Available online at www.sciencedirect.com
ScienceDirect
European Journal of Integrative Medicine 3 (2011) e201–e207
European Journal of INTEGRATIVE MEDICINE
www.elsevier.com/eujim

Original article

Clinical efficacy of Stragol™ herbal heart drop in ischemic heart failure of stable chest angina

Sedigheh Khastkhodaei [a,**], Gholamreza Sharifi [a,1], Reza Salahi [b], Mohammad Rahnamaeian [c,*,1], Fariborz Moattar [d]

[a] *Department of Physical Education, Khorasgan (Isfahan branch), Islamic Azad University, Isfahan, Iran*
[b] *Kowsar Cardiovascular Hospital, Shiraz, Iran*
[c] *Department of Plant Biotechnology, Shahid Bahonar University, P.O. Box: 76169-133, Kerman, Iran*
[d] *School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences and Health Services, Isfahan, Iran*

Received 15 April 2011; received in revised form 3 July 2011; accepted 5 July 2011

Abstract

Introduction: Medicinal plants possessing significant beneficial properties are an ideal choice as complementary medicinal strategies. Positive effects of medicinal plants on the cardiovascular system have been consistently reported. Here, we report the improvement of exercise tolerance of patients suffering from stable chest angina as a result of reduction in serum lipids by administration of Stragol™ oral drop, a consortium of seven medicinal plant extracts.

Methodology: Forty patients suffering from stable chest angina were treated with or without Stragol™ herbal heart drop for four weeks besides taking conventional medicines. The study assessed the effects of Stragol™ on critical influential factors in cardiovascular functions, i.e., serum lipids, blood sugar and exercise tolerance. Biochemical examination of blood for serum lipids and blood sugar was performed before and after treatment in both experimental and control groups.

Results: Analysis of data revealed a considerable reduction in serum LDL cholesterol, total cholesterol and triglyceride in experimental group. In addition, a significant improvement in exercise tolerance of the patients was observed after treatment with Stragol™, most likely by reducing the level of blood lipids and resultant reduction of atherosclerosis.

Conclusion: Four weeks administration of seven medicinal plant extracts with high levels of glycosides and flavonoids in the form of Stragol™ oral drop is an effective complementary strategy to significantly lower the risk of atherosclerosis and downstream heart problems.

Keywords: Exercise tolerance; Serum lipids; Blood sugar; Stragol™ herbal heart drop; Heart rate; Atherosclerosis

Introduction

Aging is often characterised by poor cooperation of different organs in supplying routine physical needs, which results from malnutrition, stresses, and competitive life style. The primary goal of modern health care is to prevent the incidence of sickness and malfunction of different organs, and secondarily to heal disease with a prescription enriched with natural medicines, if possible. Therefore, natural medicine systems, such as Ayurveda, phytomedicine, homeopathy, massage therapy, and aromatherapy have drawn much attention recently. Phytomedicines can be prescribed alongside other medicines. They are of nutritional as well as pharmaceutical value, positively influencing the organs' functions and thereby leading to persistence of the body in different stress conditions. Many believe that phytomedicine is superior to conventional medicine, because while the former have no or little side effects, the later imposes some side effects on functions of other organs [1,2]. Since phytomedicines can affect the physiological processes directly, their use for medical purposes is suggested [3,4].

Most medicinal plants possess cardiac glycosides, which play crucial roles in strengthening and harmonising the heart rate. Medicinal plants are most likely beneficial due to their roles in

* Corresponding author. Tel.: +98 917 473 2237; fax: +98 341 211 9889.
** Co-corresponding author.
E-mail addresses: Rahnamaeian@mail.uk.ac.ir (M. Rahnamaeian), Sedighe.Khodaei@yahoo.com (S. Khastkhodaei).
[1] These authors contributed equally to this work.

1876-3820/$ – see front matter © 2011 Elsevier GmbH. All rights reserved.
doi:10.1016/j.eujim.2011.07.004

Table 1
Active ingredients present in plants used in formulation of Stragol™ oral drop.

