract [16].

Thyme *(Thymus vulgaris)* (Figure 2) extract has been shown to improve the hepatic function [17]. In a study investigating the impact of an aqueous extract of oregano (*Origanum vulgare)* in a STZ-induced diabetic rat model, the glucose lowering effects of this herb have been shown, although plasma basal insulin concentration was not affected [18]. The beneficial effects of the extract of basil (*Ocimum basilicum)* against the disturbed lipid and carbohydrate metabolism have been documented as it is displayed in experimental studies [19, 20, 21]. Recent studies provide significant results on the therapeutic value of Chios Mactic *(Pistacia lentiscus)* Gum, a resin produced by the Chios Mastic trees exclusively cultivated on "Chios" island in Greece, against the disturbed lipid profile and the alterations in serum glucose levels [22, 23]. A quite notable part of the existing literature about saffron (Kozani Crocus or saffron derived from Kozani Regional Unit (*Crocus sativus*)) which is the vernacular name for the stigmata from flowers of *Crocus sativus*, focuses on its antidiabetic and hypolipidemic effects [24-26]. The information on the design of some of the above studies as well as their main outcomes are presented in Table 2.

Fig 1: *Salvia officinalis*, Kefalonia Island

Fig 2: *Thymus vulgaris*, Kefalonia island

Table 2: Studies on the lipid and glucose lowering effects of plants

Plant species	Study design	Intervention	Major findings	References
Sage	Forty hyperlipidemic and/or hypertriglyceridemic type 2 diabetic patients	Administration of a sage leaf extract (a capsule of 500 mg, 3 times/day) for 3 months	Improved fasting serum glucose levels, amelioration of glycosylated hemoglobin levels, decreased serum total cholesterol, LDL cholesterol and triglyceride concentrations and increase in HDL cholesterol levels	59
	Sixty-seven hyperlipidemic patients	Two-month sage supplementation (administration of a capsule of 500 mg every 8 hours)	Beneficial hypolipidemic activity	65
	Streptozotocin (STZ) induced diabetic rats	Ip injection of a methanolic extract (100, 250, 400 and 500 mg/kg) and essential oil (0.042, 0.125, 0.2 and 0.4 ml/kg). Blood sampling at 1, 3 and 5 h after administration	Hypoglycemic properties of the methanolic extract	66

