IJBPAS, October, 2016, 5(10): 2673-2682

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

EVALUATION OF CHEMICAL AND HERBAL DRUGS ON MYOCARDIAL INFARCTION

FARIA ALIPOURMAZANDARANI

Department of Veterenery, Islamic Azad University, Babol, Mazandaran, Iran

Received 30th June 2016; Revised 30th July 2016; Accepted 1st Sept. 2016; Available online 1st Oct. 2016

ABSTRACT

Comparison usage of chemical and herbal drugs show that chemical drugs beside having good effects also have side effects some of which will remain to the end of life and even transfer to the next generation. While the side effects of herbal drugs are lower, and they have no side effects or very few in some cases. Since chemical drugs have made many problems for people in recent decades, intention and procedures of using herbal drugs have increased. Another important issue is that herbal drugs have better effects in some diseases, and there are just using herbal drugs prescription for some disease. This study examines heart disease and myocardial infarction by popular used drugs and their side effects.

Keywords: Myocardial infarction, herbal drugs, chemical drugs.

INTRODUCTION

Standard definition was provided by WHO for myocardial infarction in 1971. Research continues to complete this definition. The definition of WHO didn't mention the related biomarkers of cardiac necrotic for being specialized. Therefore, this way is open for various interpretations. Since 1980, troponin biomarkers with high attribution and sensitivity were defined. The main specification of myocardial infarction is making necrotic in heart muscles and its intensity is determined by the range of damaged area and time. Therefore, myocardial infarction has the following symptoms: 1- cardiac ischemia, 2- visible changes in ST-segment/T-wave or left bundle branch block, 3- pathologic Q waves on, 4- reduction in the diameter of the heart muscle or observation non-natural movements in imaging, 5- determination intracoronary thrombus by angiography or autopsy. [1]

Heart troponins are part of cardiac contractility ingredients which can be used as myocardial infarction biomarkers. Myocardial necrosis damages the membranes of myocytes and myocytes release special proteins into the blood circulation. Isoforms of cTnI and cTnI can be detected using specific monoclonal antibodies. When the creatine kinase MB amount is natural, this technique can be used to detect myocardial infarction. Some structural changes made in pathological molecule ad cell mechanism after myocardial infarction that are called Remodeling [2].

Methods

This study is a systematic review and about myocardial infarction that is collected by searching in the databases PubMed, Science Direct, and Highwire (Stanford University) with keywords, Herbal Hyperlipidemia, Heart failure, Cardiovascular and Hypertension for clarification on the definition of myocardial infarction, active mechanical techniques, gerbil compounds, side effects, interruptions, and training to patient.

Herbal Treatments of Afflicted Patients to Myocardial Infarction and Depression

It was indicated in research of Bagherian et al. (2011) that depression symptoms in patients is popular after myocardial infection and can have negative effects on Prognosis. Depression was reported in 35-50% of MI patients. Depression is known as dangerous factor of MI incidence, mortality, and complications, and reduced quality of life in patients after MI. the relationship between depression and MI is reciprocal. The intermediate mechanisms in making relationship between depressions after MI and increasing mortality include behavioral and biological mechanisms. Arrhythmia, changes in vital balance, inflammation, neuro-hormonal mechanisms, and flocculation are examples of biological mechanisms. Combination of both of them may increase mortality danger in these patients. Epidemiological studies showed the relationship between depression and danger of next MI, cardiovascular disease, and cardiac death. The negative effect of depression on prognosis can be prevented by accurate treatment. There are various medical methods to cure depression after MI including cardiac rehabilitation, social support, cognitive behavioral therapy, and antidepressants. It is recommended to prevent taking tricyclic drugs for their undesirable effects in depression treatment. If

SSRI anti-depression drugs start with short gap ager MI, it won't have significant side effects. [3]

Cardiac Rehabilitation after Angioplasty, bypass Surgery, and Myocardial Infarction

In research by Saeedi et al. (2004) in three surgical groups of bypass (165 members), angioplasty 44 members), and medical (110 members), it was indicated thatfunctional capacity, ejection fraction and body mass index were significantly improved after rehabilitation of lipid profile. Comparison the changes percentage of these variables didn't show significant difference, and all groups usedcardiac rehabilitation similarly. Therefore, it can be concluded that different patients attending cardiac rehabilitation benefited equally and results from two different groups were similar. The infected patents to MI benefit significantly as patients who had undergone revascularization interventions. Therefore, attended patients are recommended to rehabilitation before doing any invasive interventions in delaying surgery and treatment due to their lower costs. It must be noticed that their research was retrospective analytical- descriptive. The profiles of 310 patients in 1999-2003 were studied who referred to cardiovascular research center of Isfahan University of medical sciences, who were gone under the angioplasty surgery, bypass surgery, or for medical reasons such as s angina or myocardial Infarction for cardiac rehabilitation. The rehabilitation plans was for 2 month (3 sessions a week) including aerobic exercise, patient education and dietary modification, and variables such as exercise capacity, ejection fraction, lipid profiles and body mass index before and after rehabilitation were measured. The collected data was analyzed using SPSS software, and t-test and Chi-squared test[4].