Hawthorn
• Flavonoid
- Hyperoside
- Vitexin
- Chlorogenic acid
- Coffeic acid
Bilberry
• Catechin tannins
• Oligomeric procyanidins
• Anthocyanoids
• Flavonoids
- Hyperoside
- Chlorogenic acid
Ginger
• Zingiberene
• Beta-bisabolene
• Gingerols
• Shogaols
Garlic
• Alliin
• Allicin
• Flavonoids
• Nicotinamides
Red pepper
• Capsaicinoids
• Steroidal Saponins
• Flavonoids
Chamomile
• Bisabolol
• Chamazulene
• Flavonoids
Willow bark
• Salicin
• Salicortin

improving the heart functions without causing any changes in oxygen levels of myocardium [5,6]. Heart diseases result mainly from inadequate blood supply because of coronary artery blockade. It is believed that medicinal plants like garlic, chamomile, ginger, hawthorn, red pepper, willow (Salix species) bark, and bilberry positively regulate the cardiovascular system due to their flavonoid content. In this study, the extracts of above-mentioned plants in the form of Stragol™ oral drop (Table 1) were used to investigate their synergistic positive effects on exercise tolerance of patients suffering from stable chest angina. Stable chest angina is a form of heart disease where the oxygen transferred by the coronary artery is inadequate for ideal cardiac performance during activity [7,8]. In such patients, based on determined exercise tolerance level, the activity limit is restricted. It appears that heart strengthening results in improvement of heart efficacy. On the other hand, decrease in casual agents of heart failure such as arterial hypertension or excessive blood sugar could result in elevation of exercise tolerance threshold and hence the activity limit in these patients, which per se leads to decrease in heart stroke. In this study, the exercise tolerance before and after administration of Stragol™ oral drop were measured to determine the efficacy of these medicinal plants in increasing the exercise tolerance threshold of patients with stable chest angina.

Table 2
Inclusion and exclusion criteria.

Inclusion criteria
• Ischemic heart failure of stable chest angina
• Age between 40 and 60 years
• Nonsmoker
• Having at least 15 min walking everyday
• Normal weight (18 < MBI < 25)
• Clear treatment history within past 3 months
Exclusion criteria
• Severe organic or mental disease
• Pregnancy or lactation
• Severe cerebral deterioration
• Severe blood pressure elevation (diastolic > 120 mmHg)
• Cardiac infarction within past 6 months
• Unstable angina pectoris
• Participation in other clinical trials simultaneously or within past 4 weeks

Methodology

Phytomedicines and extraction of plants extracts

Stragol™ oral drop contains a mixture of hydro alcoholic extracts of chamomile, willow bark, garlic, red pepper, bilberry, ginger, and 1.5% dry extract of hawthorn prepared using percolation method according to the German pharmacopeia procedure 10 (DAB_{10}) at pharmaceutical company Goldaru (Isfahan, Iran).

Data collection and follow-up

All procedures were executed in accordance with the ethical standard of Iranian Universities of Medical Sciences. Forty patients suffering from stable chest angina aged between 40 and 60 years were randomly categorised into control and experimental groups. Random number tables were used where each value was randomly selected with an equal chance of choosing any integer among 1–40 by QuickCalcs online calculator (http://www.graphpad.com/quickcalcs/randomn2.cfm) (Table S1), which allocated the numbers randomly to control and experimental groups.

At initial clinical visit, a basic examination as well as recording of case history, health condition, previous/concomitant diseases, and medical treatment was done. Patients were eligible if they met the inclusion criteria as listed in Table 2. Patients were encouraged to maintain their concomitant medications on constant doses. Patients in the experimental group were subjected to blood tests as well as exercise tests to record data on blood factors and exercise tolerance. The patients were then administered with medicines, i.e., Methoral (50 mg/day), Aspirin (80 mg/day), and sublingual Nitroglycerin in case of discomfort. As well, sixty drops of Stragol™ (Table 3) were additionally taken by patients in the experimental group, daily. The control group did not take the Stragol™ oral drop. After four weeks administration of medications, blood tests as well as exercise tests were repeated and the data recording was performed. The recorded data included

Table 3
Different ingredients in Stragol™ herbal heart drop (standardised to 0.060 mg vitexin-2-rhamnoside).

Ingredient	mg per 1 ml oral drop
Garlic extract	407.4
Hawthorn	44.4
Ginger	14.8
Bilberry	20.4
Red pepper	9.3
Chamomile	14.8
Willow bark	26.6

total cholesterol, LDL cholesterol, triglycerides, and fasting blood sugar from blood samples as well as blood pressure, heart rate, and exercise tolerance from exercise tests. VO_2 was calculated using 3.5 × MET value formula, where MET is Functional Capacity determined by Bruce exercise test [9]. The exercise test was performed as per Bruce protocol and on a treadmill, which included four stages of exercise with ascending slope and speed followed by three stages of recovery. Meanwhile, arm blood pressure, heart rate, and ECG were recorded. The test was interrupted in the case of any chest discomfort, severe asthma, hypotension, or exhaustion, and the disease was diagnosed based on recorded data by cardiologist. Exercise tolerance was determined in this stage. In addition, blood test was performed in specialised laboratories from 5 ml blood sample of arm vein of each patient. The data from exercise tests and blood tests were collectively recorded in separate sheets.

