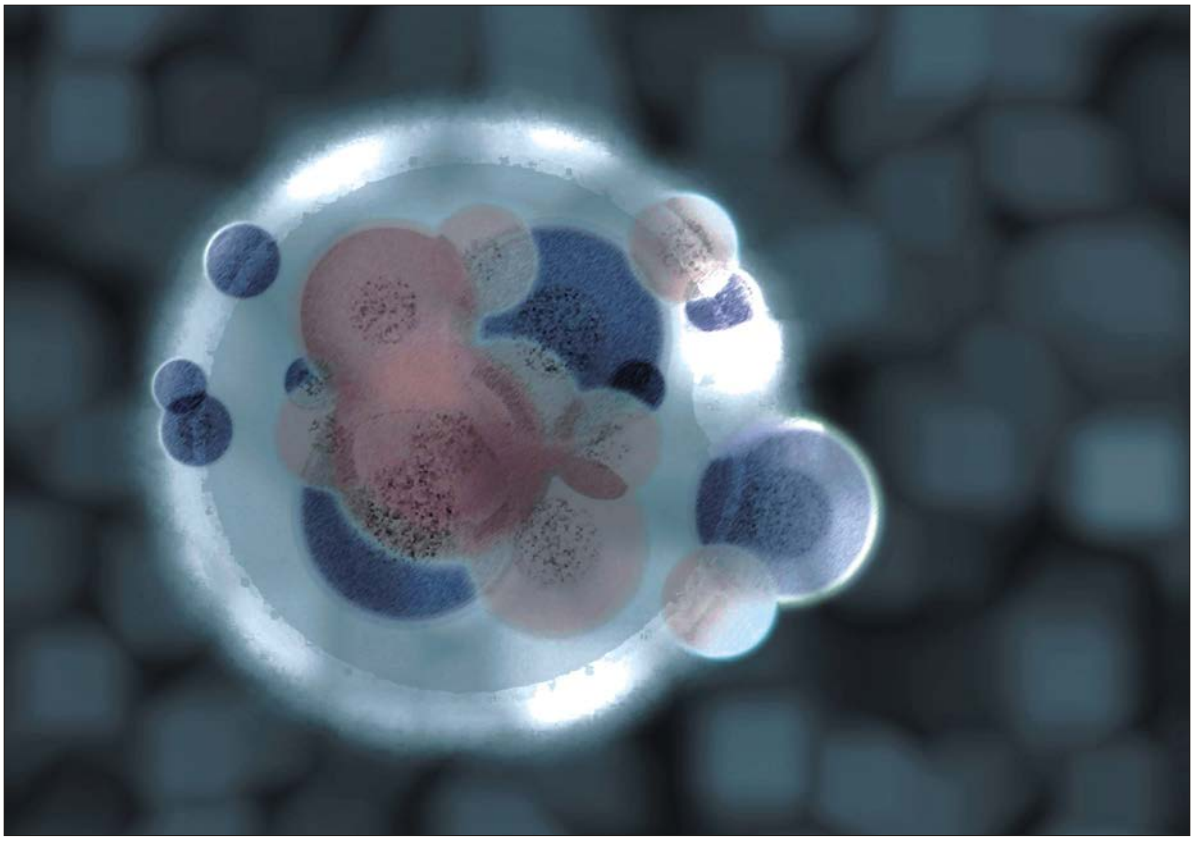

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Phytotherapy in Cardiovascular Diseases: From Ethnomedicine to Evidence Based Medicine

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Abstract: Cardiovascular diseases are now considered to be one of the major causes of mortality in the developed and developing world. With the advent of better diagnostic procedures and therapeutic strategies their management has become more efficient, yet the role of herbal and plant remedies is paramount in the developing and remote areas of the world. Phytotherapy or therapeutics using plants and herb based compounds or crude drugs are an indispensable part of Complementary and Alternative Medicine (CAM). The benefits of most of these plants are controversial as their toxicology and pharmacological activities are not well studied and documented. However certain plants species like *Ginko biloba* and *Crataegus* have shown promise in experimental and clinical trials. In the present review, some anthropo-geographical and historical perspectives of phytotherapy are mentioned. Some important manifestations of cardiovascular pathology and their phytotherapy are reviewed. The holistic approach of phytotherapy and folkloric ethno medical practices indeed have opened new horizons for quality care in cardiovascular diseases. Phytotherapy and traditional medicine have proven their potential place in the modern and more skeptical evidence based medicine.

