Journal of
Health & Medical Informatics

Saeed et al., J Health Med Informat 2015, 6:6
DOI: 10.4172/2157-7420.1000212

Research Article Open Access

The Heart and Herbs: Back to the Nature

Aamer Saeed*, Fayaz Ali Larik, Pervaiz Ali Channar and Urooj Muqadar

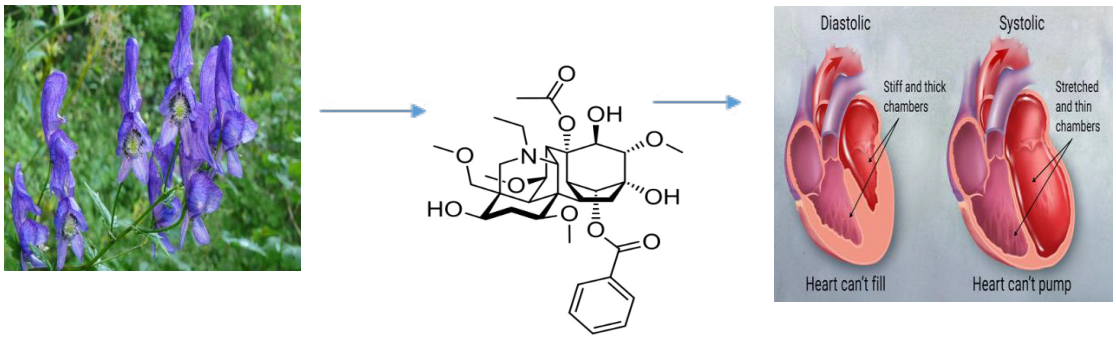
Department of Organic Chemistry,Quaid-i-Azam University, Islamabad-45320, Pakistan

Abstract

It is believed that herbal medicines act in a holistic way, but been derived from nature they can be specific in response. Herein, we review herbal medicines which are used for the treatment of cardiovascular diseases (CVDs) and their interactions with other drugs. CVDs have a high mortality rate and morbidity in the world, therefore, prevention and reduction of risk factors, which are associated with CVD, are the major tasks of healthcare professionals and scientists. Modern medicines despite having promising effects are unable to bring to a standstill the CVDs, consequently people are are paying attention to CAM (complementary and alternative medicines) -the herbal medicines.

GAraphical Abstract

Herbal medicines, play an important role in the treatment of heart failure. An illuminating example is Aconite (*Aconitum variegatum* also known as blue rocket or devil's helmet), one of the Chinese medicine, useful for treatment of heart failure. The cardiac function was observed prior to and following the treatment, and no significant side effects were noticed



"The picture is worth of a million words."

Keywords: CVDs; Herbal medicine; Molecular; Drug interaction

Introduction

Herbal medicines can be defined as, plant structures capable of showing phytomedicinal or phytopharmaceutical effects. The peoples are looking outside the decorated glass of conventional medicines to improve their health care needs. In the light of critics and proponents the treatment of cardiovascular diseases with herbal medicines is a charged subject. However, medical practitioners can no longer turn a deaf ear to herbal medicines. The World Health Organization (WHO) estimated that approximately 17.1 million people died from CVDs and its complications in 2004, and the number of deaths will dramatically increase to almost 23.6 million by 2030 (WHO, 2010). Herbal medicine is a heritage that is thousands of years old and is still used by millions of people all over the world—even after the development of modern scientific medicine, however several fundamental questions are still unanswered. What are the mechanisms of action of the herbs? What are the precise targets of these herbs? What are the relationships between these herbals and diseases? How to explain one of the basic theories of TCM, i.e., "multiple herbal drugs can treat one disease"? Herbal medicine has been widely used in China as well as other Asian countries for the treatment of cardiovascular diseases for hundreds of years. Cardiovascular disease (CVD) is the major cause of mortality and morbidity in the Western world. Therefore, prevention and reduction of risk factors, which are associated with CVD, are the major tasks of health care professionals and scientists. According to the Centers for Disease Control and Prevention (CDC) and the American Heart Association, heart disease is the leading cause of death in the United States with a mortality rate of more than a quarter of total deaths in 2004. Angina (pain from decreased blood flow to the heart), coronary syndrome, heart failure, pulmonary embolism, arrhythmias, aortic valve disorders, or bacterial endocarditis are some of the cardiovascular diseases that account for the most deaths worldwide, with heart disease responsible for 7.2 million deaths in 2004.

Through the ages, humans have relied on nature for their basic needs for the production of foodstuffs, shelter, clothing, means of transportation, fertilizers, flavors and fragrances, and, not least, medicines. Apart from their cultural significance, herbal medicines are generally more accessible and affordable. There is evidence concerning the participation of reactive oxygen species (ROS) in the etiology and physiopathology of human diseases. Cardiovascular disease (CVD) is one of the top menaces of human lives and a global burning issue and CVD, encompasses a spectrum of diseases, including, Coronary

***Corresponding author:** Aamer Saeed, Department of Organic Chemistry, Quaid-i-Azam University, Islamabad 45320, Pakistan, Tel: +92-51-9064-2128; E-mail: aamersaeed@yahoo.com

Received November 02, 2015; **Accepted** December 26, 2015; **Published** December 31, 2015

Citation: Saeed A, Larik FA, Channar PA, Muqadar U (2015) The Heart and Herbs: Back To The Nature. J Health Med Informat 6: 212. doi:10.4172/2157-7420.1000212

Herbal drug	Clinical use	Pharmacological effects
Garlic	Hypertension	↓ SBP, ↓DBP
Danshen	Moderate gestational	↓ HCT, ↓ BV, ↓ PV
	hypertension	
Red yeast rice	Hyperlipidemia	↓ Total cholesterol, ↓LDL
	Coronary heart disease	↓ coronary events ↓ Death from coronary heart disease.
Hawthorn	Primary mild hypertension	↓SBP, ↓DBP
	Coronary heart disease	↓ cardiac mortality
Ginkgo biloba	Cerebral insufficiency	Improvement off memory
Panax notoginsengg	Spontaneous Intracerebral hemorrhage	↓NIHSS score ↓ Hematoma volume ↓Inflammatory responses ↑Hematoma absorption
	Ischemic stroke	↑ score of ESS ↑Score of BI
Berberine	Acute coronary syndrome	Ameliorates inflammation following percutaneous coronary intervention
	Chronic congestive heart failure	↑ LVEF, exercise capacity and Dyspnea-Fatigue Index, ↓ Frequency of VPCs
Tetamethylpyrazine	Acute coronary syndrome	Preventing coronary thrombosis after PCI
	Myocardial infarction	↓ Attack of angina pectoris, ↓ LPO, ↑ SOD