Blood test

Biochemical examination was carried out in specialised laboratories to determine the levels of LDL cholesterol, triglyceride, total cholesterol, and fasting blood sugar in blood samples of patients.

Data analyses

Data analysis was done based on mean values of different factors obtained from twenty patients of both experimental and control groups and the *t*-test was carried out in order to analyse significance of differences between two corresponding arrays.

Results

Descriptive analyses of data

Levels of LDL cholesterol, triglyceride, total cholesterol, fasting blood sugar, resting heart rate and blood pressure, VO_2, and exercise tolerance of patients were determined before and after administration of corresponding medications in experimental and control groups. The relevant data are presented in Tables 4 and 5 for respective control and experimental groups.

Administration of Stragol™ drop improves the exercise tolerance

Data presented in Tables 4 and 5 revealed that administration of Stragol™ herbal heart drop improved the exercise tolerance of patients suffering from stable chest angina. In contrast to control group, exercise tolerance values of pre- and post-treatment in experimental group were statistically ($P < 0.05$) different (Fig. 1).

During ischemic heart failure

VO_2, which refers to consumable oxygen by myocardial tissues, was significantly (>13%) elevated after administration of Stragol™ oral drop. In contrast, no significant improvement in VO_2 value was achieved after taking only the chemical medications (Table 5).

Herbal components of Stragol™ heart oral drop significantly lowered the LDL cholesterol level in the patients suffering from stable chest angina. While in control group almost no change ($\Delta \approx 0.02\%$) was observed after treatment with chemical medications, considerable decrease in LDL cholesterol ($\Delta \approx 24\%$) was observed in experimental group after Stragol™ oral drop administration (Fig. 2A).

Table 4
Clinical records of patients in control group on different blood and cardiac factors.

Variant	Parameter		
	Mean ± SE (Pre-treatment)	Mean ± SE (Post-treatment)	Δ% (pre- and post-treatment)
LDL cholesterol	156.32 ± 7.516	156 ± 8.372	−0.20^{ns}
Triglyceride	305 ± 13.74	307.85 ± 13.60	0.93^{ns}
Total cholesterol	255.11 ± 11.363	252.1 ± 11.132	−1.20^{ns}
Fasting blood sugar	116.47 ± 7.787	116.53 ± 3.68	0.05^{ns}
Exercise tolerance	8.79 ± 0.363	9.69 ± 0.503	10.24^{ns}
Resting mean blood pressure	107.96 ± 2.29	92.39 ± 1.30	−14.5**
Resting heart rate	87.55 ± 3.23	72.6 ± 3.00	−17.08**
VO_2	30.765 ± 1.273	33.92 ± 1.761	10.24^{ns}

The patients were under treatment by Methoral (50 mg/day), Aspirin (80 mg/day), and sublingual Nitroglycerin in case of discomfort. The values are the means of twenty values in each control and experimental group. SE represents standard errors among values.
** Represents the significant differences at $P \leq 0.01$ between corresponding values before and after treatment.
^{ns} Shows non-significant difference between corresponding values before and after treatment.

Table 5
Clinical records of patients in experimental group on different blood and cardiac factors.

Variant	Parameter		
	Mean ± SE (Pre-treatment)	Mean ± SE (Post-treatment)	Δ% (pre- and post-treatment)
LDL cholesterol	149.16 ± 9.012	113.42 ± 6.766	−23.96**
Triglyceride	226.31 ± 13.654	189.37 ± 10.895	−16.33*
Total cholesterol	238.56 ± 11.222	208.56 ± 9.615	−12.58*
Fasting blood sugar	116.67 ± 7.324	106.5 ± 6.912	−8.71ns
Exercise tolerance	8.7 ± 0.241	9.845 ± 0.442	13.16*
Resting mean blood pressure	103.06 ± 1.787	91.73 ± 4.981	−6.3*
Resting heart rate	76.6 ± 1.66	70.42 ± 1.409	−8.07**
VO_2	30.45 ± 0.824	34.46 ± 1.582	13.16*

The patients were administered with Methoral (50 mg/day), Aspirin (80 mg/day), and sublingual Nitroglycerin in case of discomfort plus Stragol™ herbal heart drop. Data are the means of twenty values in each control and experimental group. SE refers to as standard errors among values.
* Represent significant differences at $P \leq 0.05$ and $P \leq 0.01$ between corresponding values before and after treatment.
** Represent significant differences at $P \leq 0.01$ between corresponding values before and after treatment.
ns Shows non-significant difference between corresponding values before and after treatment.