Key words: Cardiovascular diseases, phytotherapy, folk medicine, evidence based medicine, herbal medicine, ethnopharmacology

INTRODUCTION

Since time immemorial, disease has threatened the integrity and socio-economic welfare of humans. In every era and in every era of every community humans took up the challenge of seeking the cure for disease in the surrounding nature. The advent of traditional and nature based medicine thus improved the quality of lives and facilitated the lengthening of life spans. Traditional medicine continues till the present day to form an integral part of human cultures in many remote and under developed parts of the globe where it is the conventional form of health care. The geo-anthropological and floral diversity is a major factor in the vast array of ethno-medicine and traditional herbal and natural therapies.

The current system of health care in developed countries is steadily incorporating phytotherapy in pharmacotherapy predominantly based on synthetic drugs. With advances in pharmacognosy and experimental pharmacology the toxicological and therapeutic potential of drugs has become easier to determine. Phytotherapy is now an important domain of the complementary and alternative form of medicine. Complementary and alternative medicine is widely used in the developed world (Eisenberg *et al*., 1998). Complementary and Alternative Medical (CAM) practices are those health care and medical practices that are not currently an integral part of conventional medicine and not routinely taught in western medical schools (Eisenberg *et al*., 1993). CAM therapies broadly include yoga, relaxation/hypnosis, acupuncture, spiritual healing, chiropractic care, massage and nutrition and naturopathic remedies. CAM therapy use increased 25% and the number of Americans taking herbs nearly quadrupled (Eisenberg *et al*., 1998; Miller *et al*., 2004). In a broader sense traditional medicine and CAM are described as Hippocratic, holistic, integrative and preventive where as, conventional medicine is considered Gaelenic, analytical, curative and specific (Fulder and Munro, 1985). Some current terms associated with CAM are: folkloric, holistic, integrative, traditional, unorthodox, unconventional, unofficial, natural, mind-body etc., but there are certain more assertive terms like ineffective, questionable, dubious etc. (McGinnis, 1991). There is just as much evidence in favor of CAM as there is against it (Syed Minnatullah Qadri, 2001).

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ANTHROPO-GEOGRAPHICAL AND HISTORICAL USE OF MEDICINAL PLANTS

The evidence of the use of plants for medicinal purposes dates as far back as 60,000 years ago, in both Western and Eastern cultures and in both developed and undeveloped countries (Gossel *et al*., 2006). The Egyptian pharmacopoeia of *Ebers Papyrus*, written about 1500 BC, documents the use of medicinal plants such as the poppy of opium oil and the oil of castor beans (Ackernecht, 1973). The Indian subcontinent has witnessed the growth of two of very important systems of medicine Ayurvedic and Unani (Greco-Arabic) medicine, related but distinct in many ways. They have a standardized pharmacopoeia of herbal and natural crude drugs. Both these systems still flourish in modern times and have been widely adapted as Oriental/Eastern medicine along with Chinese medicine. There has been an upsurge in demand for the Phyto-pharmaceutical products of Ayurveda in western nations, because of the fact that the synthetic drugs are considered to be unsafe (Said, 1977; Subhose *et al*., 2005). Several herbs described in the Chinese folklore are presently used in the Chinese herbal system of medicine popularly known as Traditional Chinese Medicine (TCM). The Chinese materia medica comprises herbal formulations and other crude drugs used in various diseases (Zhu *et al*., 2007). Human beings have been involved in plant derived medicine or herbal medicines since prehistoric times. Herbal medicine and phytotherapy has enabled scientists to make many contributions to commercial drug preparations manufactured today (Yilmaz *et al*., 2006).