Changing the Health Behaviors of Patients 4-6 Months after MI

In research of Rahimiha et al. (2000) by aim of changing health behavior of patients 4-6 months after MI, it was indicated that 3.84% heath behavior stayed unchanged and proper 4-6 months after MI. Most patients had unhealthy behavior about their diet before and after MI and 5.68% stayed unchanged and improper. How to change health behavior in exercises showed that the maximum percentage (36%) was unchanged and proper and 8.34% stayed unchanged and improper. More than 50% of patients had unchanged and proper behavior and others had proper changed to cope with psychological pressure. Consequently, it can be stated that afflicted patients to MI must be educated and health advice are given to them according to their gender, age, educational level, habits, and cultures to cure them. In addition, it is suggested to prioritize curing elderly patientsin outpatient clinics and homes to continue cares and necessary trainings. It must be stated that 89% of MI patients that they first had MI passing 4-6 monthin this research were selected by stratified method and participated in research that had no specific disease[5].

Relationship between Depression after MI and Left Ventricular Function

In futuristic research by Bagherian et al. (2008) by aim of determination the relationship between depression and the left ventricular function, it was indicated that low function of left ventricular determined by LVEF has significant relationship with depression three months after MI. In addition, the exploratory model, that only has LVEF variable, has prediction validity of 64.8% with sensitivity of 55.7% and feature of 72.1%. Consequently, it can be stated that left ventricular dysfunction is related with incremental danger of depression after MI. it must be started that in this research, 176 32-84 years old patients with gen average of 556 years (st.dev of 10.05), who were hospitalized in acute myocardial infarction in a coronary care unit (CCU) of the city of Isfahan during the first five months of 2006, were selected ad studied by available sampling method.

Demographic and medical and evaluation of left ventricular function (LVEF) was collected using echocardiography, angiography immediately after MI. then, they were evaluated by Beck Depression scale for the first three caring months after MI. the collected data during hospitalization and follow-up stage was analyzed using logistic regression. [6]

Used Drugs in Cardiovascular Disease [7]

Anethum: it is used for hyperlipidemia, prevention, and treatment of atherosclerosis and bile colic in 650 gr tablets and also granules in 100 gr pack. Anethum is made from extraction of anethum graveolens, cichorium intybus, fumaria parviflora, Citrus Sp. Active substances in anethum includes Volatile oils such as Karun, glycosides, bitter lactucopicrin and alkaloids protopine, hespéridine and quercetin. Mechanism of this drug is unknown. It was indicated in a research on high-fat diet without diabetes on mice that using edible anethum significantly reduces triglycerides and LDL and increase HDL. However, anti-aging effect wasn't seen in the high-fat diet without diabetes on mice and increased their glycemic. Results of this study showed that this drug is used cautiously to reduce diabetic patients' glycemic. It was shown in another study that the anti-lipid effects of anthenum leaf extraction had protective effect of liver from oxidative damage caused by high-fat diet. [8]

Training to patient: it is trained to patient to take tables with water or fruit juice. 9. To take granule, please take each time a teaspoonful of granules in a glass of boiling water and after 10 minute. The security of this product hasn't been proved in pregnant and lactating women; nonetheless, its advantages must be evaluated against disadvantages. Therefore, this point must be included in training.Anethum graveolens is full of sodium, so an overdose of sodium restriction is not recommended for patients such as those suffering from myocardial Infarction or kidney failure. The sensitive patients to anethum graveolens must be prohibited of using any type of its products.

Generally,cichorium intybusis known as a non-dangerous plant, yet patient blood pressure and heart beat must be controlled. It is recommended to patient to report all types of cardiac disease to doctor. Taking anethum compound should be along with doctor permission due to the presence of sucrose in combination, in patients with diabetes. In addition, long-time taking of this drug (more than 1 year) is prevented for incidences of toxicity with beta-carotene. Taking anethum is not recommended in patients with urinary tract infections.Long-term exposure of this drug to sunlight and UV exposure should be avoided for probability of creating photo-dermatitis. There must be at least 1 hour gap between taking this drug if it has interruption with other drugs.

