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Anti-hyperelipidemic effects of Sumac (*Rhus coriaria* L.): Can sumac strengthen anti-hyperlipidemic effect of statins?

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ABSTRACT

People believe that sumac is used as reducing fat. In the present study, the hypolipidemic effect of sumac fruits was compared with lovastatin in patients suffered hypercholesterolemia. In a randomized double-blinded-controlled trial, 172 patients diagnosed as hypercholesterolemia (high LDL level) and indicated for lipid-lowering schedules were randomly allocated to receive lovastatin (20 mg/day) or a combination of lovastatin (20 mg/day) and sumac (1 gram equivalent to a teaspoon/day, soluble in water). Immediately before initial assessment and also after a 3-month period of drugs prescription, the level of serum lipid profile was measured in both intervention groups by enzymatic assay and serum LDL level was determined using the Friedewald's equation. At baseline, the mean level of LDL was 149.26±22.36 mg/dL in the group received combination therapy, and 146.25±19.89 mg/dL in the group received lovastatin alone with no significant different (p=0.352). However, following administration of the two treatment schedules, the level of LDL was significantly more reduced in combination treatment group compared with another group that the serum level of LDL after 3-month study period was 105.75±21.21 mg/dL in combination therapy group and 117.04±15.78 mg/dL in single therapy group (p<0.001). The positive response rate in the two groups was 93.0% and 75.6%, respectively (p=0.002). Using Multivariable logistic regression model, the use of sumac combined with statin led to higher response rate indicated by lowering serum LDL level (p=0.019). Sumac has a potential role in lowering LDL level especially when combined with anti-hyperlipidemic drugs as statins.

Key words: Sumac, Antihyperlipidemia, *Rhus coriaria* L., Lovastatin.

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INTRODUCTION

Medicinal plants and their derivatives are a rich resource for discovering new drugs [1-4]. In traditional medicine, they have been used for prevention of human disorders [5-12]. Also their effects have been investigated in various studies [13-19]. They have been shown the antioxidant activity, anti-inflammatory, anti-hyperlipidemic effects, etc. Sumac (*Rhus coriaria* L.), is one of the main medicinal plants from the family Anacardiaceae that the long history of its use has been noted in ancient medicine [20]. Sumac plant usually grows in subtropical and temperate regions throughout the world, especially in Africa, North America, and Southeast Asia [21]. In Iranian alternative medicine, sumac is used as a preventive agent in cardiac diseases and consumed with some common foods [22,23]. Phytochemical analysis have indicated that Sumac is a rich source of phenolic compounds, such as delphinidin, chrysanthemin, myrtillin, tannins, and some types of organic acids including malic acid, citric acid, and tartaric acid [24, 25]. Furthermore, some studies have shown a considerable amount of water-soluble tannins with antioxidant

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properties effective for prevention of development and progression of cancer [26]. In addition, because of its phenolic acids, flavonols and anthocyanins components, it has been identified as a main source of phenolic compounds that act as antioxidants as well as a hypoglycemic agent. Recently, attentions have been focused on anti-lipidemic properties of sumac so that long-term consumption of this herb has been accompanied with lowering serum lipids [27]. Also, glycoprotein extracted from sumac fruit result in decreasing serum cholesterol, triglyceride, and low-density lipoprotein (LDL) [28]. Because hyperlipidemia is a major risk factor for development of atherosclerosis and occurrence of new cardiac ischemic events, and also due to serious side effects of biochemical-based drugs for lowering serum lipids, the use of a food additive and herbal medicine particularly for a long time is superior to achieve an appropriate level of serum lipid profile, leading reduced risk of coronary atherosclerosis and its life-threatening consequences. In the present study, the hypolipidemic effect of sumac fruits was compared with common used anti-lipidemic drugs in patients suffered hypercholesterolemia.

MATERIALS AND METHODS

In a randomized double-blinded-controlled trial, 172 consecutive patients diagnosed as hypercholesterolemia (high LDL level) and indicated for lipid-lowering schedules were entered into the study. The patients aged 40 to 80 years with a LDL cholesterol level of >or=130 mg/dl (>or=100 mg/dl if diabetes mellitus or cardiovascular disease was present) or on treatment. Those with the recent history of anti-lipids consumption, or suffered from any metabolic disturbances were excluded from the study. All participants were under a regular routine meal program. The study was performed according to the Declaration of Helsinki, and its protocol was approved by the Institutional Ethics Committee.

According to the study protocol, the patients were randomly allocated to receive lovastatin (20 mg/day) or a combination of lovastatin (20 mg/day) and sumac (1 gram equivalent to a teaspoon/day, soluble in the warm water). Administered sumac for all subjects was purchased from a single location. Randomization was done by an independent investigator blinded to the type of drugs. Allocation also concealed using a random allocation chart. Immediately before initial assessment and also after a 3-month period of drugs prescription, the level of serum lipid profile was measured in both intervention groups by enzymatic assay and serum LDL level was determined using the Friedewald's equation. Within the study time, none of the participants used other types of anti-lipid drugs. The end-point of the study was to compare the changes in serum LDL level between the interventional groups. The proper response rate to anti-lipid drugs was defined as "at least a 40 mg/dL decrease in LDL-C level following treatment".

Data were presented as mean ± SD for continuous variables and percentages for categorical variables. Comparisons of categorical variables across the groups were performed using an overall chi-square test or Fisher's exact test if required; while comparisons of continuous variables were performed using an independent t-test or Mann-Whitney U test. The difference in drug response rate was finally examined by the multivariable logistic regression modeling with the presence of baseline characteristics as probable confounders. P values of 0.05 or less were considered statistically significant. All the statistical analyses were performed using SPSS version 13 (SPSS Inc., Chicago, IL, USA).