Table 1: Herbal medicine their clinical use and pharmacological effects.

artery disease,peripheral vascular disease,congestive heart failure, dyslipidemias, ,hypertension [1]. Despite being promising effects, peoples are turning faces away from modern medicines mainly due to unsatisfying treatment results, redundant side effects, Economic issues.During the last two to three decades, developed countries, such as the United States, Canada, Australia, and members of the European Union, judiciously promoted the use of herbal medicine in the form of complementary and alternative medicine. However, efficacy or safety of the majority of herbal medicines in CVDs has not been fully established through an evidence-based approach. Further, other issues, such as scientific, cultural, educational, economical, and legal, need to be addressed. Safety is a major concern for the use of herbs in humans. It is generally believed that herbal medicines approach a patient in a holistic way. Nevertheless, to make it easier to understand and to study these herbs, in this review, we chose to introduce these herbs one by one individually and even introduce the main components in molecular level. Following Table 1 depicts the role of herbal medicines in the treatment of CVDs [2].

The theme of this MS is uncler.The materials including the effect of 34 kinds Japanese herbal medicines, anoxidant effect of resvertrol, effect of strawberry, etc, are loosely put together

Effectively put together. Effect of strawberry has been replaced by another exciting topic, that is troika of herbal medicines. Antioxidant effects of resveratrol are reorganized. Also effect of 34 kinds Japanese herbal medicines has been improved.

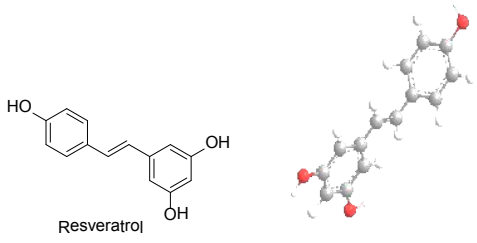
Effect of 34 kinds of japanese herbal medicines on sustainability of cardiac allograft survival

Herbal medicines have been used for over 3,000 years in Asia as alternative therapy for their varying effects and recently have become popular in Europe and the United States. In this study, X Jin et al investigated the effect of 34 kinds of traditional Japanese herbal medicines (prior to this gynecological effect also treated with herbal medicines [3], on alloimmune responses in a murine model of cardiac allograft transplantation [4-6]. In this study, the effect of 34 kinds of traditional Japanese herbal medicines of alloimmune responses in a murine model of cardiac allograft transplantation was examined at molecular level. Table 1 shows the major components found in all 34 Japanese herbal medicine.

Antioxidant effects of resveratrol in cardiovascular diseases.

Resveratrol—a natural polyphenolic compound—was first discovered in the 1940s. It has shown beneficial effects against most cardiovascular diseases. A large part of these effects are related to its antioxidant properties [7].

Structure of resveratrol:



Resveratrol

Effects of resveratrol on antioxidant mechanisms protecting against oxidative cardiovascular pathophysiology: It has been recently demonstrated that resveratrol reduces endothelial dysfunction in vessel from dyslipidemic patients with hypertension; this antioxidant action of resveratrol was mediated by up regulation of manganese superoxide dismutase (Mn-SOD) via a mechanism dependent upon nuclear factor (erythroid-derived 2)-like 2 (NRF2). This finding in humans was in agreement with experimental models showing that resveratrol was able to increase Mn-SOD expression in the mouse myoblast line C2C12 via nuclear translocation and activation of sirtuin 1 (SIRT1), a NAD+-dependent class III histone deacetylase. It also hampers platelet aggregation and activation of phytoalexin seems to inhibit the interaction of platelets with collagen and thrombin in vitro in isolated platelets and in animal models. Reduction in the rate of cytochrome C oxidation by hydroxyl radicals Jiian et al. reported that resveratrol significantly reduced cytochrome C protein levels in the heart tissue of

rats subjected to trauma-hemorrhage.Mechanism of action is shown in Figure 1.

Use of herbal medicines, evidence dominates over belief in case of treatment of cardiovascular diseases.

Modern medicines used for the treatment of various cardiovascular diseases provide symptomatic relief or slow down the progress of disease. In the treatment of heart failure, adverse effects of medicines may be observed in the form of rise in frustration in patient, scientists have gone to apply extreme alternatives like gene therapy and stem cell therapy. Under such sensitive circumstances, understanding the high risk of morbidities and mortality of CVD hybrid with the limitations of modern medicines, there is an dire need to explore (Table 2) herbs for the prevention and possible, "cure" of CVDs.

Table 3 List of medicinal plants and their application against cardiovascular diseases in humans [8].

A troika of herbal medicines (*Crataegus monogyna, Ginkgo biloba,* and *Aesculus hippocastanum*) on the treatment of cardiovascular diseases

The cardiovascular diseases that account for the most deaths worldwide, with heart disease responsible for 7.2 million deaths in 2004 [9] many of the components and complications of cardiovascular diseases including the damage caused by oxidants in the aftermath of ischemic heart failure. McCune investigated the role of these herbal medicines in cardiovascular. Flavonoids and other antioxidants have the ability to regulate the metabolism of cholesterol, triglyceride and induction of inflammatory cytokinese, which inhibit the build up of foam cells, platelets and fatty acids deposits in arteries.

The German Commission E Monographs, the standard reference for prescription herbal products in some of the countries of Europe, lists the following plants for treatment of cardiovascular indications: *Ginkgo biloba* leaf extract (*Ginkgo biloba* L.), onion (*Allium cepa* L.), motherwork herb (*Leonuri cardiacae* L.), hawthorn leaf with flower (*Crataegus monogyna* Jaquin emend. Lindmand or *C. laevigata* (Poiret) de Candolle), lily of the valley herb (*Convallariae majalis* L.), pheasants eye herb (*Adonidis vernalis* L.), squill (*Urginea maritime* (L.) Baker), butcher's bloom (*Ruscus aculeatus* L.), camphor (*Cinnamomum camphora* (L.) Siebold), lavender flower (Lavandulae *angustifolia*

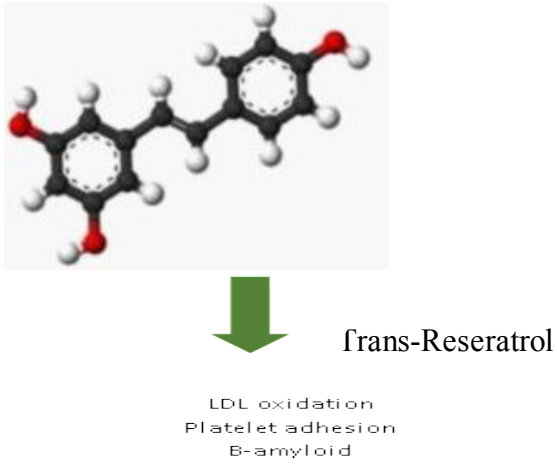


Figure 1: Resveratrol reduces cardiovascular diseases.