The role of CAM in general and phytotherapy in various diseases in particular has been of extreme interest to various scientific and non scientific communities throughout the world. Phytotherapy is broadly defined as the use of natural therapeutic agents derived from plants or crude herbal drugs.

Cardiovascular diseases are now considered a major cause of mortality in not only the developed world but also in the developing countries. In the age of genomics, nanotechnology and proteomics, cardiovascular diseases continue to remain a major challenge to therapeutically manage and the search for a viable evidence-based alternative continues (Burta *et al*., 2007).

Folk and ethno medicine records have been of extreme value in this regard. In 350-377 BC, Hippocrates, the father of medicine, advised the use of diet and plant medicines. He tried to relieve the pain of his patients by asking them to chew Willow bark, which contains salicylic acid. Long before Hippocrates, the ancients Egyptians, Sumerians, Indians and Chinese were noted to use herbs such as onions, garlics, ginger, thyme etc. In 1775, it is reported that William Withering cured people with dropsy, swelling of the legs and shortness of breath related to heart failure with a herbal poly formulation that also contained fox glove plant, *Digitalis purpurea*. Since then for more than 200 years digitalis (digoxin) has been used to treat cardiac insufficiency (DeSmet, 2002).

Avicenna in about 1000 AD, in his pioneering work. The Canon of Medicine, logically and scientifically presented perhaps for the first time in the history of medicine through a classified description of cardiac diseases. He was inspired by the earlier works of Greek scholars, Aristotle and Galen. He is considered the first physician to correlate the diseases of the heart with the temperament and psychic make up of an individual and wrote an elaborate pharmacopoeia on heart remedies (Said, 1995).

The Ayurvedic treatment practiced since ancient times in the India consists of the use herbal preparations, diet, yoga, meditation and other practices. Studies have shown that the dietary principles and herbal formulations have a positive impact on cardiovascular diseases like essential hypertension, dyslipidemia and cardiac insufficiency (Mamtani, 2005). The Chinese system of medicine popularly known as Traditional Chinese Medicine or TCM has been very successful in the phytotherapy of cardiovascular diseases. Acupuncture along with TCM is beneficial as an adjunctive therapy in the management of congestive heart failure, arrhythmias and systemic hypertension (Smith, 1992).

CARDIOVASCULAR PATHOLOGY AND PHYTOTHERAPY

Cardiovascular diseases are a broad entity including all diseases that affect the circulation of blood and distribution of oxygen to healthy tissues. They include ischemic cardiopathy, hypertension, hypotension, conduction defects and arrhythmias, valve defects and an eventual dysfunction known as heart failure (Burta *et al*., 1998). The phytotherapy of cardiovascular diseases is always set with pros and cons just like any other pharmacotherapy. With years of research and clinical trials, many plants have been approved by various drug associations and commercially marketed for treating heart and circulation diseases. Majority of these drugs owe their origins to the traditional and folkloric practices where they were accidentally discovered and through trial and error have been used for centuries (Zbiden *et al*., 2002). The discussion about the benefit of these drugs is still controversial because of lack of scientific evidence. However, certain drugs like *Ginko biloba*, *Crataegus* and

garlic, often recommended substances for patients with cardiovascular diseases. For these substances there is a lot of data available from experimental and clinical studies, unfortunately not always adhering to the criteria of evidence based medicine (Dennehy, 2001). The present review encompasses of succinct outlines of some common plants used in the pharmacotherapy of various cardiovascular ailments consisting of both drugs used in traditional medicine worldwide and under experimental and clinical studies but also clinically approved herbs that have proven to be evidenced based medicine.

