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Therapeutic efficacy of *crategus oxyacantha* L. For treatment of heart diseases: a cross-sectional study

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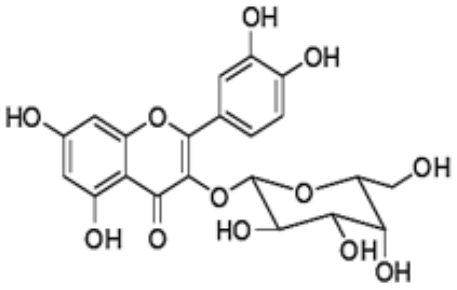
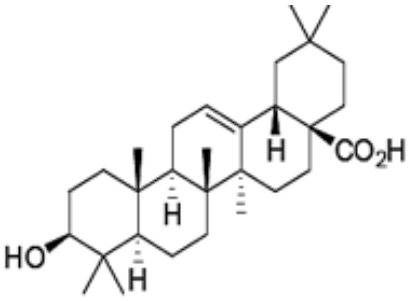
Abstract
Objectives: The purpose of the study was to explore the efficacy and drug interaction of *Crataegus oxyacantha* L. with other conventional medicines.
Methodology: Patients using *Crataegus oxyacantha* L. were interviewed to evaluate the medicine's efficacy and any interaction with other conventional medicines. Data of 500 patients was collected and explored by direct interviewing and from their medical record.
Results & Conclusion: The results of the study revealed that *Crataegus oxyacantha* L. acts as a heart tonic and is best used in the form of mother tincture. Its efficacy was found in all the cases of different heart diseases and their symptoms probably due to its flavonoids content and diversity in mechanism of action. No drug interactions were observed in the studied population due to effective history taking for proper diagnosis and avoiding any drug interactions.

Keywords: hawthorn, cardiac tonic, anti-oxidant, flavonoids

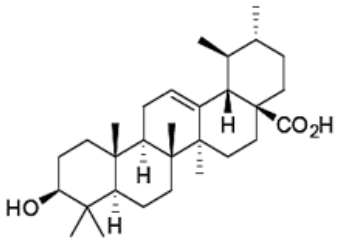
Introduction
World Health Organization (WHO) has conducted the statistical analysis of disease burden globally. According to which cardiovascular diseases ranks 1st because of high rates of morbidity and mortality associated with them. The approximate number of deaths yearly is 17.1 million according to WHO [1]. According to WHO report, 'Capitalizing on the Demographic Transition: Tackling Non – Communicable Diseases in South Asia', an estimated 17.5 million people died from CVDs in 2012, representing 31 percent of all global deaths. Of these deaths, an estimated 7.4 million were due to coronary heart disease and 6.7 million were due to stroke.
Out of the 16 million deaths under the age of 70, due to non-communicable diseases, 82% are in low and middle income countries like Pakistan, of which 37% are caused by CVDs.
Most cardiovascular diseases can be prevented by addressing behavioural risk factors such as: tobacco use, unhealthy diet, obesity, physical inactivity, use of alcohol and stress.
Crataegus oxyacantha Linn belongs to family Rosaceae and is commonly known as Hawthorn. It is an official plant in Homoeopathic System of medicine to treat various conditions of cardiovascular system due to the presence of flavonoids, oligomeric procyanidins, cardiotonic amines, tripterpenes and purine derivatives as the major constituents [2-3]. It is native to Asia, Europe and North America [4].



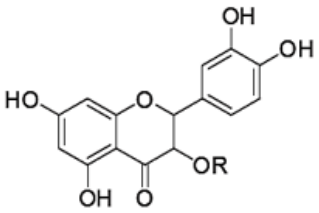
Hyperoside



Oleanolic acid



Flavonoglycosyls, vitexin-4′-rhamnoside, epicatechol, tyramine, isobutylamine, O-methoxyphenylethylamine, ursolic acid



20 R=H
21 R=Rham-Glu

Rutin and Quercetin

Fig 1: Chemical Constituents of *Crataegus oxyacantha*

Crataegus oxyacantha is an official drug in United States Pharmacopoeia, National Formulary, British Pharmacopoeia, European Pharmacopoeia and Homoeopathic Pharmacopoeia of India, Homoeopathic material medica and German Commission E due to its safety and efficacy as a heart remedy [3, 5].