Miller), rosemary leaf (*Rosmarinus officinalis* L.), scotch broom herb (*Cytisus scoparius* (L.) Link), garlic (Allium sativum L.), soy lecithin and phospholipid (Glycine max (L.) Merrill), Indian snakeroot (*Rauwolfia serpentine* (L.) Bentham ex Kurz), arnica flower (*Arnica Montana* L. or *A. chamissonis* Less. subsp. foliosa (Nutt.) Maguiere), sweet clover (*Melilotus officinalis* (L.) Pallas and/or M. *altissimus Thuillier*), and horse chestnut seed (*Aesculus hippocastanum* L).

Hawthorn

Hawthorn (*Crataegus monogyna* or *laevigata* frequently referred to as *C. oxyacantha*) has other common names such as may bush and white thorn and is found in Europe, North America, and Asia as a deciduous tree in the Rosaceae family [10]. Hawthorn contains polycyclic flavonoids including epicatechin, chlorogenic acid, rutin, isoquercitin, and hyperoside [11] .Vitexin-4-O-glucoside and vitexin-2-O-rhamnoside have been described as the major flavonoids present in hawthorn leaves that are readily absorbed when the products are fed to rats [12]. Hawthorn shows antiarrhythmic properties. Many flavonoids found in it have shown increased coronary blood flow. Problems of heart contraction and blood flow can be successfully solved by using hawthorn.

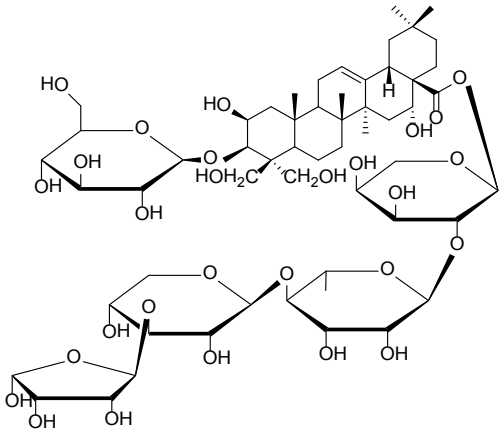
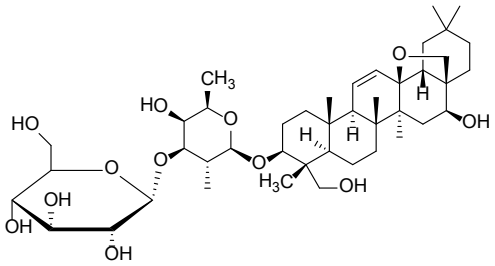
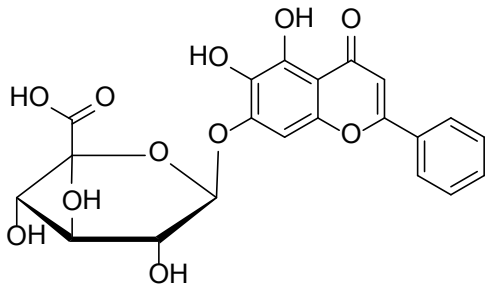
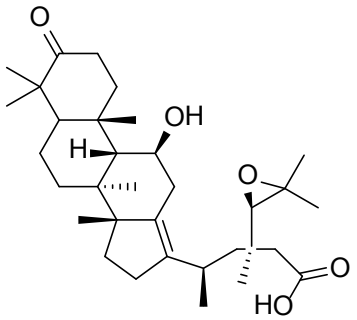
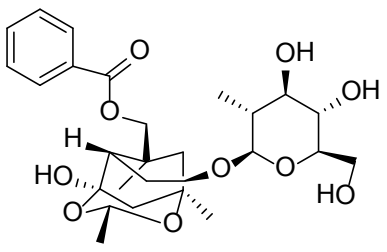
Horse chestnut seed