	Six 40-50 years old healthy women	Consumption of a beverage produced by sage (4 g leaves of sage in 300 ml boiling water) for 4 weeks	Improvement of lipid metabolism	67
	Thirty-six alloxan-induced diabetic Wistar rats	Administration of a methanolic extract of leaves of sage 250 mg/kg, for 21 days	Increase in the activity of superoxide dismutase, declined serum triglycerides and LDL cholesterol levels	68
	Fisher 344 rats	Administrations of a dietary supplement containing sage, two other herbs and two vitamins	No significant impact on serum lipid profile or the metabolic function of liver or kidneys	69
Rosemary	HepG2 cell lines	Rosemary extract at doses 0.4, 2, 10 and 50 μg/mL	The doses of 2, 10 and 50 μg/mL increased the glucose consumption in HepG2 cells by 6%, 13% and 21% respectively	3
	Diet induced hyperlipidemic mice	Administration of carnocic acid - a major component of sage- for a period of 12 weeks	Decrease in fatty tissue deposition in liver, amelioration of their metabolic disorders and improved insulin resistance	4
Lavender	Forty-eight alloxan-induced diabetic Wistar rats	Administration of a lavender extract (50 mg/kg) for a period of 15 days	Protective action against the increased serum glucose levels	5
Lemon balm	Hyperlipidemic rats	*Per os* administration of lemon balm extract (2 g/kg) for 28 days	Ameliorated serum lipid and hepatic enzymes levels, reduced lipid peroxidation in liver, increased hepatic glutathione concentration	6
	High fat diet-induced hyperlipidemic mice	Administration of a mixture of species *Melissa officinalis L.*, *Morus alba L.*, and *Artemisia capillaris Thunb* for a 12-week period	Reduced body weight and fat deposition, improved serum total cholesterol and triglycerides levels and diminished fat deposition in liver	7
	db/db mice	Lemon balm extract administration	Improvement in serum glucose levels and insulin resistance	8
Peppermint	Adult rats that were offspring either of streptozotocin-induced diabetic female rats or healthy female rats	0.29 g/kg water-peppermint "juice" once a day for 30 consecutive days	Reduced serum glucose levels and serum total cholesterol, LDL cholesterol and triglyceride levels/increased HDL cholesterol levels	9
	Diabetic rats	Administration of alcoholic extract of peppermint	Improved serum glucose levels	10
	Wistar rats receiving normal chow or high saturated fat diet	Administration of peppermint juice (100 g of leaves per /l of water) at a dose 0.29 g/kg twice a day by the intra-gastric route (gavage) for 30 days	Reduction in the weight gain percentage, significant reduction of triglycerides and increase in HDL-c has been achieved	11
	Twenty-four Sprague Dawley rats, receiving increased fructose content diet	Administration of aqueous peppermint extract (100 mg/Kg, 250 mg/Kg p.o. daily) for 3 weeks	Dose dependent improvement of glucose and lipid profile.	12
	25 students (18-45 years old)	Peppermint juice consumption for a period of 30 days	Reduction of serum glucose levels, serum total cholesterol levels, serum triglycerides and serum LDL cholesterol levels, improved serum HDL cholesterol levels	14
Basil	Control and alloxan-induced diabetic rats	Ip injection of basil (400 mg/kg) basil methanol extract	Reduced blood glucose levels both in control and diabetic rats	21
Chios Mastic Gum	133 volunteers over 50 years of age	Intake of a high dose of Chios Mastic Gum (5 g mastic powder daily diluted in one glass -250 ml- of water) for a period of 18 months or a solution of a lower dose of mastic gum (approximately one-seventh of the dose received by the high-dose group) for 12 months	The intake of high dose resulted in reduced serum total and LDL cholesterol levels, decreased apo-A and apo- B serum concentration and improved levels of hepatic enzymes. The hypoglycemic activity of Chios Mastic Gum was also recorded in the low dose group	22
	Twenty-seven streptozotocin induced diabetic mice	Administration of 500 mg/kg and 20 mg/kg per day of Chios Mastic Gum for 8 weeks	Both doses resulted in declined serum glucose, total cholesterol, LDL cholesterol and triglyceride levels and increased HDL levels at the 4th week of the study. Mice receiving the lower dose had lower serum glucose, cholesterol, low-density lipoprotein cholesterol, and triglyceride levels and improved high-density lipoprotein cholesterol levels at the 8^{th} week	23

Antioxidant action
The antioxidant activity of sage, as it is displayed in experimental studies, resides mainly in its composition in different compounds such as di- and triterpenoids, phenolic acids, essential oils, tannins and flavonoids [27, 28, 29]. Similar to sage, rosemary's antioxidant activity derives from the flavonoids and polyphenolic acids that it contains (particularly hydroxycinnamic acids) [30]. Additionally, the antioxidant potential of lavender is well documented and are attributed to its polyphenolic and flavonoid composition [5, 31, 32, 33, 34]. Many compounds of lemon balm (phenolic ingredients, oils, monoterpenes, flavonoids, tannins) are implicated in its antioxidant properties [35, 36, 37, 38, 37, 39]. Different species of mint including *Mentha piperita* contain thymol and carvacrol which are associated with Free Oxygen Radicals (ROS) lowering effects [40-42]. The main antioxidant molecules in marjoram belong to the categories of flavonoids and tepenoides [43, 44, 45].

Oregano is considered as one of the most important sources of natural phenols that can reduce lipid peroxidation and alleviate oxidative damage [46].

The beneficial antioxidant properties of the aqueous extract of basil are ascribed at least in part to the antioxidant mechanism of its compounds [20]. The afore mentioned health benefits of Chios Mastic Gum regarding the lipid and glucose metabolism are mainly related to its antioxidant activity that engages in the metabolic pathway of protein kinase C (PKC) that further attenuates the production of superoxide radicals by NADPH oxidases [47]. A methanol extract of *Crocus sativus* has shown marked antioxidant action [48] while a methanol extract of saffron, crocin ot crocetin can positively influence the human monocyte system [49]. The antioxidant properties of a methanolic extract of *Daucus carota* seeds have been exhibited in rats, in which oxidative stress was induced by thioacetamide administration [15] (Table 3).