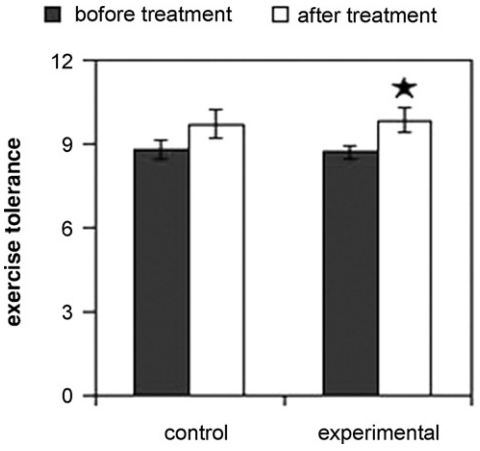

Fig. 1. Exercise tolerance of patients suffering from stable chest angina. Exercise tolerance of all patients before and after treatment were determined by exercise test using Bruce protocol. Data are the means of values of twenty patients in each control and experimental group. Error bars indicate the standard errors among the values. *Displays the significance of difference at $P \leq 0.05$ between corresponding values before and after treatment.

A four-week administration of Stragol™ herbal drop resulted in a statistically significant reduction (≈12%) in total cholesterol amount, whereas in control group only ≈1% reduction was observed. This demonstrates the efficacy of Stragol™ herbal drop in lowering the total-cholesterol level, which is a main limiting factor for cardiac activity (Fig. 2B).

Another important factor investigated during treatment of ischemic heart failure with Stragol™ herbal drop was the triglyceride level, which critically threatens cardiovascular performance. A significant decrease in triglyceride level (more than 16%) was noticed in experimental group after administration of Stragol™ drop; while almost no decrease (less than 1%) was recorded after treatment with chemical medicines in control group (Fig. 2C).

Elevated fasting blood sugar (FBS) is another casual agent of heart failure as it affects the vessels carrying blood. The four-week administration of Stragol™ herbal drop did not reduce FBS level significantly, although reduction (≈9%) was greater in the experimental group compared to that observed (≈0.045%) in control group (Fig. 3).

In ischemic heart diseases, the blood pressure is high mainly due to blockade of vessels. Therefore, the remedies are aimed at reducing the blood pressure by resolving blockades. Administration of Stragol™ oral drop resulted in reduction of blood pressure. Hence, Stragol™ herbal drop can eliminate the vessel blockades, which is of high importance in remedies for ischemic heart diseases (Fig. 4A).

Monitoring the heart rate of patients suffering from stable chest angina before and after treatment in either group revealed

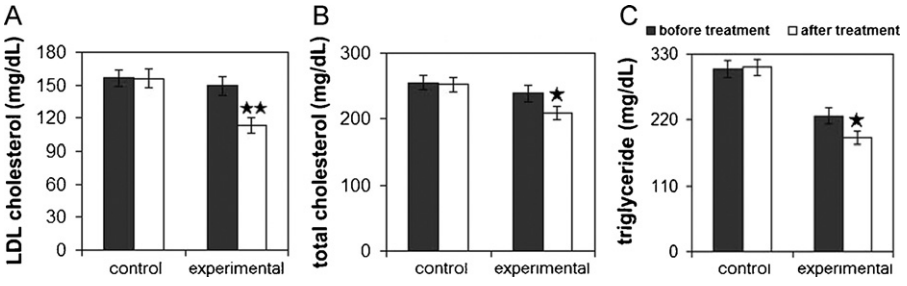

Fig. 2. Changes in serum lipids of patients stricken by stable chest angina. (A) LDL cholesterol; (B) Total cholesterol; (C) Triglycerides. Biochemical examinations of blood for serum lipids were performed before and after treatment in both experimental and control groups using 5 ml of arm vein of each patient. Data are the means of values of twenty patients in each control and experimental group. Error bars illustrate the standard errors among the corresponding values. * and ** show the significant differences at respective $P \leq 0.05$ and $P \leq 0.01$ between corresponding values before and after treatment.

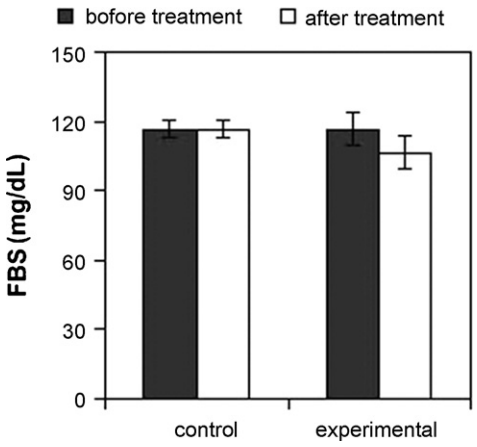

Fig. 3. Changes in fasting blood sugar (FBS) in blood samples of patients suffering from stable chest angina. Biochemical examination of blood for fasting blood sugar was performed before and after treatment in each experimental and control group. Data are the means of values of twenty patients in both control and experimental groups. Error bars represent the standard errors among the corresponding values.