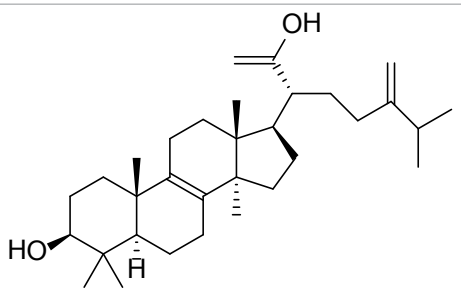
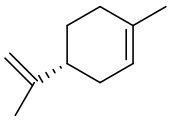
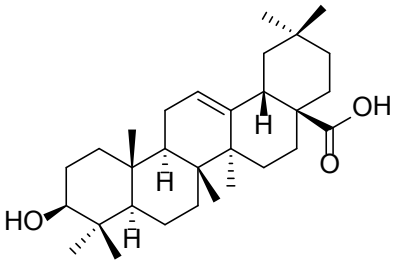
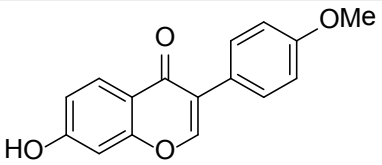
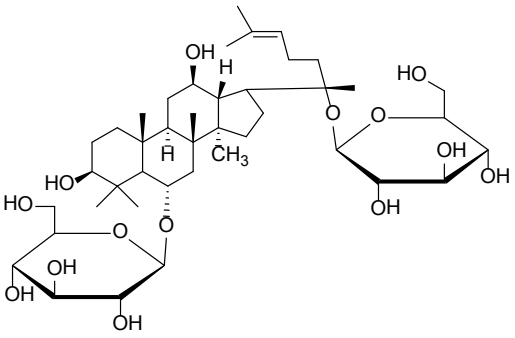
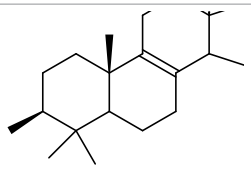
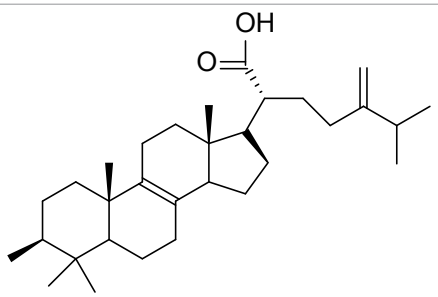
Horse chestnut seed (*Aesculus hippocastanum* L.), of the family Hippocastanceae, is a medicinal tree species cultivated widely for ornamental and shade purposes.Horse chestnut is one of the top 20 herbal supplements sold in the United States with sales of $558946 in 2009 in the mass market alone [13]. Extracts of horse chestnut are commonly standardized to about 20% of triterpene saponin glycosides (the natural mix of these is commonly referred to as aescin). Aescin is found in A. hippocastanum seeds at the rate of 9.5% dry matter as well as the flavonoids quercetin, kaempherol, epicatechin, and anthocyanins; and the fatty acids lauric acid, palmitic acid, myristic acid, stearic acid, arachidic acid, and oleic acid. Dosages in these trials ranged from 100 to 150 mg aescin daily.Experiments in animal and cell culture systems have demonstrated the effectiveness of horse chestnut in decreasing inflammation and platelet aggregation, increasing venous contractions and protecting venous endothelium relaxation.In ADP-induced human platelet aggregation studies, it was determined that horse chestnut extract reduced platelet aggregation. Endothelial dysfunction is a precursor to hypertension, atherosclerotic disease, hypercholesterolemia,and chronic venous insufficiency (CVI). There are many studies on the effects of horse chestnut extracts on the traits and symptoms of CVI (these can includevaricose veins, venous ulcers, leg-tiredness, swelling, and the hardening of the skin caused by lipidermatosclerosis) [14,15]

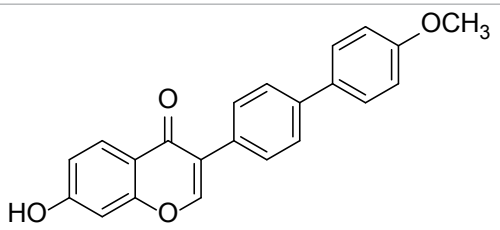
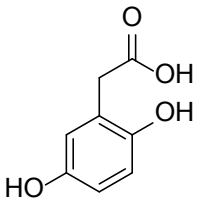
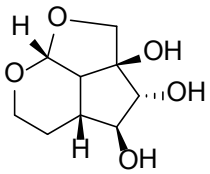
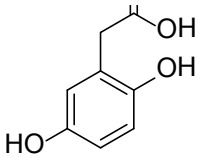
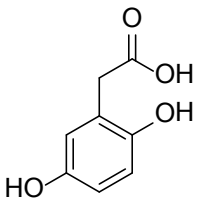
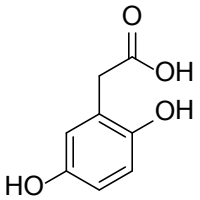
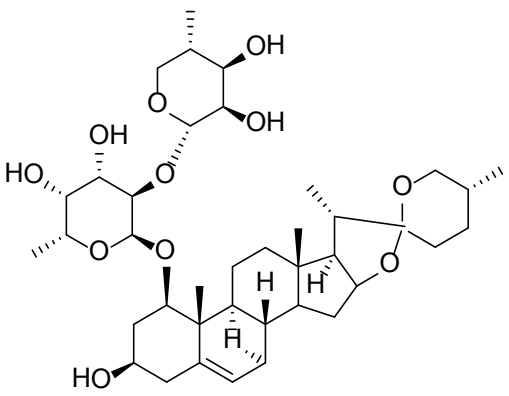
Ginkgo

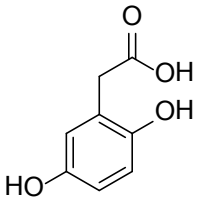
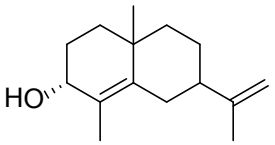
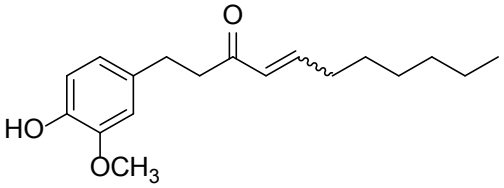
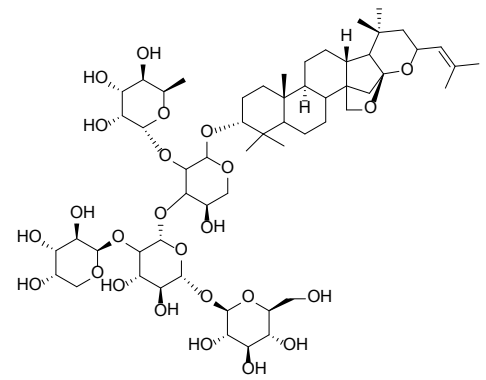
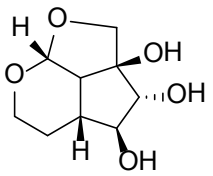
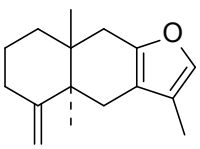
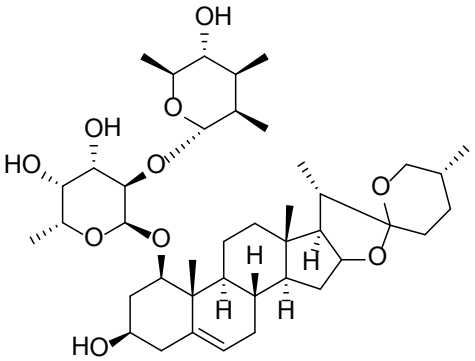
Ginkgo (*Ginkgo biloba* L.) is an ancient tree species that has been used as a heart medicine in Chinese phytomedicine since at least 1509 .The German Commission E Monographs listed the leaf extract as an approved herb due to established results in experimental research. In the United States, it is one of the top-selling herbal supplements with over 16 million US$ in sales in the mass market in 2009 and $4 276 489 in the US natural and heath food retailers alone. Ginkgo leaves have diterpene terpenoids (chiefly the ginkgolides and bilobalide) and flavonoids (including quercetin, kaempferol, and isorhamnetin). Suggested dosages are between 120 and 240 mg daily in multiple increments.