Train the patients that this medication during pregnancy and lactation and severe allergy to this drug is contraindicated. Train patients about side effects such as skin reactions and photo-dermatitis, spotting in some women and yellowing of the skin (especially on the palms and soles) due to long-term use or more than the recommended dose. Train patient also about drug interactions as: anethum exacerbate the effects of other lipid lowering drugs; PUVA therapy is contraindicated with concomitant use anethum; anethum with concomitant use of vitamin A should be done with caution and under medical supervision for being rich in beta-carotene dill (precursor of vitamin A); simultaneous consumption of anethum with potassium-sparing diuretics should be performed by a physician for having high potassium in anethum graveolens plant.

Diuretic: Diuretic is available in granule and 100 gr pack. Diuretic is used to reduce human body symptoms such as congestive heart failure and hypothyroidism, kidney, urinary tract infection and help to ward off urinary tract stones, and high blood pressure. The diuretic plant mixture powder is made from compounds of Prunus Cerasus, Zea Mays, Tribulus Terrestris, Mentha Longifolia. Its active ingredients include potassium, calcium, glucose, Levulose, volatile oils and flavonoids. Effect mechanism of this product is not known completely. Probably the present ions and sugars in water similar to osmosis increases the osmolality fluid filtered in the glomerulus and facilitates the excretion of water and inhibit reabsorption of water and salts. The present volatile oil in menthapulegium causes smooth muscle relaxation and facilitate the flow of urine is urinary tract for anti-spasmodic effect.

Training to People: patients can drink plant mixture after clearing in one glass of boiling water twice in a day, each time one eating spoon. There is probability of allergic reactions such as contact dermatitis and urticarial in sensitive people to tassel. The reliability of taking this drug isn't proved in pregnancy and lactation; nonetheless, its advantages are measured against its disadvantages. High usage of this product may lead to water and electrolyte disturbance. Effects of other diuretic drugs are intensifies in simultaneous taking of this drug and can lead to water and electrolytes disorders. [10 &11]

Alicom: this is the coated 260 mg alicom including 100 mg allium sativum. This drug is used to reduce cholesterol and triglycerides and increase HDL. In addition, it helps to prevent rigid arteries due to the impact on blood pressure and platelet aggregation. On the other hand, it is used to reduce the risk of MI and strokes. Therefore, alicom is used in hypertension, hyperlipidemia, atherosclerosis, and prevention of thrombosis. Its usage it three time a day, each time one to two tablets after eating. Its active ingredients are thiol alkyl and their derivatives, such as allicin, Ajoene, Allyl propyl disulfide, and diallyltrisulfide. Studies have shown that allium sativum with direct effect on the straight muscles of vessels wall makes peripheral vascular vasodilatation. It seems that this drug hyperpolarize potassium membrane and membranes and artery vasodilatation by opening potassium channels. In addition, experimental studies on aqueous extract, alcoholic extract, and allium sativum powder increase nitric oxide production resulting in lower blood pressure by activating nitric oxide synthase. These results were confirmed by experiments in human, too. [12] The effect of allium sativum usually appears in lowering cholesterol and triglyceride synthesis probably by inhibiting key enzymes of cholesterol and fatty acids such as hydroxyl methyl coenzyme A glutaryl, and CoA acetyl carboxylase. Allium sativum prevents from flocculation by increasing fibrinolytic activity, increased coagulation, and platelet aggregation suspension. Clinical trial administered in 1993 on allium sativum effects, reduction of total cholesterol, and its impact on reducing platelet aggregation showed reducing hypotension and its antioxidant properties. Moreover, other plant drugs made from allium sativum are garlet, garlic, garlicap, and garsin. Garlet is in 570 mg coated tablet. Garlet tablet has 400 mg allium sativum granules, and the amount of allicin and allicin per tablet is 1000µg. Its active ingredients are similar to alicom. This drug is taken three time a day, each time 1 or 2 tablets with food. Garlic is in 15 ml drop. Each 10 drops includes 250 g garlic abstract and it is taken 1-3 tablets with food or fruit juice every day. Garlicap is as 330 mg capsule. Garlicap capsule has 330 mg garlic granules. It is taken three times a day each time 1-2 capsules with a glass of water after food. Garsin is 600 mg coated tablet. Garsin includes 85.42% allium sativum granules (equal to 8.9 mg alleyne) and it should be taken three times a day, each time one tablet after food.