RESULTS AND DISCUSSION

The two groups received combination therapy (including lovastatin and sumac) or single therapy (with lovastatin alone) were matched for baseline characteristics such as gender, age, body mass index, previous history of hypertension and diabetes mellitus, current smoking status, as well as for educational level (table 1).

At baseline, the mean level of serum LDL was 149.26±22.36 mg/dL in group received combination therapy, and 146.25±19.89 mg/dL with no significant different (p=0.352). However, following administration of the two treatment schedules, the level of serum LDL was significantly more reduced in combination treatment group compared with another group that the serum level of LDL after 3-month study period was 105.75 ± 21.21 mg/dL in combination therapy group and 117.04±15.78 mg/dL in single therapy group, p<0.001). In this regard, the positive response rate in the two groups was 93.0% and 75.6%, respectively (p=0.002). Using Multivariable logistic regression model (table 2), and considering a reduce at least a 40 mg/dL decrease in LDL-C level as positive response to treatment, the use of sumac combined with statin led to higher response rate indicated by lowering serum LDL level (OR=1.745, 95% CI: 1.094 – 2.786, p=0.019).

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Table 1: Baseline characteristics and clinical data in study subjects

Characteristics	Lovastatin Group (n = 86)	Lovastatin +Sumac group (n = 86)	P-value
Male gender	46 (53.5)	48 (55.8)	0.868
Age (yr)	56.62 ± 7.79	58.35 ± 9.91	0.205
History of hypertension	12 (14.0)	14 (16.3)	0.715
History of diabetes mellitus	6 (7.0)	7 (8.1)	0.789
Body mass index (kg/m$^{2)}$)	26.25 ± 3.32	26.02 ± 4.41	0.699
current smoking	9 (10.5)	12 (14.0)	0.537
Educational level			
Primary	18 (20.9)	16 (18.6)	0.754
Secondary	42 (48.9)	40 (46.5)	0.856
college degree	26 (30.2)	30 (34.9)	0.642

Table 2: Multivariable logistic regression model for determining difference in response rate in the two interventional group

Characteristics	Multivariate p-value	Odds Ratio	95% Confidence Interval
Drug pattern (L+S vs. L)	0.019	1.745	1.094 – 2.786
Male gender	0.469	0.850	0.547 – 1.320
Age	0.162	0.725	0.462 – 1.138
History of hypertension	0.820	1.052	0.683 – 1.618
History of diabetes mellitus	0.015	1.782	1.116 – 2.849
Body mass index (kg/m$^{2)}$)	0.028	1.696	1.058 – 2.716
Current smoking	0.352	1.261	0.773 – 2.056
Educational level	0.655	1.115	0.691 – 1.801

L: Lovastatin; S: Sumac.

Various effects of sumac have been revealed in terms of its therapeutic effects as an antimicrobial and antioxidant [28]. The fruit of this plant has been also applied for improving fever, diarrhea, dermatitis and a variety of gastrointestinal disorders. The sumac plant serves also as a traditional medicine, which has pharmacological functions such as anti-hemorrhoidal, antiseptic, blood purifier, diuretic, stomachic and tonic [29, 30]. Despite different beneficial effects of this agent noted in ancient and also in modern medicines, up to now, few studies focused on its therapeutic effects on metabolic disturbances especially hypercholesterolemia as a main risk factor for cardiovascular disorders leading high mortality and morbidity whole of the world. The present study attempted to determine therapeutic impact of sumac as a lowering serum LDL level compared with common drug regimens such as statins. We aimed to consider sumac as a supplement to statin for reducing LDL level in hyperlipidemic patients and could show higher response rate to combination therapy compared to use statin alone. In a study, the plant extract raised markedly serum high-density lipoprotein (HDL) by 34% and also reduced low-density lipoprotein (HDL) by 32% [31]. Also showed that the treatment with aqueous methanol extract of sumac fruits reduced the serum lipids alterations observed in hypercholesterolemic animal models [32]. Oh et al. (2006) by extracting a special plant glycoprotein from sumac showed anti-hyperlipidemic effects of this agent along with its antioxidative characteristic. In total, the fruits of sumac can potentially reduce serum level of LDL and thus its administration in combined with anti-hyperlipidemic drugs such as statins can increased therapeutic response to these drugs effectively. On the other hand, by co-administration of statins and sumac, the need for elevating statin dosages or their use prolongation can be unnecessary and hence the side effects of these drugs may be significantly reduced [33]. According to few recent studies on the mechanisms of sumac for reducing serum lipids or related metabolism, lipid peroxidation had the main role in neutralizing processes involving increase of circulating lipids [34]. Lipid oxidation is a highly deteriorative process in foods, as it leads to unacceptable properties for the customer and a loss in nutritional value [35]. Various kinds of antioxidants with different functions inhibit lipid peroxidation and the deleterious effects caused by the lipid peroxidation products on different organs [36-47]. This effect is very vast, causing a wide variety of complications [48-52]. It should be noted that the biological role of lipid peroxidation products has recently received a great deal of attention, but its physiological significance remained unclear [53-55]. According to this fact that extracts and fractions of sumac have moderate lipid peroxidation inhibition effects, it seems that sumac not only has a major role for preventing lipid oxidation, it may also reduce lipid levels and thus prevent progression of cardiovascular disorders.

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CONCLUSION

In conclusion, along with antimicrobial and antioxidant effects of sumac, the level of serum lipids can be effectively reduced following use of this agent, especially in combination of anti-lipidemic drugs. On the other hand, adding this material to statins can strengthen drug efficacy to lowering serum LDL.

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