Table 3: Summary of the medicinal and biological properties of the plants

Common name of plant	Reduction in lipid levels	Reduction in serum glucose levels	Antioxidant activities	Anti-inflammatory action	PPAR-γ agonist activity
Sage	x	x	x	x	x
Rosemary	x	x	x	x	x
Lavender		x	x		
Lemon balm	x	x	x	x	x
Peppermint	x	x	x		
Marjoram		x			
Thyme	x		x		
Oregano		x	x	x	
Basil		x	x		
Chios Mastic Gum	x	x	x		x
Kozani Crocus	x	x	x	x	
Wild carrot		x	x		

Anti-inflammatory properties
Sage has been shown to present remarkable anti-inflammatory activity [50]. Sage extracts contributed to a decreased production of the pro-inflammatory agents IL-6 and TNF-α and an enhanced release of the anti-inflammatory IL-10 attenuating cyclooxygenase-2 (COX-2) or nitric oxide synthase expression [39]. Sage oil has also inhibited the generation of nitric oxide in murine macrophage cell lines following their stimulation with lipopolysaccharide (LPS) [51]. In addition, other studies revealed the beneficial anti-inflammatory properties of rosemary [52, 53].

Scientific reports also describe the anti-inflammatory potential of lemon balm [37, 38]. Different components of this herb, such as phenolic compounds, oils, flavonoids and tannins, are implicated in this action [37]. The in vitro anti-inflammatory properties of lemon balm have been also shown [39], while this activity has been evaluated and further validated in an animal study with rats [54] (Table 3).

Thyme and oregano have been studied as anti-inflammatory agents. An extract of oregano exhibited significant inhibitory action against inflammation in an in vitro atherosclerosis model, by determining the production of cytokines from THP-1 macrophages [55, 56]. Saffron has been indicated to show strong anti-inflammatory properties [57, 58] (Tables 2, 3).

Other actions
It has been demonstrated that extract from sage leaves acts as a Peroxisome proliferator-activated receptor gamma (PPAR-γ) agonist in vitro, obstructs pancreatic lipase in vitro, obstructs the absorption of lipids, decreases the triglycerides levels in the muscle, decreases lipid peroxidation in the brain and the liver of mice, strengthens the action of insulin and obstructs gluconeogenesis in hepatic cells in healthy mice [59]. It is shown that the increase of insulin levels in diabetic mice is connected with an increase in the expression of both insulin and Glut-4 genes as well as a decrease in the functionality of a-glucosidase [60]. PPAR-γ activation has been also demonstrated for sage extract in vitro [61]. Sage's action as a PPAR-γ agonist is crucial to this herb being helpful in hyperlipidemia and Type-2 DM treatment [59].

The beneficiary actions of various plants such as *Melissa officinalis,* are partly due to their effect in the expression of genes in the liver which are targets of PPAR-a transcription factors such as lipoprotein lipase, C-III apolipoprotein and acetyl-CoA synthetase, which are actively involved in lipid metabolism [7]. *Melissa officinalis* acts in NF-kB and PPARs and contains various components such as rosmarinic acid, which define *Melissa officinali's* action as an antioxidant and anti-inflammatory factor [39]. Further molecular research of this exact plant in db/db mice has shown an increase in hepatic glucokinase and Glut4 expression as well as an increase in the expression of Glut-4, PPAR-γ, PPAR-α and SREBP-1c genes in adipose tissue. On the contrary, there was a decrease in the expression of glucose 6 phosphatase and phosphoenolpyruvate carboxykinase in liver tissue. The hypoglycemic action of *Melissa officinalis* oil is related to increased intake and metabolism of glucose in adipose tissue and liver and decreased gluconeogenesis in the liver [8].

Rosmarinus officinalis extract activates both AMPK signaling and PPAR pathways, thus regulating glucose and lipid metabolism in HepG2 cells. It increases AMPK phosphorylation and its substrate as well as acetylo-CoA carboxylase (ACC). In addition, the same extract takes part in the transcriptional control of several genes which are involved in metabolism, like SIRT1, PGC1a (Peroxisome proliferator-activated receptor gamma coactivator 1-alpha), G6Pase, ACC and LDLR. GW9662, a PPAR-γ antagonist, is shown to decrease the effect of *Rosmarinus officinalis* in glucose metabolism [3].

Lavender extract may exert an antihyperglycemic action through an increase in plasma insulin action, insulin secretion and insulin's detachment from its attached form [5]. The beneficiary actions of *Thymus vulgaris* extract are possibly related with its effects on plasma levels of nitrogen monoxide and liver and kidney MDA [17].