Training to patient: you must be aware why patient use this drug. Allium sativum is not recommended to patients with diseases such as diabetes, insomnia, pemphigus, rheumatoid arthritis, organ transplantation, and also in patients after surgery. The extra usage of raw garlic increases danger of undesirable reactions. Patient must be controlled based on blooding symptoms and signs. In some studies, garlic products usage leads to glycemic improvement beside anti-lipid activity in patients with type 2 diabetes. [13] Anyway, diabetes patients that use garlic may shows lower blood cholesterol. If a patient uses anti-diabetic drug, pay attention to signs and symptoms of blood sugar reduction and control the serum glucose levels. Using garlic is harmful for afflicted patients to skin disorders and also feeding mothers and must prevent it, because it irritates the mucosa of baby. Garlic must be used cautiously in treated patients with acetylsalicylic acid or other anticoagulants and blood glucose lowering drugs. High consumption of garlic cause bleeding after surgery. No side effects were seen by the suggested amount consumption, but its high consumption or usage with empty stomach may make gastrointestinal disorders such as heartburn, nausea, vomiting, and diarrhea. In addition, garlic consumption has been reported to make allergic reactions such as contact dermatitis and asthma attacks in sensitive people. This product is forbidden to be used by sensitive people to garlic and afflicted to acute gastrointestinal ulcer. Experimental studies have shown that garlic will cause uterine contractions and make use of it during pregnancy and lactation has not been proved yet; therefore, it is suggested not to be used in this period.

It is suggested to patients to consult with other physicians before consuming plant products, because treatment or proved effectiveness may be accessible. It is said to patient to make the pharmacist aware of prescription if using any type of nutritional or herbal supplements. Recommend patient not delay proper medical evaluation, because doing this action may endanger detection of a disease symptoms seriously in future. It is suggested to patient to prevent extra usage of garlic to minimize the danger of undesirable reactions. Before surgery, extra usage of garlic must be prevented. If a patient uses garlic to reduce blood serum cholesterol levels, suggest him/her to consult with his/her doctor to control blood serum cholesterol levels. Suggest to patient that garlic along with the anticoagulant may increase the risk of bleeding. [14] If patient use garlic as position antiseptic, prevent from its long-term lasting on skin, because this action may cause burning.

Olea-crat:olea-crat is used in treatment of hypertension as granule and 100 gr pack. Olea-crat is made by collection of Olea Europaea, CrataegusMicrophilla, VacciniumArctostaphylos, Zizyphus Vulgaris, and MenthaPulegium. Its active ingredients include Flavonoids, procyanidine, and oleuropein. The cardiovascular effects of these products are attributed to flavonoid compounds in crataegus, particularly procyanidine. Studies on human in laboratory have shown that olea-crat increase coronary blood flow, increase peripheral blood flow (in the head, skeletal muscle and kidney), decrease peripheral blood flow (cutaneous and gastrointestinal tract), and decrease peripheral resistance and reduce blood pressure. Examinations have shown that olea-crat decrease blood-pressure probably by dilation of blood vessels.

Training to Patient: it is trained to patient to make olea-crat 2-3 time a day, each time 1 table spoon in a glass of boiling water for 15 min then clear it and drink. The patients under treatment of cardiovascular drugs are more sensitive to pharmacologic crataegus. Therefore, using this drug in the mentioned cases must be with caution. Using product including crataegus has been reported with side effects of nausea, fatigue, sweating, and skin rashes. Therefore, the patients must be trained efficiently before accidence of them. High consumption of these products may make toxicity, bradycardia, and respiratory depression.

Rucardin:rucardin (red hawthorn) is used in congestive heart failure, coronary artery disease elimination, and thrombolytic therapy,dysrhythmia, and thrombolytic therapy. This product is used in cardiovascular and hypertension disease treatments by the dilation of blood vessels (especially in the coronary arteries). The existed flavonoids and procyanidine in this product increase calcium storage in heart cells by controlling CAMP phosphodiesterase enzyme, increases cAMP concentration in heart muscle. These effects increase cardiac contractility and are useful in congestive heart failure. This drug separates the phospholipids of the epithelial cells of the vascular walls and prevents their blockage by forming complexes between phospholipids anthocyanoside in these products and some deposits in artery walls. X glycosides and catechins of these products accelerate blood flow to the coronary arteries of the heart and improve general condition of patients with arrhythmias. Red hawthorn intensified heart glycosides surgery such as digoxin. Reduce digoxin dose as much as possible while simultaneous prescription of extract of digoxin and rucardin. Its maximum effect is dilution blood and the treatment of hypertension. Moreover, it prevents from forming fat layers in vessel walls leading to hypertension.