Its free radical scavenging action has been responsible for protecting

Name of Japanese Herbal Medicine	Main Component	Major Element	Molecular Formula	Chemical Structure
Jumihaidoku-to (TJ-6)	*Platycodon root*	Platycodin D	$C_{57}H_{92}O_{28}$	
Saikokaryukotsuborei-to (TJ-12)	*Bupleuri radix*	Saikosaponin A	$C_{42}H_{68}O_{13}$	
Orengedoku-to (TJ-15)	*Ogon*	Baicalin	$C_{21}H_{18}O_{11}$	
Gorei-san (TJ-17)	*Alismatis rhizoma*	Alisol B 23-acetate	$C_{28}H_{44}O_4$	
Tokishakuyaku-san (TJ-23)	*Paeoniae radix*	Paeoniflorin	$C_{23}H_{28}O_{11}$	

Shinbu-to (TJ-30)	*Poria sclerotium*	Eburicoic acid	$C_{31}H_{50}O_3$	
Hangebyakujutsutenma-to (TJ-37)	*Citrus unshiu peel*	(R)-(+)-Limonene	$C_{10}H_{16}$	
Tokishigyakukagoshuyushokyo-to (TJ-38)	*Zizyphi fructus*	Oleanolic acid	$C_{30}H_{48}O_3$	
Hochuekki-to (TJ-41)	*Astragalus root*	Formononetin	$C_{16}H_{12}O_4$	
Rikkunshi-to (TJ-43)	*Ginseng radix*	Ginsenoside Rx	$C_{42}H_{72}O_{14}$	
Yokukan-san (TJ-54)	*Atractylodis lanceae rhizoma*	Hinesol	$C_{15}H_{26}O$	
Gorin-san (TJ-56)	*Poria sclerotium*	Eburicoic acid	$C_3H_{50}O_3$	

Kihi-to (TJ-65)	*Astragalus root*	Formononetin	$C_{16}H_{12}O_4$	
Jinsoin (66)	*Pinellia tuber*	Homogentisic acid	$C_8H_8O_4$	
Simotsu-to (TJ-71)	*Rehmannia root*	Rehmaglutin A	$C_9H_{14}O_5$	
Sikunsi-to (TJ-75)	*Atractylodis lanceae rhizoma*	Hinesol	$C_{15}H_{26}O$	
Yokukansankachinpihange (TJ-83)	*Pinellia tuber*	Homogentisic acid	$C_8H_8O_4$	
Nijutsu-to (TJ-88)	*Pinellia tuber*	Homogentisic acid	$C_8H_8O_4$	
Seihai-to (TJ-90)	*Ophiopogonis tuber*	Ophiopogonin B	$C_{39}H_{62}O_{12}$	

Chikujountan-to (TJ-91)	*Pinellia tuber*	Homogentisic acid	$C_8H_8O_4$	
Jiinsiho-to (TJ-92)	*Cyperi rhizoma*	Cyperol	$C_{15}H_{24}O$	
Daikenchuto (TJ-100)	*Processed ginger*	[6]-Shogaol	$C_{17}H_{24}O_3$	
Sansonin-to (TJ-103)	*Jujube seed*	Jujuboside A	$C_{58}H_{94}O_{26}$	
Gosyajinkigan (TJ-107)	*Rehmannia root*	Rehmaglutin A	$C_9H_{14}O_5$	
Ninjinyoei-to (TJ-108)	*Atractylodis rhizoma*	Atractylon	$C_{15}H_{20}O$	
Seisinrensiin (TJ-111)	*Ophiopogonis tuber*	Ophiopogonin B	$C_{39}H_{62}O_{12}$	

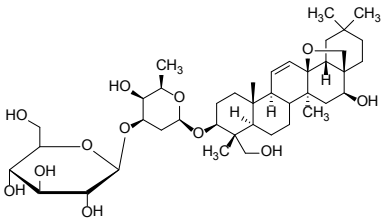
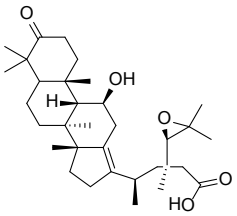
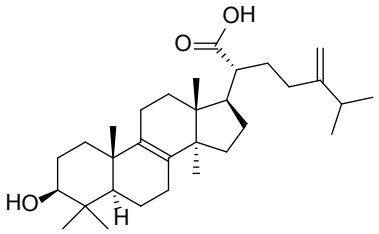
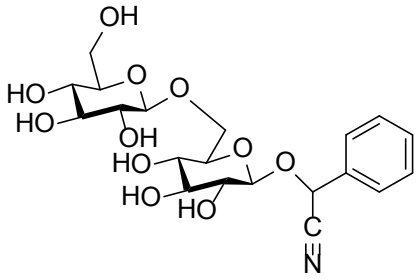
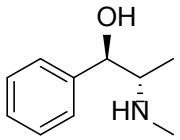
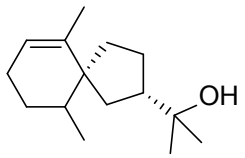
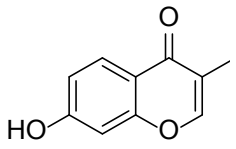
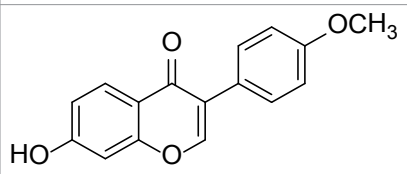
Sairei-to (TJ-114)	*Bupleuri radix*	Saikosaponin A	$C_{24}H_{68}O_{13}$	
Inchingorei-san (TJ-117)	*Alismatis rhizoma*	Alisol B 23-acetate	$C_{28}H_{44}O_4$	
Ryokyojutsukan-to (TJ-118)	*Poria sclerotium*	Eburicoic acid	$C_{31}H_5O_3$	
Ryokankyomishingenin-to (TJ-119)	*Apricot kernel*	Amygdalin	$C_{20}H_{27}NO_{11}$	
Maobushisaishin-to (TJ-127)	*Ephedra herb*	(-)-Ephedrine	$C_{10}H_{15}NO$	
Keihi-to (TJ-128)	*Atractylodis lanceae rhizoma*	Hinesol	$C_{15}H_{26}O$	
Inchinko-to (TJ-135)	*Artemisiae Capillaris herba*	6,7-Dimethylesculetin	$C_{11}H_{10}O_4$	
Kamikihi-to (TJ-137)	*Formononetin*	Formononetin	$C_{16}H_{12}O_4$	

Table 2: Herbal medicines with molecular information.

nitric oxide and prostaglandin I2 activity, thereby ensuring continued blood flow via smooth muscle relaxation .clinical trials have reported antioxidant activity, improved blood flow, and anti-inflammatory properties against cardiovascular disease development.