According to the study of Aydin *et al*. in 2005, even small quantities of *Thymus vulgaris* oil are capable of protecting human lymphocyte DNA from various gene toxins [(2-amini-3-methylimidazo [4,5-f]-quinoline (IQ), mitomycin C (MMC), hydrogen peroxide] [62].

The normalization of glucose levels in diabetic mice is appointed to the increase in AGEs inhibitors (Advanced Glycation End) after the intake of *Origanum majorana* extract [16]. These exact inhibitors are used as a powerful and effective cure of Type2 DM patients [16].

The antidiabetic action of *Origanum vulgare* has been related to a decreased gluconeogenesis in the liver or an increased glucose consumption from peripheral tissues, mainly muscles and adipose tissue. The same paper appoints the hypoglycemic action of *Origanum vulgare* to its various components, such as flavonoids, alcohols, phenols and tyrpenies [18]. Furthermore, the hypoglycemic action of *Ocimum basilicum* is appointed to the inhibition of a-glycosidase and a-amylase [20].

A recent study suggests that the synergistic action of some constituents of Chios Mastic Gum on PPARs, could be considered as a main mechanism via which this spice exerts its multiple effects [63] (Table 3).

Four stems of endophytic microorgansims which derive from the root of *Daucus carrota* are capable of reducing the carbonylic group in ketones both to enantiomeres and diastereomers. These results show that endophytic organisms take part in enantiomeric reduction of ketones and ketoesters when somebody chews fresh pieces of *Daucus carrota* roots [64] (Table 2).

Conclusions

Although the use of medicinal natural products and the classical medicine are recognized as two separate philosophies, they may be combined with aim to promote the prevention and control of the different pathological conditions. In the antiquity, the use of plants and plant derived products as medicines was based on the experience gained as the knowledge on the exact cause of an illness or on the specific properties of the plant components were scarce. Currently, science emphasizes on the identification of the specific biological properties of medicinal plants.

Some of these herbs and spices have been already extensively studied as treatments against disorders of lipid and glucose metabolism. It remains to further elucidate in more detail the molecular mechanisms of their action in order to validate their scientific accuracy and extent their use in the cure of different pathological conditions.

Conflict of interest

The authors of this article have not any possible conflict of interest to declare.