Training to Patient: Since the effect of rucardin on heart is similar to digoxin, simultaneous consumption of them can increase hypertension on heart muscles and dysrhythmia. Rucardin has similar performance to anti-dysrhythmia class III. Therefore, simultaneous consumption must be avoided. Since rucardin may increase bleeding danger if it is used simultaneously withanticoagulants, taking these two drugs in the study of signs and symptoms of bleeding must be with caution. Train the patient not to use rucardin in treatment of cardiac symptoms such as edema and angina, because delaying raking this drug may be dangerous. Moreover, patients must be trained to aware any symptoms such as dizziness, drowsiness, irregular heartbeat to doctor. Patient must report any dyspnea and chest pain.

Cratagus: using extraction of this plant goes back to the ancient time and was used in

Arab traditional medicine to treat cardiovascular disease, cancer, diabetes, and impotency. Its useful effects are for having antioxidant properties. Cratagus is available in 30 ml drop. Cratagus is used as reducer of blood pressure and coronary vasodilator in the treatment of mild heart failure (Class II) and hypertension for having cardiotonic effects. The cratagus drop is made from Crataegusmicrophylla whose each 100 ml has 02 gr has active ingredient flavonoid. Active ingredients include flavonoids, proanthocyanidins, and procyanidin. Cardiovascular effects of flavonoid compounds of this product in the crataegus, has been attributed to the procyanidins. Studies have shown that cratagus increase coronary blood flow, increase blood flow to the head, skeletal muscle and kidney blood flow in the skin and gastrointestinal tract, reduce peripheral resistance, and reduce blood pressure (via inhibition of the action of the enzyme ACE and dilation of blood vessels). Studies have shown that cratagus improve dysrhythmias (by increasing the excitability of heart muscle by blocking the potassium channels). The flavonoid and proanthocyanidins compounds of this plant have positive inotrope and negative cronotrope effects. [16]

Cratagus is herbal plant that has been popularly used for treatment failure and psychosomatic disorders. The benefits of cratagus Lavigata was examined on the biomarkers of coronary artery disease in a double-blind study. This study included 40 diabetic patients with coronary artery disease who were selected randomly for six-month treatment with 400 mg of placebo flower and leaves, three times per day. Blood cell count, lipid profile, CRP, neutrophil elastase, and malondialdehyde were measured at the beginning, one month, and six months. Results showed that neutrophil elastase reduced in treatment group in comparison to placebo group. In addition, cragatus reduces LDL cholesterol in diabetic patients who are afflicted to coronary artery disease, too. In a random double-blind study,multicenter, efficacy, and safety of crataegus extract were indicated in patients with heart failure (class II).

63 from 143 patients were examined per day by 30 drops of this herbal drop, and 74 members in placebo group for 8 weeks. The initial variable of evaluating the effectiveness of change in test was bicycle exercise tolerance. Secondary variables include hypertension and heart rate. Results showed that patients with heart failure class II did the highest exercise tolerance test level without

dyspnea and fatigue. Therefore, it can be expected that these patients are in recovery period with long-term treatment plant with standardized extract. [18]

Training to Patient: its initial consumption amount is 60-70 drops, three time day, for 3-4 days, and its containing amount is 3 time a day and each time 25 drops. It is better to use drop with a little diluted water. Patients under the cardiovascular drugs are more sensitive to effects of pharmacological crataegus. Therefore, taking this product in the mentioned patients must be with caution, raking recommended and normal dose of this drug has rare reported side effects. However, high doses can makehypotension, bradycardia, severe sedation, nausea, sweating, dizziness, and skin rashes (usually on the hands). In addition, since relative prevention from the ACE enzyme performance that finally prevents from aldosterone synthesis, long-term taking of this drug canput a person at risk of hypokalemia. Cratagus may intensify effects of cardiac glycosides (such as digoxin). Simultaneous taking of crataegus with beta-blockers (such as propranolol) may reduce hypertension. Since crataegus have antiarrhythmic effects similar to anti-arrhythmic drugs class III (potassium channel blockers, such as amiodarone), their simultaneous taking is not recommended. The strengthening cardiovascular effects of this drug are increased by simultaneous taking with vitamin B6, onions, garlic, and magnesium supplements. This drug interferes with cisapride, and simultaneous taking of this drug is not recommended. Contraindications of taking this drug are in the three first months of pregnancy, in children under 12 years old, gastrointestinal discomfort, and sensitivity to this drug.