Cardiovascular herbal medicines: The risk of drug interaction

Herbal medicines are widely used for the treatment of cardiovascular diseases, so it is important to support credible research on the use of herbal medicines by focusing and explaining herb-drug interactions to provide a reliable alternative path to cardiovascular patients [16]. Recent data have revealed that all herbal medicines contain many active ingredients including those used in the therapy of cardiovascular diseases [17-21], Like all the other things of the world (excess of everything is very bad) herbal medicines (HB) are not always right, so medical professionals must care and know that HBs are not completely risk free [22].

Table 3 clinical interaction between herbal medicines and conventional cardiovascular drugs [23].

PC-PCS is a mixture of eight herbal drugs, namely, *Dendrathema morofolium* (Chrysanthemum), *Isatis indigotica* (Dyer's woad), and *Glycyrrhiza glabra* (liquorice), Ganoderma lucidum (reishi), *Panax pseudoginseng* (san-qui ginseng), *Rabdosia rubescens* (rubescens), *Serenoa repens* (saw palmetto) and *Scutellaria bacicalensis* (Baikal skullcap).

Conclusion

Herbal medicine, almost by definition, is the application of a group of compounds rather than single pure entities. These compounds can have synergistic or antagonistic properties that affect how the compounds interact and the potential to affect multiple aspects of a disease. Plant products, whether food, herb, or spice, can contribute antioxidants to ameliorate symptoms of cardiovascular diseases.

Name of herbal product	Country of study	Disease indication	Efficacy
Terminalia arjuna	India	Post myocardial infarction Ischemic cardiomyopathy	↓ Symptoms of angina, left ventricular ejection fraction, and left ventricular mass Terminalia group, severity of cardiomyopathy also improved from NYHA class III to class I in two patients during the study
Terminalia arjuna	India	Congestive heart failure with severe refractory heart failure (NYHA class IV)	Improvement of edema, fatigue and dyspnea along with walking toleranc, stroke volume, left ventricular ejection fractio, with decrease in end-diastolic and end-systolic left ventricular volume
Terminalia arjuna	India	Patients with coronary artery disease (CAD)	↓ Total cholesterol, ↓ LDL cholesterol, ↓ lipid peroxide levels after 30-day follow up.
Allium sativam	Australia	Progression of carotidatherosclerosis	Anti-atherosclerotic effect on carotid atherosclerosis
Allium sativum	India	Hyperttension, Oxidative stress	↓ 8-hydroxy-2-deoxyguanosine, ↓ nitric oxide level, ↓ lipid peroxidation, ↑ Vitamins C, ↑ vitamin E
Allium sativum	India	Effect of garlic powder (Kwai) on plasma lipids and lipoproteins in mild hypercholesterolemia	No change in blood lipids and lipoproteins levels
Apium graveolens	China	Hypertension	↓ Blood pressure ↓ Blood pressure
Achllea Wilhelmsi	Iran	Antihyperlipidemic and antihypertensive effects	↓ Triglyceride after 2 months, ↓ total cholesterol and LDL-C after 4 months ↑ HDL-C levels after 6 months of treatment, ↓ diastolic and systolic blood pressure after 2 and 6 months, respectively
Fenugreek Trigonella foenum	India	Coronary artery disease (CAD) patients and patients with type 2 diabetes without CAD	↓ Total cholesterol ↓ triglycerides
Curcumin	India	Lipid level in patients with acute coronary syndrome	Moderate-dose curcumin showed the minimal effect of increase, followed by the low-dose curcumin and finally,high-dose ccurcumin that showed the highest effect of increase.
Curcumin	India	Overweight hyperlipidemia	Reduction in lipids profiles such as serum total cholesterol, triglyceride and LDL-cholesterol and VLDL-cholesterol
(Ginger) Zingiber officinale Saudi	Saudi	Lipid levels in patients with hyperlipidemia after 45 days.	↓ Triglyceride, ↓ LDL-C,↑ HDL-C
Artichoke (Cynara cardinculus var. scolymus)	India	Hyperlipoproteinemia	↓ Total cholesterol, ↓ LDL-C
Artichoke (Cynara cardunculus var. scolymus)	UK	Hypercholesterolemia	↓ Total cholesterol
Rhubarb (Rheum rhapontiam)	USA	Cholesterol-lowering effect in hypercholesterolemic men	↓ Total cholesterol (8% and) LDL-C (9%), while HDL-C concentrations remained unchanged. The depressed total and LDL-C levels returned to baseline after the fiber supplementation was withdrawn for 1 month.
Hibiscus sabdariffa L.tea	Boston	Pre-and mildly hypertensive adults	↓ Blood pressure in pre-and mildly hypertensive adults