PHYTOTHERAPY IN ISCHEMIC HEART DISEASE, PLATELET AGGREGATION AND HYPERLIPIDEMIA

Diseases that cause the ischemia of the myocardium are potentially fatal. They belong to the wider class of acute coronary syndromes. In modern day medicine they are well managed by vasodilators and nitroglycerine compounds, calcium channel blockers and beta blockers that are regarded as the cornerstone of cardiac therapy (Khan, 1999). *Arnica montana* is often described for anti-inflammatory activities but there are strong suggestions made in literature regarding its anti anginal activity. The flavonoids of these compounds are suggested for its activity against coronary insufficiency. The pharmacological activity of Arnica is well recorded in homeopathic tinctures (Rutten, 2004). Danshen (*Salvia miltiorrhiza*) is believed to posses' vasoactive free radical scavenger and demonstrable properties. Because of its properties of improving microcirculation, causing coronary vasodilatation, suppressing the formation of thromboxane, inhibiting platelet adhesion and aggregation and protecting against myocardial ischemia, it is widely used either alone or in combination with other herbal ingredients for patients with coronary artery disease and other cardiovascular diseases especially in China (Tsung, 2006, 2007).

Garlic (*Allium sativum*) and its supplements are considered to outnumber any other supplements in the pharmaceutical market sales and consumption by the general population (Radimer *et al*., 2000). It is believed to reduce cholesterol, decrease blood pressure, inhibit atherosclerosis and improve circulation. Since hyperlipidemia is directly associated to atherosclerosis and coronary heart disease. Drugs improving the lipid profiles help against atherosclerosis (Burta *et al*., 2000a, b). The active substance is allicin, formed by the action of alliinase on alliin when crushed (Ali *et al*., 2000). A trial of garlic versus fibrates reported similar efficacy. Both forms of treatments produced parallel reductions in Low-Density Lipoprotein (LDL) and increases in High-Density Lipoprotein (HDL) cholesterol, thus remarkably reducing the risk of an acute coronary event (Stevinson *et al*., 2000; Holzgartner *et al*., 1992). Other plants with potential against ischemic heart disease currently under pharmacognostical and ethnopharmacological study worldwide and used by indigenous folk medical practitioners include, coronary dilators like *Coffeae semen*, *Cacao semen*, *Theae folium*, Gurana (soft extract of *Paullina cupana* seeds) and antispastic agents such as *Ammi visagnae fructus*, volatile oils containing methyl salicyclates like *Betulae lentae aertherleum* and *Ulmariae herba*. (Duarte *et al*., 1999; Zambel *et al*., 2006; Lee *et al*., 2003). *Olea europaea* or olive is now known to reduce the risk of coronary heart disease and is more of a dietary therapy than an exclusive phytotherapy (Caramia, 2006). *Avena sativa*, *Amaranthus hypochondriacus* and red grapefruit are all known to be beneficial against coronary artery disease (Cerwiñski *et al*., 2004). For the treatment of coagulation imbalance related to atherosclerosis and coronary artery diseases certain plants like *Allium sativum*, *Ginko biloba*, *Salvia miltiorrhiza*, *Zingiber officinale*, *Angelicae sinensis* (Dong Quai) etc. are known to inhibit platelet aggregation and are beneficial in patients with acute coronary syndromes (Tsung, 2007; Burta, 2000b; Grant and Lutz, 2000; Diamond *et al*., 2000). *Ginko biloba* is a strong anti oxidant and has a strong free radical scavenging properties. It has the propensity for protection to reperfusion injury and markers of oxidative stress and cardiac performance, including cardiac index and left ventricular stroke volume improved after surgical intervention on the heart (Diamond *et al*., 2000).

ARTERIAL HYPERTENSION AND PHYTOTHERAPY

Treatment of hypertension has been a major accomplishment of phytotherapy. There are several studies to substantiate the anti hypertensive effects of drugs used in ethnomedicine and folk practitioners. Some of the well elaborated and studied crude herbal drugs are derived from the Chinese, Ayurvedic and Unani systems of Eastern and oriental medicine. Reserpine, the purified alkaloid of *Rauwolfia serpentina*, was the first potent drug widely used in the long-term treatment of hypertension. It was used as an integral part of the Indian folk medicine in Ayurveda and Unani. There have also been reports that it was used by the indigenous Indian population of India and Africa for other ailments like insomnia and snake bites (Jerie, 2007).