REFERENCES

- Hani Jneid،MahboobAlam، Salim S. Virani and Biykem Bozkurt، Redefining Myocardial Infarction: What Is New In The ESC/ACCF/AHA/WHF Third Universal Definition Of Myocardial Infarction? Methodist DebakeyCardiovasc J. 2013 Jul-Sep; 9(3): 169–172.
- Hani Jneid،MahboobAlam, Salim S. Virani and Biykem Bozkurt، Redefining Myocardial Infarction: What Is New In The ESC/ACCF/AHA/WHF Third Universal Definition Of Myocardial Infarction? Methodist DebakeyCardiovasc J. 2013 Jul-Sep; 9(3): 169–172.

- R .,BagherianSaravardi, H., Saneei, A., Baghban stroke and depression; Isfahan Medical School: the third week of April 2011, Volume 29, Number 127; From page 102 to page 114.
- M., Saeedi, K., Rabiei, J., Najafian. Compare the efficiency of cardiac rehabilitation in heart patients after angioplasty, bypass surgery and coronary heart disease. ArmaghanDanesh. 2004; 9 (4): 41-49.
- F., Rahimiha, A., Baheshti, M., Gholami, Health behaviors and 6-4 months post-MI patients. Iran Journal of Nursing. 2000; 13 (24): 8-15
- R. Bagherian Saravardi, B., Gilani, E. Bahrami, H., Saneei (2008) Relationship of depression after myocardial infarction and left ventricular function. Iranian Journal of Psychiatry and Clinical Psychology, p. 13.
- Kostka-rokosz, M. D., Vibbard، K. J., Dvorkin, L. & Couris, R. R. 2005. Selected herbal therapies: A review of safety. Nutrition today، 40، 17-28.
- Bahramikia, S. & Yazdanparast, R. 2009. Efficacy of different fractions of Anethumgraveolens leaves on serum lipoproteins and serum and liver oxidative status in experimentally induced hypercholesterolaemic rat models. The American journal of Chinese medicine, 37, 996-586.
- Piri، M., Shahin, M. &ORYAN, S. 2010. The effects of Anethum on plasma lipid and lipoprotein in normal and diabetic rats fed high fat diets. Journal of Shahrekord University of Medical Sciences، 11, 15-25.
- Lindquist, R., Snyder, M. & Tracy, M. F. 2013. Complementary & alternative therapies in nursing، Springer Publishing Company.
- Halberstein, R. A. 2005. Medicinal plants: historical and cross-cultural usage patterns. Annals of epidemiology، 15، 686-699.
- Rahman, K. & Lowe, G. M. 2006. Garlic and cardiovascular disease: a critical review. The Journal of nutrition، 136،736S-740S.
- Ashraf, R., Khan, R. A. & Ashraf، I. 2011. Garlic (Allium sativum) supplementation with standard antidiabetic agent provides better diabetic control in type 2 diabetes patients. Pakistan journal of pharmaceutical sciences، 24.

- Beikangge، Z. Z.،Zuo، Z. & Shatin، N. Updates on the Clinical EvidencedHerb-Warfarin Interactions.
- Halberstein، R. A. 2005. Medicinal plants: historical and cross-cultural usage patterns. Annals of epidemiology، 15، 686-699.
- Halberstein، R. A. 2005. Medicinal plants: historical and cross-cultural usage patterns. Annals of epidemiology، 15، 686-699.
- Dalli، E.،Colomer، E.،Tormos، M.،Cosin-Sales، J.،Milara، J.، Esteban، E. & Saez، G. 2011. <i>Crataeguslaevigata</i> decreases neutrophil elastase and has hypolipidemic effect: A randomized، double-blind، placebo-controlled trial. Phytomedicine.577-967 ،81.
- Degenring، F.، Suter، A.، Weber، M. & Saller، R. 2003. A randomised double blind placebo controlled clinical trial of a standardised extract of fresh Crataegus berries (Crataegisan®) in the treatment of patients with congestive heart failure NYHA II. Phytomedicine، 10، 363-369.
- Halberstein، R. A. 2005. Medicinal plants: historical and cross-cultural usage patterns. Annals of epidemiology، 15، 686-699