Researches were conducted by various researchers to determine the mechanism of action of cardio-active activity of *Crataegus oxyacantha*. The studies done revealed that cardiotonic effect of *C. oxyacatha* is obtained through multiple mechanisms of action. According to Jayalakshmi & Devaraj (2004) and Jayalakshmi *et al.* (2006), the alcoholic extract of *C. oxyacantha* maintains mitochondrial anti-oxidant level and prevents mitochondrial lipid peroxidative damage as well as decrease in Kreb cycle enzymes by inhibiting phosphodiesterase, angiotensin converting enzyme (ACE) and Na^+/K^+ ATPase. The above mentioned mechanism of actions promotes dilation of peripheral blood vessels, increases in metabolism of the heart muscle and dilation of coronary vessels [6-7]. This improves blood supply to the heart and aids in treating heart disease and mitigating symptoms in early stage of heart failure [8-10].

Crataegus oxycantha (hawthorn), probable mechanism of action includes: to induce cAMP-independent positive inotropy by increasing intracellular Ca2+ concentration; cause peripheral and coronary vasodilation by increasing the supply of energy and oxygen to the myocardium; provide protection against ischemia-induced ventricular arrhythmias by lengthening the refractory period, possess anti-oxidative properties and exhibit anti-inflammatory effects. Crataegus may directly inhibit sodium-potassium ATPase and indirectly influence intracellular processes by interacting with cardiac β-1 receptors [11-13].

According to Chang *et al.* (2005), *C. oxyacantha* is a slow-acting herb and should be used for at least 4 to 8 weeks for full benefit. The dosage depends on the type of preparation (standardized extract, tincture) and source material (berry, leaf and flower) [14].

C. oxyacantha mother tincture acts on heart muscles, having no impact on endocardium and therefore known as a heart tonic. The cardinal symptoms for its prescription include; irregularity of heart beat, high arterial tension, as a sedative in cases of cross and irritable patients with cardiac symptoms. It may be used in chronic heart disease, with extreme weakness, very feeble and irregular heart action, pain sensation of pressure in the left side of chest below the clavicle and arteriosclerosis [15].

Crataegus oxyacantha is a non-toxic herb if taken in proper dose. *C. oxyacantha* has probable drug interaction with drugs having cardio-active effects. For instance it has synergistic effect with digitalis; therefore dose needs to be adjusted if giving concomitantly with digitalis [16]. It can have drug interactions with medications for male sexual dysfunction that increase blood flow to the heart, for high blood pressure [17].

Methodology

Patients visiting Dr Mahboob Alam Homoeopathic clinics were interviewed and their medical records were checked and recorded on their consent. All the patients who participated in the study filled the informed consent form before conduction of their interview and reviewing of their medical records. Data of 500 patients was explored and interpreted using Microsoft Excel.

Results

The study revealed that *C. oxyacantha* improved the condition of cardiovascular patients due to its lipid-lowering, vasodilating, positive inotropic and anti-arrhythmic effects. It exhibited efficacy without any side effects. The results observed in studied population are shown in figure 2.

The results of the study revealed that *C. oxyacantha* L. acts as an effective heart tonic and is best used in the form of mother tincture. Its efficacy was found in all the cases of different heart diseases and their symptoms probably due to its flavonoids content and diversity in mechanism of action. No drug interactions were observed in the studied population due to effective history taking for proper diagnosis and avoiding any drug interactions.