References

1. Ahvazi M, Khalighi-Sigaroodi F, Charkhchiyan MM, Mojab F, Mozaffarian VA, Zakeri H. Introduction of medicinal plants species with the most traditional usage in alamut region. Iranian journal of pharmaceutical research: IJPR. 2012; 11(1):185-94.
2. Aristatile B, Al-Numair KS, Veeramani C, Pugalendi KV. Effect of carvacrol on hepatic marker enzymes and antioxidant status in d-galactosamine-induced hepatotoxicity in rats. Fundamental & Clinical Pharmacology 2009; 23(6):757-65.
3. Tu Z, Moss-Pierce T, Ford P, Jiang TA. Rosemary (Rosmarinus officinalis L.) extract regulates glucose and lipid metabolism by activating AMPK and PPAR pathways in HepG2 cells. Journal of agricultural and food chemistry. 2013; 61(11):2803-10.
4. Park MY, Mun ST. Dietary carnosic acid suppresses hepatic steatosis formation via regulation of hepatic fatty acid metabolism in high-fat diet-fed mice. Nutrition research and practice 2013; 7(4):294-301.
5. Sebai H, Selmi S, Rtibi K, Souli A, Gharbi N, Sakly M. Lavender (Lavandula stoechas L.) essential oils attenuate hyperglycemia and protect against oxidative stress in alloxan-induced diabetic rats. Lipids in health and disease. 2013; 12:189.
6. Bolkent S, Yanardag R, Karabulut-Bulan O, Yesilyaprak B. Protective role of Melissa officinalis L. extract on liver of hyperlipidemic rats: A morphological and biochemical study. Journal of Ethnopharmacology. 2005; 99(3):391-8.
7. Lee J, Chae K, Ha J, Park B-Y, Lee HS, Jeong S *et al*. Regulation of obesity and lipid disorders by herbal extracts from Morus alba, Melissa officinalis, and Artemisia capillaris in high-fat diet-induced obese mice. Journal of Ethnopharmacology. 2008; 115(2):263-70.
8. Chung MJ, Cho S-Y, Bhuiyan MJH, Kim KH, Lee S-J. Anti-diabetic effects of lemon balm (Melissa officinalis) essential oil on glucose- and lipid-regulating enzymes in type 2 diabetic mice. British Journal of Nutrition. 2010; 104(02):180-8.
9. Barbalho SM, Damasceno DC, Spada AP, da Silva VS, Martuchi KA, Oshiiwa M *et al*. Metabolic Profile of Offspring from Diabetic Wistar Rats Treated with Mentha piperita (Peppermint). Evidence-based complementary and alternative medicine: eCAM. 2011; 2011:430237.
10. Narendhirakannan RT, Subramanian S, Kandaswamy M. Biochemical evaluation of antidiabetogenic properties of some commonly used Indian plants on streptozotocin-induced diabetes in experimental rats. Clinical and experimental pharmacology & physiology. 2006; 33(12):1150-7.
11. Barbalho SM, Spada APM, Oliveira EPd, Paiva-Filho ME, Martuchi KA, Leite NC *et al*. Mentha piperita effects on wistar rat’s plasma lipids. Brazilian Archives of Biology and Technology. 2009; 52:1137-43.
12. Mani Badal R, Badal D, Badal P, Khare A, Shrivastava J, Kumar V. Pharmacological Action of Mentha piperita on Lipid Profile in Fructose-Fed Rats. Iranian journal of pharmaceutical research: IJPR. 2011; 10(4):843-8.
13. Randle PJ. Regulatory interactions between lipids and carbohydrates: the glucose fatty acid cycle after 35 years. Diabetes/metabolism reviews 1998; 14(4):263-83.
14. Barbalho SM, Machado FMVF, Oshiiwa M, Abreu M, Guiger EL, Tomazela P *et al*. Investigation of the effects of peppermint (Mentha piperita) on the biochemical and anthropometric profile of university students. Food Science and Technology (Campinas) 2011; 31:584-8.