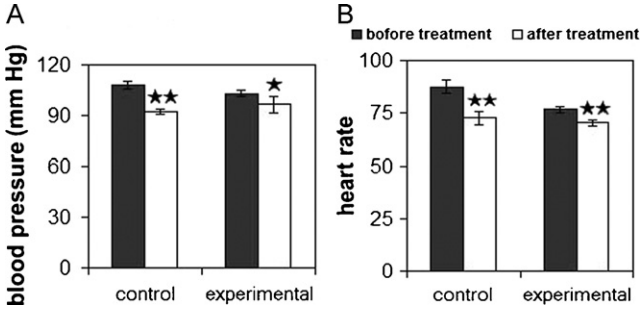

Fig. 4. Improvement of blood pressure and heart rate of patients affected by stable chest angina. Exercise tests using Bruce protocol were carried out before and after treatment in control and experimental groups and the corresponding data of blood pressure (A) and heart rate (B) were recorded accordingly. Data are the means of values of twenty patients in each control and experimental group. Error bars denote the standard errors among corresponding values. * and ** demonstrate the significance of differences at respective $P \leq 0.05$ and $P \leq 0.01$ between corresponding values before and after treatment.

that both remedial strategies were statistically effective in harmonising the heart rate of patients (Fig. 4B).

Discussion

Stable chest angina is a form of atherosclerosis which may change to unstable form in the case of no prophylaxis or careless treatment, which gradually leads to myocardial infarction and heart stroke. Major threatening factors causing heart failure are high level of LDL cholesterol, low level of HDL cholesterol, arterial hypertension, smoking, and diabetes. These factors can cause inadequate blood circulation in myocardial tissues and hence the oxygen tension resulting in collapse of tissues, which may lead to mechanical, biochemical, and electrical transient dysfunction of myocardium. Therefore, elimination or reduction of these factors could result in increase of oxygen availability for tissues, and reduce the heart problems. The ideal method for achieving this outcome is the one with the least side effects and costs. Recent investigations revealed that phytomedicines play an important role in prophylaxis and treatment of heart diseases (for review, see [10]). Plants are rich in some useful active ingredients with positive physiological impacts on different organs.

Garlic acts selectively in blocking the synthesis of effective enzymes involved in formation of platelets, while acting neutrally towards synthesis of important veins' prostaglandins [11]. In addition, garlic lowers the age-dependent vessel atherosclerosis [12] leading to lowering of blood pressure. Chamomile possesses some effective antibiotics and has antimicrobial and anti inflammatory properties [13]. Moreover, chamomile strengthens the nervous system by its anxiolytic and sedative nature, and can decrease the heart discomfort [14]. It is believed that ginger inhibits the synthesis of prostaglandins [15] and could be used as a cholesterol-lowering, antithrombotic and anti-inflammatory agent [16]. Hawthorn extract blocks the thromboxane production, lowers the probability of platelet aggregation, and broadens blood vessels [17,18], resulting in decreased blood pressure. Because of its broadening effect on the coronary artery, the overall output is the lowered probability of angina incidence. Moreover, it blocks the phosphodiesterase activity, thereby increasing the concentration of cAMP in myocardium, which per se increases the heart contractility [19]. Additionally, hawthorn flavonoids effectively preserve the vessels' collagen and thus protect the vessels against atherosclerotic plaques [20]. Capsapsin in red pepper along with vitamins A and C can increase the blood circulation in coronary vessels, decrease the cholesterol and triglyceride, and prevent the development of atherosclerosis [21]. Bilberry improves the blood circulation in different organs and effectively induces the formation of new capillary vessels [22]. It is also well-known that Salix as the source of aspirin possesses nerve strengthening and anxiolytic properties, relieves the cardiac discomforts, and is useful for prophylaxis of cardiovascular failures.