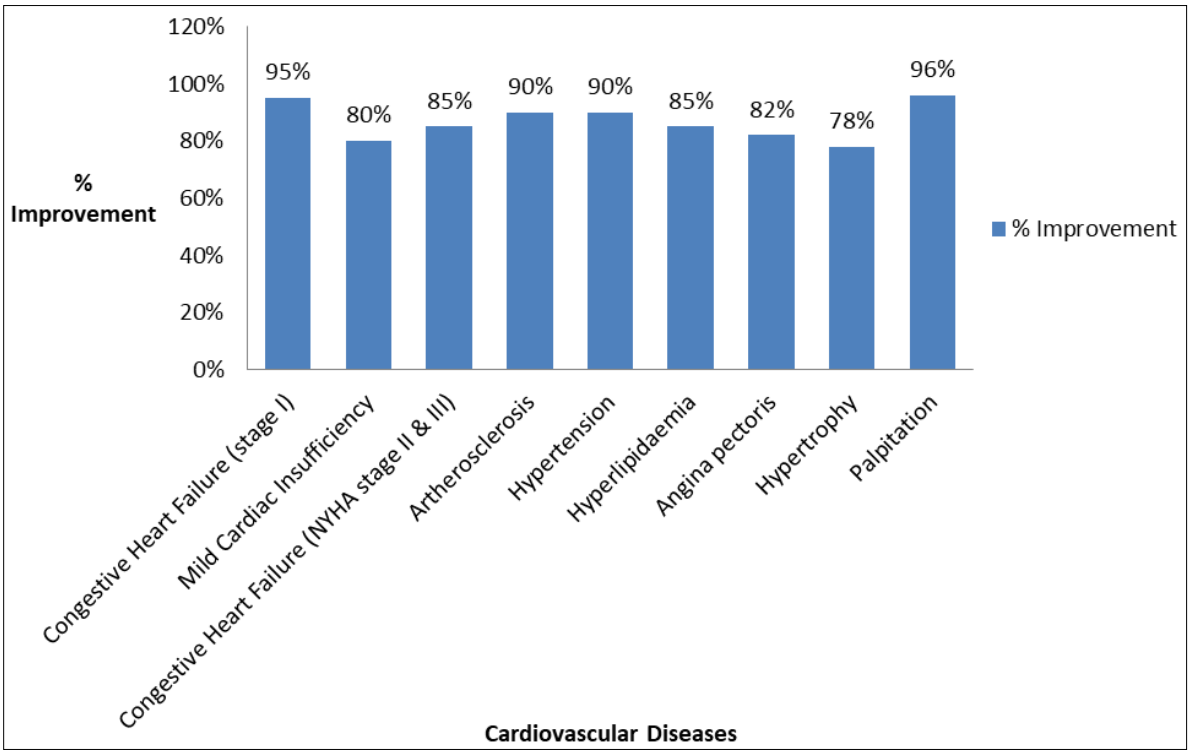


Fig 2: Effectiveness of *Crataegus oxyacantha* observed in population under study (n = 500).

Discussion

Results of our current research endeavor confirm the safety and effectiveness of *C. oxyacantha* mother tincture. The overall cardiovascular symptoms encountered by patients were observed to be better controlled according to the patients' feedback. The overall improvement in derranged lab report values was also observed that supported the feedback got from the patients themselves. Our clinical survey validates the work done by various researchers (pre-clinical and clinical trials) in confirming the therapeutic efficacy of *C. oxyacantha*.

Daniele *et al.* (2006) has reported in his review article that flavonoids are to be credited for the therapeutic efficacy of *C. oxyacantha* in facilitating the alleviation and cure of heart failure patients. Crataegus is found to improve following functions of the heart: left ventricular function, improves exercise capacity and tolerance, reduces blood lipid levels, improves circulation of blood and relieves hypertension [18].

One way of organizing the healing properties of hawthorn has been supplied by a noted European expert in hawthorn research, R.F. Weiss, who maintains that hawthorn products are characterized by three basic healing properties that complement one another: Improvement of coronary blood supply; which leads to reducing of anginal attacks and general declining of subjective complaints; Improvement of metabolic processes in the myocardium, which results in an improvement of the functional heart activity; abolishment of some types of rhythm disturbances [19].

In pre-clinical (*in vivo* and *in vitro*) studies carried out by various researchers, *C. oxyacantha* extract was found exhibit anti-oxidant, anti-inflammatory, positive inotropic effect, anti-inflammatory effect, anti-platelet aggregation effect, vasodilating effect, endothelial protective effect, reduction of smooth muscle cell migration and proliferation, protective effect against ischemia/reperfusion injury, anti-arrhythmic effect, lipid-lowering effect and decrease of arterial blood pressure effect. Apart from that in placebo-controlled clinical trials *C. oxyacantha* was observed to improve the condition of patients that suffered from cardiac disease (NYHA-I-II), hypertension and hyperlipidaemia [20-34]. All these effects ultimately contribute to cardiac tonic effect of *C. oxyacantha*. In meta-analysis study carried out by Pittler *et al.* (2003), Crataegus was found to exhibit several efficacious cardiovascular effects as compared to placebo [35].

In accordance with the research work done on animals and human clinical trials; *C. oxyacantha* may be prescribed for the treatment of following cardiovascular conditions: Hypertension, angina, arrhythmias, congestive heart failure (NYHA class I & II), peripheral vascular disorders, anti-oxidant and lipid regulating agent [36-41].

Further clinical trials needs to be carried out to further validate the *C. oxycantha* doses, time duration and combination of other cardio effective drug along with it in order to better alleviate different cardiovascular symptoms and curing cardiovascular diseases.

Conclusion

Our study validates the safe and effective use of *C. oxycantha* mother tincture according to doctor's prescription. The excellent safety profile of this remedy, coupled with the lack of herb–drug interactions detected to date in clinical trials would further support its inclusion in treatment strategies surrounding CVD, especially in the early stages of disease progression.

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