15. Singh K, Singh N, Chandy A, Manigauha A. In vivo antioxidant and hepatoprotective activity of methanolic extracts of Daucus carota seeds in experimental animals. Asian Pacific Journal of Tropical Biomedicine. 2012; 2(5):385-8.
16. Perez Gutierrez RM. Inhibition of Advanced Glycation End-Product Formation by Origanum majorana L. In Vitro and in Streptozotocin-Induced Diabetic Rats. Evidence-based complementary and alternative medicine: eCAM. 2012; 2012:598-638.
17. Cerda A, Martinez ME, Soto C, Poirrier P, Perez-Correa JR, Vergara-Salinas JR *et al*. The enhancement of antioxidant compounds extracted from Thymus vulgaris using enzymes and the effect of extracting solvent. Food chemistry. 2013; 139(1-4):138-43.
18. Lemhadri A, Zeggwagh NA, Maghrani M, Jouad H, Eddouks M. Anti-hyperglycaemic activity of the aqueous extract of Origanum vulgare growing wild in Tafilalet region. J Ethnopharmacol. 2004; 92(2-3):251-6.
19. Bravo E, Amrani S, Aziz M, Harnafi H, Napolitano M. Ocimum basilicum ethanolic extract decreases cholesterol synthesis and lipid accumulation in human macrophages. Fitoterapia. 2008; 79(7-8):515-23.
20. El-Beshbishy H, Bahashwan S. Hypoglycemic effect of basil (Ocimum basilicum) aqueous extract is mediated through inhibition of alpha-glucosidase and alpha-amylase activities: an in vitro study. Toxicology and industrial health. 2012; 28(1):42-50.
21. Aguiyi JC, Obi CI, Gang SS, Igweh AC. Hypoglycaemic activity of Ocimum gratissimum in rats. Fitoterapia. 2000; 71(4):444-6.
22. Triantafyllou A, Chaviaras N, Sergentanis TN, Protopapa E, Tsaknis J. Chios mastic gum modulates serum biochemical parameters in a human population. J Ethnopharmacol. 2007; 111(1):43-9.
23. Georgiadis I, Karatzas T, Korou LM, Agrogiannis G, Vlachos IS, Pantopoulou A, *et al*. Evaluation of Chios mastic gum on lipid and glucose metabolism in diabetic mice. Journal of medicinal food. 2014; 17(3):393-9.
24. Lee IA, Lee JH, Baek NI, Kim DH. Antihyperlipidemic effect of crocin isolated from the fructus of Gardenia jasminoides and its metabolite Crocetin. Biol Pharm Bull 2005; 28(11):2106-10.
25. Xi L, Qian Z, Xu G, Zhou C, Sun S. Crocetin attenuates palmitate-induced insulin insensitivity and disordered tumor necrosis factor-alpha and adiponectin expression in rat adipocytes. Br J Pharmacol. 2007; 151(5):610-7.
26. Xi L, Qian Z, Shen X, Wen N, Zhang Y. Crocetin prevents dexamethasone-induced insulin resistance in rats. Planta Med. 2005; 71(10):917-22.
27. Kontogianni VG, Tomic G, Nikolic I, Nerantzaki AA, Sayyad N, Stosic-Grujicic S *et al*. Phytochemical profile of Rosmarinus officinalis and Salvia officinalis extracts and correlation to their antioxidant and anti-proliferative activity. Food chemistry. 2013; 136(1):120-9.
28. Walch SG, Tinzoh LN, Zimmermann BF, Stuhlinger W, Lachenmeier DW. Antioxidant Capacity and Polyphenolic Composition as Quality Indicators for Aqueous Infusions of Salvia officinalis L. (sage tea). Frontiers in pharmacology. 2011; 2:79.
29. Lima CF, Andrade PB, Seabra RM, Fernandes-Ferreira M, Pereira-Wilson C. The drinking of a Salvia officinalis infusion improves liver antioxidant status in mice and rats. Journal of Ethnopharmacology. 2005; 97(2):383-9.