The above-mentioned properties of these medicinal plants and their valuable positive influences on the cardiovascular system encouraged us to investigate the effect of administration of these plants as an oral drop, Stragol^{TM}, on exercise tolerance of patients suffering from stable chest angina. A 4-week administration regime of Stragol^{TM} oral drop resulted in a significant reduction in blood lipids, namely LDL cholesterol, total cholesterol and triglyceride (Fig. 2A–C). These are important deteriorating factors in oxygen circulation, and hence resulted in heart strengthening and increase of exercise tolerance (Fig. 1). Many believe that medicinal plants, due to their lack of or negligible side effects and relative low cost, are preferable to conventional medicines. The present results regarding the positive correlation between administration of botanicals and naturaceuticals, prophylaxis and treatment of heart diseases, and diminishing their casual agents are in accordance with previous observations [1–6,10,23–28]. Increase of exercise stability along with decrease of heart rate and blood pressure during maximum activity was observed after administration of garlic and hawthorn [5,6,23]. Verma et al. [5] correlated the increase of exercise stability with decrease in isoprenaline level, as the isoprenaline-induced myocardial damage was reduced dramatically. This mechanism may relate to stress induced by

environmental sympathetic system activity without any influence upon cerebellum and hypophyseal–adrenocortical system. Moreover, garlic was recommended to patients as an adaptogen due to the increase of adaptability to stress in patients with ischemic heart disease [28]. In the present study a significant increase in exercise tolerance of patients was observed in the experimental group who received Stragol^{TM} oral drop. Heart rate and blood pressure were significantly decreased in both experimental and control groups, which agrees with the results of other research. Employment of a combination of phytomedicines with diverse modes of mechanism seems promising in improving the heart function. The considerable decreases in LDL cholesterol (24%), TG (16%), and total cholesterol (12%) during a short period of Stragol^{TM} oral drop administration (four weeks) were highly influential in increasing the exercise tolerance of the patients. Investigations on ginger have demonstrated that it is anti-inflammatory, antioxidant, anti-platelet, hypotensive, and hypolipidemic in an experimental setting [26]. Ansari et al. [26] used ginger for treatment of oxidative necrosis of myocardium induced by isoproterenol and described the underlying mechanism as follows: The ginger extract causes elevation of endogenous myocardial antioxidant levels, decreases serum marker enzymes, and increases myocardium lipid peroxides, all of which have protective effects on the heart [26]. It is expected that this mechanism is also applicable in the present study, culminating in elevated exercise tolerance. Based on provided data, usage of this botanical oral drop affected the body physiology very effectively due to the synergistic effects of its components. Ghayur et al. [24] reported vessel contraction and blood pressure decreases due to administration of ginger extract. These data revealed that ginger extract lowers the blood pressure mediated by a double inhibitory effects, i.e., provoking the moscarinic receptors and blocking Ca^{2+} channels. In other words, it suggests that the blood pressure-lowering effect of ginger is mediated through blockade of voltage-dependent calcium channels [29]. In addition, zingerone, an active ingredient of ginger, is able to efficiently scavenge native $ONOO^{(-)}$ as well as $ONOO^{(-)}$ derived from the peroxynitrite donor 3-morpholinosydnonimine hydrochloride (SIN-1), thus improving the functionality of endothelium [30]. Although the methodology of present study contrasts from that of Ghayur et al. [24], based upon provided data, the proposed mechanism for ginger in Stragol^{TM} oral drop is most probably identical. Young et al. [31] compared the influence of two medicinal groups, i.e., Aspirin and Nifedipine and phytomedicines of ginger. Consequently, the authors recommended the daily integrative consumption of 10 g ginger and 10 mg of Nifedipine for relieving cardiovascular as well as brain problems by anti-platelet property. However, it implicated the side effects of Aspirin. Here, results of administering a combination of chemical medicines and naturaceuticals are in accordance with Young et al. [31] as in stable chest angina patients. Stragol^{TM} oral drop could remove the vessel atherosclerosis, which leads to better and more effective blood circulation and higher exercise tolerance (Fig. 1). As per Young et al. [31], side effects imposed by conventional medications and satisfaction of taking phytomedicines were observed in patients, and chralonine adaptability with other medicines confirmed its value for prescription. According to the results of the present study, significant contribution of mentioned phytomedicines to lowering the serum LDL cholesterol, triglyceride, and total cholesterol was not comparable with that by chemical medicines. Interestingly, lowering of blood pressure in experimental group was also significant and comparable with that in control group. Chen et al. [10] recommended the administration of garlic, ginger, and hawthorn as a medication for high blood pressure, which is confirmed by the present results. It is reported that chamomile is an anti-anxiety medicine through epigenic functions as linkers of benzodiazepine receptors, producing anti-anxiety and sedative effects. It is plausible that here the resulting anxiolytic effect from chamomile influences the vessels, which are all controlled by the sympathetic nervous system. The fine-tuned function of this system harmonises the cardiovascular performance that per se conducts a better blood circulation and transfer into myocardium.