*Combination of **Commiphora mukul and Irula racemosa** (1:1 ratio)*	India	Ischemic heart disease	↓ Total cholesterol ↓ Triglycerides,↓ Total blood lipids	
Inula racemosa	India	Ischemic heart disease	All nine subjects showed improvement in ST-segment depression on ECG.	
Crataegus	China	Cardiac insufficiency stage NYHA II heart failure	Reduced performance in the exercise tolerance test, fatigue, palpitation, and exccercise dyspnea	
C.mukul Guggul	USA	Hypercholesteromia	No improvement of cholesterol level	
***C.mukul (Guggul)* in combination with Irula racemosa**	India	Ischemic heart disease	Improved electrocardiogram readings and decreased episodes of dyspnea and chest pain	
Crataegus monogyna (Hawthorn)	USA	Heart failure	Provides no symtomatic or functional benefit when given with standard medical therapy to patients with heart failure	
Conventional drug	**Herbal medicine**	**Result of interaction**	**Possible mechanism**	**Ref**
Interaction with cardiac drugs				
Digoxin	Gum guar	↓ plasma digoxin concentration	Reduced absorption	[20]
Digoxin	St.John's	↓ plasma digoxin concentration	Induction of P-glycoprotein	[24]
Digoxin	Siberian ginseng	↑ plasma digoxin concentration	Some component of Siberian ginseng might impair digoxin elimination or interfere with the digoxin assay.	[25]
Digoxin	Wheat bran	↓ plasma digoxin concentration	Reduced absorption	[26]
Interactions with antihypertensive drugs				
Diuretic thiazide	Ginkgo	↑ in blood pressure	Not known	[27]
Antihypertensive	Liquorice	Hypokalemia	Additive effect on potassium excretion	[28]
Interactions with antiplatet drugs				
Aspirin	Ginkgo	Spontaneous hyphema	Additive inhibition of platelet aggregation	[29]
Aspirin	Tamarind	↑ bioavailability of aspirin	Not known	[30]
Interactions with anticoagulants				
Warfarin	Boldo/Fenugreek	↑ anticoagulant effect	Additive effect on coagulation mechanisms	[31]
Warfarin	Danshen	↑ Additive effect on coagulation mechanisms and/or increased	In addition to its antiplatet activity, Danshen decreases warfarin elimination in rats.	[32-34]
Warfarin	Devil's claw	↑ anticoagulant effect, purpura	Unknown	[27]
Warfarin	Garlic	↑ anticoagulant effect; increase in clotting time	Additive effect on coagulation mechanisms	[35]
Interactions with anticoagulants				
Warfarin	Ginkgo	Intracerebral hemorrhage	Additive effect on coagulation mechanism	[36]
Warfarin	Ginseng	Decreased anticoagulant effect	Unknown	[37]
Warfarin	Green tea	↓ anticoagulant effect	Pharmacological antagonism	[38]
Warfarin	Lycium	↑ anticoagulant effect	Uknown	[23]
Warfarin	Mango	↑ anticoagulant effect	Hepatic enzyme inhibition	[22]
Warfarin	Papaya	↑anticoagulant effect	Unknown	[27]
Warfarin	PC-SPES	↑ anticoagulant effect	Additive effect on coagulation mechanisms	[14]
Warfarin	Soy	↓ anticoagulant effect	Not known	[15]
Warfarin	St. John's wort	↓ anticoagulant effect	Hepatic enzyme induction	[15]
Phenprocoumon	St. John's wort	↑"Quick-Wert test (indicating decreased anticoagulant effect)	Hepatic enzyme induction	[40,41]
Phenprocoumon	Wheat bran	↓ plasma level of Phenprocoumon; increase in the free plasma Phenprocoumon fraction	↓ Absorption can explain the decreased plasma level; however, the mechanism of the increase of free plasma Phenprocoumon fraction is Unknown.	[42,43]
Interactions with antilipidaemic drugs				
Simvastatin	St.john's wort	↓ plasma simvastatin concentration	Hepatic enzyme induction	[37]
Lovastatin	Oat bran	↓ lovastatin absorption	Bran contains fibers which can trap digoxin	[38]
Lovastatin	Pectin	↓ lovastatin absorption	Pectin can trap digoxin	[39]

Table 3: Clinical interaction between herbal medicines and conventional cardiovascular drugs [23].

Hawthorn can improve exercise tolerance, pressure-heart rate product, fatigue, maximal workload, and has antiarrhythmic properties. Gingko's antioxidant and anti-inflammatory properties improve brachial artery endothelial vasomotor function (flow-mediated dilation) and coronary artery blood flow.Horse chestnut seed decreases inflammation and platelet aggregation, increases venous contractions, and protects venous endothelium relaxation in animal and cell studies, while in humans it has been shown to improve conditions of CVI. The search for plant medicines should encompass the food, herb, and spice use of cultures around the world. Human pharmacokinetic studies are needed on plants used for food, herbs, and spice