30. Aprotosoaie AC, Raileanu E, Trifan A, Cioanca O. The polyphenolic content of common lamiaceae species available as herbal tea products in Romanian pharmacies. Revista medico-chirurgicala a Societatii de Medici si Naturalisti din Iasi 2013; 117(1):233-7.
31. Amira S, Dade M, Schinella G, Rios JL. Anti-inflammatory, anti-oxidant, and apoptotic activities of four plant species used in folk medicine in the Mediterranean basin. Pakistan journal of pharmaceutical sciences. 2012; 25(1):65-72.
32. Gilani AH, Aziz N, Khan MA, Shaheen F, Jabeen Q, Siddiqui BS *et al*. Ethnopharmacological evaluation of the anticonvulsant, sedative and antispasmodic activities of Lavandula stoechas L. Journal of Ethnopharmacology. 2000; 71(1–2):161-7.
33. Goren A, Topcu G, Bilsel G, Bilsel M, Aydogmus Z, Pezzuto JM. The chemical constituents and biological activity of essential oil of Lavandula stoechas ssp. stoechas. Zeitschrift fur Naturforschung C, Journal of biosciences. 2002; 57(9-10):797-800.
34. Messaoud C, Chograni H, Boussaid M. Chemical composition and antioxidant activities of essential oils and methanol extracts of three wild Lavandula L. species. Natural product research. 2012; 26(21):1976-84.
35. Dastmalchi K, Damien Dorman HJ, Oinonen PP, Darwis Y, Laakso I, Hiltunen R. Chemical composition and in vitro antioxidative activity of a lemon balm (Melissa officinalis L.) extract. LWT - Food Science and Technology. 2008; 41(3):391-400.
36. Cabrera AC, Prieto JM. Application of artificial neural networks to the prediction of the antioxidant activity of essential oils in two experimental in vitro models. Food chemistry 2010; 118(1):141-6.
37. Martins EN, Pessano NTC, Leal L, Roos DH, Folmer V, Puntel GO *et al*. Protective effect of Melissa officinalis aqueous extract against Mn-induced oxidative stress in chronically exposed mice. Brain Research Bulletin 2012; 87(1):74-9.
38. Carnat AP, Carnat A, Fraisse D, Lamaison JL. The aromatic and polyphenolic composition of lemon balm (Melissa officinalis L. subsp. officinalis) tea. Pharmaceutica Acta Helvetiae. 1998; 72(5):301-5.
39. Vogl S, Picker P, Mihaly-Bison J, Fakhrudin N, Atanasov AG, Heiss EH *et al*. Ethnopharmacological in vitro studies on Austria's folk medicine—An unexplored lore in vitro anti-inflammatory activities of 71 Austrian traditional herbal drugs. Journal of Ethnopharmacology. 2013; 149(3):750-71.
40. Samarth RM. Protection against radiation induced hematopoietic damage in bone marrow of Swiss albino mice by Mentha piperita (Linn). Journal of radiation research. 2007; 48(6):523-8.
41. Lee KG, Shibamoto T. Determination of antioxidant potential of volatile extracts isolated from various herbs and spices. Journal of agricultural and food chemistry. 2002; 50(17):4947-52.
42. Miura K, Kikuzaki H, Nakatani N. Antioxidant activity of chemical components from sage (Salvia officinalis L.) and thyme (Thymus vulgaris L.) measured by the oil stability index method. Journal of agricultural and food chemistry. 2002; 50(7):1845-51.
43. Cipak L, Grausova L, Miadokova E, Novotny L, Rauko P. Dual activity of triterpenoids: apoptotic versus antidifferentiation effects. Archives of toxicology 2006; 80(7):429-35.
44. El-Ashmawy IM, el-Nahas AF, Salama OM. Protective effect of volatile oil, alcoholic and aqueous extracts of Origanum majorana on lead acetate toxicity in mice. Basic