Anti-hypertensive activity of hawthorn is probably mediated by the following mechanisms [10]: First, it induces endothelium-dependent, NO-mediated vasorelaxation via eNOS phosphorylation [32]. Second, as it is rich in hyperoside (a flavonoid) and has a strong free radical scavenging activity, it can shield the NO from being attacked by superoxide radicals and scavenge the peroxynitrite radicals [33,34]. Third, procyanidins in hawthorn extract may be responsible for the endothelium-dependent nitric oxide-mediated relaxation in isolated rat aorta via activation of tetraethylammonium-sensitive K^+ channels [35]. Finally, hawthorn flavonoids and proanthocyanidins might possess diuretic activity [36]. Overall, as most researchers implicate the side effects on the performance of other organs imposed by chemical medicines, it seems that botanicals and naturaceuticals could rationally substitute for or at least assist the chemical medicines in treatment of cardiovascular failures.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgements

We thank the pharmaceutical company Goldaru (Isfahan, Iran) for providing the Stragol^{TM} herbal heart drops, and Dr. Varun Dev for critical reading of the manuscript. We also thank two anonymous reviewers for their valuable comments on this article.

Authors: All research done by the authors.

Financial support: yes.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.eujim.2011.07.004.

References

[1] Valerio CJ, Coghlan JG. Bosentan in the treatment of pulmonary arterial hypertension with the focus on the mildly symptomatic patient. Vascular Health and Risk Management 2009;5:607–19.