References

1. Li L, Zhou X, Li N, Sun M, Lv J, et al. (2015) Herbal drugs against cardiovascular disease: traditional medicine and modern development. Drug Discov Today 20: 1074-1086.
2. Liu Q, Li J, Hartstone RA, Wang J, Li J (2015) Chinese Herbal Compounds for the Prevention and Treatment of Atherosclerosis: Experimental Evidence and Mechanisms. Evidence-Based Complementary and Alternative Medicine.
3. Goto H, Satoh N, Hayashi Y, Hikiami H, Nagata Y, et al. (2011) A Chinese herbal medicine, tokishakuyakusan, reduces the worsening of impairments and independence after stroke: a 1-year randomized, controlled trial.
4. Jin X, Uchiyama M, Zhang Q, Hirai T, Niimi M (2012) Inchingorei-san (TJ-117) and Artemisiae Capillaris Herba Induced Prolonged Survival of Fully Mismatched Cardiac Allografts and Generated Regulatory Cells in Mice. Evid Based Complement Alternat Med 2012: 689810.
5. Uchiyama M, Jin X, Zhang Q, Hirai T, Amano A, et al. (2012) Auditory stimulation of opera music induced prolongation of murine cardiac allograft survival and maintained generation of regulatory CD4+CD25+ cells. J Cardiothorac Surg 7: 26.
6. Uchiyama M, Jin X, Zhang Q, Hirai T, Amano A, et al. (2012) Auditory stimulation of opera music induced prolongation of murine cardiac allograft survival and maintained generation of regulatory CD4+CD25+ cells. J Cardiothorac Surg 7: 26.
7. Jin X, Uchiyama M, Zhang Q, Harada T, Otsuka K, et al. (2014) In Effect of 34 Kinds of Traditional Japanese Herbal Medicines on Prolongation of Cardiac Allograft Survival, Transplantation proceedings, Elsevier: 1175-1179.
8. Carrizzo A, Forte M, Damato A, Trimarco V, Salzano F, et al. (2013) Antioxidant effects of resveratrol in cardiovascular, cerebral and metabolic diseases. Food Chem Toxicol 61: 215-226.
9. Maulik SK, Banerjee SK (2015) uses of herbals in cardiac diseases: priority of evidence over belief. Elsevier: 515-529.
10. http://www.who.int/mediacentre/factsheets/fs317/en/index.html.
11. (2010) Crataegus oxyacantha (Hawthorn). Monograph. Altern Med Rev 15: 164-167.
12. Dasgupta A, Kidd L, Poindexter BJ, Bick RJ (2010) Interference of hawthorn on serum digoxin measurements by immunoassays and pharmacodynamic interaction with digoxin. Arch Pathol Lab Med 134: 1188-1192.
13. Ma LY, Liu RH, Xu XD, Yu MQ, Zhang Q, et al. (2010) The pharmacokinetics of C-glycosyl flavones of Hawthorn leaf flavonoids in rat after single dose oral administration. Phytomedicine 17: 640-645.
14. McCune L (2012) A Review of the Antioxidant Actions of Three Herbal Medicines (*Crataegus monogyna*, *Ginkgo biloba*, and *Aesculus hippocastanum*) on the Treatment of Cardiovascular Diseases. Bioactive Food as Dietary Interventions for Cardiovascular Disease: Bioactive Foods in Chronic Disease States 243.
15. Izzo AA, Borrelli F, Capasso R (2002) Herbal medicine: the dangers of drug interaction. Trends Pharmacol Sci 23: 358-391.
16. Aggarwal A, Ades PA (2001) Interactions of herbal remedies with prescription cardiovascular medications. Coron Artery Dis 12: 581-584.
17. Wittkowsky AK (2001) Drug interactions update: drugs, herbs, and oral anticoagulation. J Thromb Thrombolysis 12: 67-71.
18. Villegas JF, Barabe DN, Stein RA, Lazar E (2001) Adverse effects of herbal treatment of cardiovascular disease: what the physician must know. Heart Dis 3: 169-175.
19. Chan TY (2001) Interaction between warfarin and danshen (*Salvia miltiorrhiza*). Ann Pharmacother 35: 501-504.
20. Huupponen R, Sepp P, Iisalo E (1984) Effect of guar gum, a fibre preparation, on digoxin and penicillin absorption in man. Eur J Clin Pharmacol 26: 279-281.
21. Johne A, Brockmller J, Bauer S, Maurer A, Langheinrich M, et al. (1999) Pharmacokinetic interaction of digoxin with an herbal extract from St John's wort (*Hypericum perforatum*). Clin Pharmacol Ther 66: 338-345.
22. McRae S (1996) Elevated serum digoxin levels in a patient taking digoxin and Siberian ginseng. CMAJ 155: 293-295.
23. Nordstr M, Melander A, Robertsson E, Steen B (1987) Influence of wheat bran and of a bulk-forming ispaghula cathartic on the bioavailability of digoxin in geriatric in-patients. Drug Nutr Interact 5: 67-69.
24. Shaw D, Leon C, Kolev S, Murray V (1997) Traditional remedies and food supplements. A 5-year toxicological study (1991-1995). Drug Saf 17: 342-356.
25. Cumming AM, Boddy K, Brown JJ, Fraser R, Lever AF, et al. (1980) Severe hypokalaemia with paralysis induced by small doses of liquorice. Postgrad Med J 56: 526-529.
26. Rosenblatt M, Mindel J (1997) Spontaneous hyphema associated with ingestion of *Ginkgo biloba* extract. N Engl J Med 336: 1108.
27. Mustapha A, Yakasai IA, Aguye IA (1996) Effect of *Tamarindus indica* L. on the bioavailability of aspirin in healthy human volunteers. Eur J Drug Metab Pharmacokinet 21: 223-226.
28. Lambert JP, Cormier J (2001) Potential interaction between warfarin and boldo-fenugreek. Pharmacotherapy 21: 509-512.
29. Izzat MB, Yim AP, El-Zufari MH (1998) A taste of Chinese medicine! Ann Thorac Surg 66: 941-942.
30. Tam LS, Chan TY, Leung WK, Critchley JA (1995) Warfarin interactions with Chinese traditional medicines: danshen and methyl salicylate medicated oil. Aust N Z J Med 25: 258.
31. Yu CM, Chan JC, Sanderson JE (1997) Chinese herbs and warfarin potentiation by 'danshen'. J Intern Med 241: 337-339.
32. Sunter WH (1991) Warfarin and garlic. Pharm J 246:772.
33. Matthews MK Jr (1998) Association of Ginkgo biloba with intracerebral hemorrhage. Neurology 50: 1933-1934.
34. Janetzky K, Morreale AP (1997) Probable interaction between warfarin and ginseng. Am J Health Syst Pharm 54: 692-693.
35. Taylor JR, Wilt VM (1999) Probable antagonism of warfarin by green tea. Ann Pharmacother 33: 426-428.
36. Lam AY, Elmer GW, Mohutsky MA (2001) Possible interaction between warfarin and *Lycium barbarum* L. Ann Pharmacother 35: 1199-1201.
37. Izzo AA, Di Carlo G, Borrelli F, Ernst E (2005) Cardiovascular pharmacotherapy and herbal medicines: the risk of drug interaction. Int J Cardiol 98: 1-14.
38. Kobayashi H, Ishii M, Takeuchi S, et al.(2010) Efficacy and safety of a traditional herbal medicine, hochu-ekki-to in the long-term management of Kikyo (Delicate Constitution) patients with atopic dermatitis: a 6 month, multicenter, double-blind, randomized, placebo-controlled study. Evid Based Complement Alternat Med 7: 367.
39. Felixsson E, Persson, IAL, Eriksson AC, Persson K (2010) Horse chestnut extract contracts bovine vessels and affects human platelet aggregation through 5-HT2A receptors: An in vitro study. Phytotherapy Research 24: 1297–1301.
40. Kkkurt I, Ince S, Kele H, Akkol EK, Avci G, et al. (2010) Beneficial effects of *Aesculus hippocastanum* L. seed extract on the body's own antioxidant defense system on sub acute administration. J Ethnopharmacol 129: 18-22.
41. Kuller LH, Ives DG, Fitzpatrick AL, Carlson MC, Mercado C, et al. (2010) Does Ginkgo biloba reduces the risk of cardiovascular events? Circ Cardiovasc Qual Outcomes 3: 41-47.
42. Xin W, Zhang L, Sun F, Jiang N, Fan H, et al. (2011) Escin exerts synergistic anti-inflammatory effects with low doses of glucocorticoids *in vivo* and *in vitro.* Phytomedicine 18: 272-277.
43. Dasgupta A, Kidd L, Poindexter BJ, Bick RJ (2010) Interference of hawthorn on serum digoxin measurements by immunoassays and pharmacodynamic interaction with digoxin. Arch Pathol Lab Med 134: 1188-1192.