& clinical pharmacology & toxicology 2005; 97(4):238-43.

45. Handl S, Hellweg P, Khol-Parisini A, Rossmann B, Thurner K, Luf W *et al*. Effect of oregano (O. majorana x O. vulgare) on performance and antioxidative capacity of quails fed a diet rich in omega3 fatty acids. Journal of animal physiology and animal nutrition. 2008; 92(3):242-5.
46. Kaurinovic B, Popovic M, Vlaisavljevic S, Trivic S. Antioxidant capacity of Ocimum basilicum L. and Origanum vulgare L. extracts. Molecules. 2011; 16(9):7401-14.
47. Triantafyllou A, Bikineyeva A, Dikalova A, Nazarewicz R, Lerakis S, Dikalov S. Anti-inflammatory activity of Chios mastic gum is associated with inhibition of TNF-alpha induced oxidative stress. Nutr J. 2011; 10:64.
48. Assimopoulou AN, Sinakos Z, Papageorgiou VP. Radical scavenging activity of Crocus sativus L. extract and its bioactive constituents. Phytotherapy research: PTR. 2005; 19(11):997-1000.
49. Ordoudi SA, Befani CD, Nenadis N, Koliakos GG, Tsimidou MZ. Further examination of antiradical properties of Crocus sativus stigmas extract rich in crocins. Journal of agricultural and food chemistry. 2009; 57(8):3080-6.
50. Rodrigues MRA, Kanazawa LKS, Neves TLMd, Silva CFd, Horst H, Pizzolatti MG *et al*. Antinociceptive and anti-inflammatory potential of extract and isolated compounds from the leaves of Salvia officinalis in mice. Journal of Ethnopharmacology. 2012; 139(2):519-26.
51. Abu-Darwish MS, Cabral C, Ferreira IV, Goncalves MJ, Cavaleiro C, Cruz MT *et al*. Essential oil of common sage (Salvia officinalis L.) from Jordan: assessment of safety in mammalian cells and its antifungal and anti-inflammatory potential. BioMed research international 2013; 2013:538940.
52. Wang W, Li N, Luo M, Zu Y, Efferth T. Antibacterial activity and anticancer activity of Rosmarinus officinalis L. essential oil compared to that of its main components. Molecules 2012; 17(3):2704-13.
53. Lucarini R, Bernardes WA, Ferreira DS, Tozatti MG, Furtado R, Bastos JK *et al*. In vivo analgesic and anti-inflammatory activities of Rosmarinus officinalis aqueous extracts, rosmarinic acid and its acetyl ester derivative. Pharmaceutical biology. 2013; 51(9):1087-90.
54. Bounihi A, Hajjaj G, Alnamer R, Cherrah Y, Zellou A. In Vivo Potential Anti-Inflammatory Activity of Melissa officinalis L. Essential Oil. Advances in Pharmacological Sciences. 2013; 2013:7.
55. Grespan R, Aguiar RP, Giubilei FN, Fuso RR, Damiao MJ, Silva EL *et al*. Hepatoprotective Effect of Pretreatment with Thymus vulgaris Essential Oil in Experimental Model of Acetaminophen-Induced Injury. Evidence-based complementary and alternative medicine: eCAM. 2014; 2014: 954136.
56. Ocana-Fuentes A, Arranz-Gutierrez E, Senorans FJ, Reglero G. Supercritical fluid extraction of oregano (Origanum vulgare) essentials oils: anti-inflammatory properties based on cytokine response on THP-1 macrophages. Food and chemical toxicology: an international journal published for the British Industrial Biological Research Association. 2010; 48(6):1568-75.
57. Poma A, Fontecchio G, Carlucci G, Chichiricco G. Anti-inflammatory properties of drugs from saffron crocus. Anti-inflammatory & anti-allergy agents in medicinal chemistry. 2012; 11(1):37-51.
58. Speranza L, Franceschelli S, Pesce M, Reale M, Menghini L, Vinciguerra I *et al*. Antiinflammatory effects in THP-1 cells treated with verbascoside. Phytotherapy research: PTR. 2010; 24(9):1398-404.
59. Kianbakht S, Dabaghian FH. Improved glycemic control and lipid profile in hyperlipidemic type 2 diabetic patients consuming Salvia officinalis L. leaf extract: A randomized placebo. Controlled clinical trial. Complementary therapies in medicine 2013; 21(5) 441-6.
60. Moradabadi L, Montasser Kouhsari S, Fehresti Sani M. Hypoglycemic Effects of Three Medicinal Plants in Experimental Diabetes: Inhibition of Rat Intestinal alpha-glucosidase and Enhanced Pancreatic Insulin and Cardiac Glut-4 mRNAs Expression. Iranian journal of pharmaceutical research: IJPR. 2013; 12(3):387-97.
61. Poeckel D, Greiner C, Verhoff M, Rau O, Tausch L, Hörnig C *et al*. Carnosic acid and carnosol potently inhibit human 5-lipoxygenase and suppress pro-inflammatory responses of stimulated human polymorphonuclear leukocytes. Biochemical Pharmacology 2008; 76(1):91-7.
62. Aydin S, Basaran AA, Basaran N. The effects of thyme volatiles on the induction of DNA damage by the heterocyclic amine IQ and mitomycin C. Mutation research 2005; 581(1-2):43-53.
63. Georgiadis Ioannis KT, Korou Laskarina-Maria, Katsilambros Nikolaos, Perrea Despina. Beneficial Health Effects of Chios Gum Mastic and Peroxisome Proliferator-Activated Receptors: Indications of Common Mechanisms Journal of medicinal food. 2015; 18(1):1-10.
64. Caron D, Coughlan A, Simard M, Bernier J, Piché Y, Chênevert R. Stereoselective reduction of ketones by Daucus carota hairy root cultures. Biotechnol Lett. 2005; 27(10):713-6.
65. Kianbakht S, Abasi B, Perham M, Hashem Dabaghian F. Antihyperlipidemic Effects of Salvia officinalis L. Leaf Extract in Patients with Hyperlipidemia: A Randomized Double-Blind Placebo-Controlled Clinical Trial. Phytotherapy Research 2011; 25(12):1849-53.
66. Eidi M, Eidi A, Zamanizadeh H. Effect of Salvia officinalis L. leaves on serum glucose and insulin in healthy and streptozotocin-induced diabetic rats. Journal of Ethnopharmacology. 2005; 100(3):310-3.
67. Sá CM, Ramos AA, Azevedo MF, Lima CF, Fernandes-Ferreira M, Pereira-Wilson C. Sage Tea Drinking Improves Lipid Profile and Antioxidant Defences in Humans. International Journal of Molecular Sciences. 2009; 10(9):3937-50.
68. Fehresti Sani M, Montasser Kouhsari S, Moradabadi L. Effects of Three Medicinal Plants Extracts in Experimental Diabetes: Antioxidant Enzymes Activities and Plasma Lipids Profiles in Comparison with Metformin. Iranian journal of pharmaceutical research: IJPR. 2012; 11(3):897-903.
69. Bulku E, Zinkovsky D, Patel P, Javia V, Lahoti T, Khodos I *et al*. A novel dietary supplement containing multiple phytochemicals and vitamins elevates hepatorenal and cardiac antioxidant enzymes in the absence of significant serum chemistry and genomic changes. Oxidative medicine and cellular longevity 2010; 3(2):129-44.