[2] Marin-Neto JA, Rassi Jr A, Avezum Jr A, Mattos AC, Rassi A, Morillo CA, et al. The benefit trial: testing the hypothesis that trypanocidal therapy is beneficial for patients with chronic chagas heart disease. Memòrias do Instituto Oswaldo Cruz 2009;104:319–24.
[3] Nicoll R, Henein MY. Ginger (zingiber officinale roscoe): a hot remedy for cardiovascular disease. International Journal of Cardiology 2009;131:458–9.
[4] Chrubasik S, Pittler MH, Roufogalis BD. Zingiberis rhizome: a comprehensive review on the ginger effect and efficacy profiles. Phytomedicine 2005;12:684–701.
[5] Verma SK, Rajeevan V, Jain P, Bordia A. Effect of garlic (allium sativum) oil on exercise tolerance in patients with coronary artery disease. Indian Journal of Physiological Pharmacology 2005;49:115–8.
[6] Zapfe Gj. Clinical efficacy of crataegus extract WS 1442 in congestive heart failure NYHA class II. Phytomedicine 2001;8:262–6.
[7] Braunwald E, Zipes DP, Libby P. Heart disease a textbook of cardiovascular medicine. Philadelphia: Wb Saunders; 2001.
[8] Fauci A, Braunwald E, Kasper D, Hauser S, Longo D, Jameson J, et al. Harrison's principles of internal medicine. McGraw-Hill; 2008.
[9] Kang J. Bioenergetics primer for exercise science. Champaign: Human Kinetics; 2008. p. 475–478.
[10] Chen ZY, Peng C, Jiao R, Wong YM, Yang N, Huang Y. Anti-hypertensive nutraceuticals and functional foods. Journal of Agriculture and Food Chemistry 2009;57:4485–99.
[11] Chang HS, Yamato O, Yamasaki M, Maede Y. Modulatory influence of sodium 2-propenyl thiosulfate from garlic on cyclooxygenase activity in canine platelets: possible mechanism for the anti-aggregatory effect. Prostaglandins, Leukotrienes and Essential Fatty Acids 2005;72:351–5.
[12] Koscielny J, Klüssendorf D, Latza R, Schmitt R, Radtke H, Siegel G, et al. The antiatherosclerotic effect of Allium sativum. Atherosclerosis 1999;144:237–49.
[13] Chehregani A, Mohsenzadeh F, Mirazi N, Hajisadeghian S, Baghali Z. Chemical composition and antibacterial activity of essential oils of Tripleurospermum disciforme in three developmental stages. Pharmaceutical Biology 2010;48:1280–4.
[14] Viola H, Wasowski C, Levi de Stein M, Wolfman C, Silveira R, Dajas F, et al. Apigenin, a component of Matricaria recutita flowers, is a central benzodiazepine receptors-ligand with anxiolytic effects. Planta Medica 1995;61:213–6.
[15] Han AR, Kim MS, Jeong YH, Lee SK, Seo EK. Cyclooxygenase-2 inhibitory phenylbutenoids from the rhizomes of Zingiber cassumunar. Chemical And Pharmaceutical Bulletin (Tokyo) 2005;53:1466–8.
[16] Thomson M, Al-Qattan KK, Al-Sawan SM, Alnaqeeb MA, Khan I, Ali M. The use of ginger (Zingiber officinale Rosc.) as a potential anti-inflammatory and antithrombotic agent. Prostaglandins, Leukotrienes and Essential Fatty Acids 2002;67.
[17] Walker AF, Marakis G, Morris AP, Robinson PA. Promising hypotensive effect of hawthorn extract: a randomized double-blind pilot study of mild, essential hypertension. Phytotherapy Research 2002;16:48–54.
[18] Vibes J, Lasserre B, Gleye J, Declume C. Inhibition of thromboxane A2 biosynthesis in vitro by the main components of Crataegus oxyacantha (Hawthorn) flower heads. Prostaglandins, Leukotrienes and Essential Fatty Acids 1994;50:173–5.
[19] Müller A, Linke W, Klaus W. Crataegus extract blocks potassium currents in guinea pig ventricular cardiac myocytes. Planta Medica 1999;65:335–9.
[20] Koch E, Malek FA. Standardized extracts from hawthorn leaves and flowers in the treatment of cardiovascular disorders – preclinical and clinical studies. Planta Medica 2011;77(11):1123–8.
[21] Kwon MJ, Song Y-S, Choi MS, Song YO. Red pepper attenuates cholesteryl ester transfer protein activity and atherosclerosis in cholesterol-fed rabbits. Clinica Chimica Acta 2003;332:37–44.
[22] Bell DR, Gochenaur K. Direct vasoactive and vasoprotective properties of anthocyanin-rich extracts. Journal of Applied Physiology 2006;100:1164–70.
[23] Pittler MH, Schmidt K, Ernst E. Hawthorn extract for treating chronic heart failure: meta-analysis of randomized trials. American Journal of Medicine 2003;114:665–74.
[24] Ghayur MN, Gilani AH, Afridi MB, Houghton PJ. Cardiovascular effects of ginger aqueous extract and its phenolic constituents are mediated through multiple pathways. Vascular Pharmacology 2005;43:234–41.
[25] Zareba G. Phytotherapy for pain relief. Drugs of Today (Barcelona) 2009;45(6):445–67.
[26] Ansari MN, Bhandari U, Pillai KK. Ethanolic zingiber officinale R. extract pretreatment alleviates isoproterenol induced oxidative myocardial necrosis in rats. Indian Journal of Experimental Biology 2006;44:892–7.
[27] Schröder D, Weiser M, Klein P. Efficacy of a homeopathic crataegus preparation compared with usual therapy for mild (NYHA II) cardiac in sufficiency: results of an observational cohort study. The European Journal of Heart Failure 2003;5:319–26.
[28] Head KA, Kelly GS. Nutrients and botanicals for treatment of stress: adrenal fatigue, neurotransmitter imbalance, anxiety, and restless sleep. Alternative Medicine Review 2009;14:114–40.
[29] Ghayur MN, Gilani AH. Ginger lowers blood pressure through blockade of voltage – dependent calcium channels. Journal of Cardiovascular Pharmacology 2005;45:47–80.
[30] Shin SG, Kim JY, Chung HY, Jeong JC. Zingerone as an antioxidant against peroxynitrite. Journal of Agricultural and Food Chemistry 2005;53:7617–22.
[31] Young HY, Liao JC, Chang YS, Luo YL, Lu MC, Peng WH. Synergistic effect of ginger and nifedipine on human platelet aggregation: a study in hypertensive patients and normal volunteers. American Journal of Chinese Medicine 2006;34:545–51.
[32] Brixius K, Willms S, Napp A, Tossios P, Ladage D, Bloch W, et al. Crataegus special extract WS 1442 induces an endothelium-dependent, NO-mediated vasorelaxation via eNOS-phosphorylation at serine 1177. Cardiovascular Drugs and Therapy 2006;20:177–84.
[33] Koçyildiz ZC, Birman H, Olgaç V, Akgün-Dar K, Melikoğlu G, Meriçli AH. Crataegus tanacetifolia leaf extract prevents L-NAME-induced hypertension in rats: a morphological study. Phytotherapy Research 2006;20: 66–70.
[34] Tadić VM, Dobrić S, Marković GM, Dordević SM, Arsić IA, Menković NR, et al. Anti-inflammatory, gastroprotective, free-radical-scavenging, and antimicrobial activities of hawthorn berries ethanol extract. Journal of Agricultural and Food Chemistry 2008;56:7700–9.
[35] Kim SH, Kang KW, Kim KW, Kim ND. Procyanidins in crataegus extract evoke endothelium-dependent vasorelaxation in rat aorta. Life Science 2000;67:121–31.
[36] Lacaille-Dubois MA, Franck U, Wagner H. Search for potential angiotensin converting enzyme (ACE)-inhibitors from plants. Phytomedicine 2001;8:47–52.