Ajmaline from *Rauwolfia* is of application in Brugada syndrome in modern cardiology (Satish *et al*., 2005). *Hibiscus sabdarifa* is an extensively studied plant for anti

hypertensive effects. Traditionally it is used in West African Countries. In comparison to captopril, the anti hypertensive effects were almost similar (41). *Allium sativum* due to its versatile effects can be considered as the wonder herb for cardiovascular diseases. Besides its hypoglycemic, hypolipidemic and anti platelet aggregant activity, it has also anti hypertensive activity (Etuk, 2006; Ernst, 1987). *Vitex dodiana* is widely used in Nigerian and west African folk medicine (Etuk, 2006). *Lepidium latifolium* is used by the indigenous population of the Canary islands and has a major anti hypertensive effect due to its diuretic activity in rats (Navorro *et al*., 1994). Other herbs popular as folk remedies for hypertension and with proven ethnopharmacology include *Phyllanthus amarus*, *Cassia occidentalis*, *Musanga cecropiodes*, *Rhapetalum coriaceum* etc. (Etuk, 2006).

PHYTOTHERAPY OF CARDIAC INSUFFICIENCY

Heart failure is categorized by a decrease in the inotropic activity of the heart along together with a substantial decrease in cardiac output and a generalized edema of the body due to the pathophysiology of the renin-angiotensin-aldosternone system. Phytotherapy is the cornerstone of heart failure treatment as the first line drugs of heart failure digoxin is a plant derivative. It is inappropriate to include it anymore as CAM. Cardiotonic and diuretic based phytotherapy is essential in the treatment of congestive heart failure. One very important plant with high potential in phytotherapy and tinctures in homeopathy is Hawthorn (*Crataegus* species). Hawthorn berries were reportedly used by the folk medicine in North America and Europe (Valli and Giardina, 2002). Mechanisms of action of *Crataegus* species include antioxidant, antihyperlipidemic, vasodilatory, inotropic and decreased capillary permeability. Clinical trials have decreased symptoms of congestive heart failure, as well as improved cardiac performance (Weikl *et al*., 1996; Leuchtgens, 1993).

Ginko biloba is yet another drug with multi-potential in cardiovascular diseases. Ginko biloba has been reportedly used by the Chinese for more than 3000 years and it is one of the best selling natural drugs in the US. Ginko is believed to be rich in flavonoids and terpenoids which exert their effects through radical scavenging, anti platelet aggregation and anti inflammatory activities. In a study conducted with poly herbal Chinese formulation in which Ginseng was a part revealed that there was an improvement in stroke volume and cardiac index (Fang *et al*., 1987).

ANTI ARRHYTHMIC AND ANTI HYPOTENSIVE PHYTOTHERAPY

Anti arrhythmic therapies in conventional cardiology are by drugs derived from plants like digoxin and quinidine. So they are exclusive of CAM. Ajmaline is used in Brugada syndrome (Satish *et al*., 2005). Ephedrine obtained from Ma Huang has potent sympathomimetic activity and is anti hypotensive nature (White *et al*., 1997).

PHYTOTHERAPY IN INTERMITTENT CLAUDICATION AND CHRONIC VENOUS INSUFFICIENCY

Ginko biloba has yet another benefit in the long term treatment of intermittent claudication of the limbs due to ischemia via vasoregulation. It increased the pain free walking distance for patients dramatically (Fang *et al*., 1987). Horse chestnut seed or *Aesculus hippocastanum*, is now marketed as a phyto therapeutic product useful in chronic venous insufficiency of the lower limbs together with varicose veins. The active compound Aescin decreases lower extremity edema by decreasing capillary permeability via inhibition of endothelial lysosomal enzymes (Pittler and Ernst, 1998).

CONCLUSION

CAM in general and phytotherapy in particular have heralded a new era in cardiology by bringing hope with a more efficient management of heart and circulatory diseases. The physicians and health care providers must opt for a more holistic approach in their practice and judgment of therapeutics. CAM continues to grow world wide regardless of he economic and social status of nations. The future is steadily embracing the legacies of our ancestors and folk medicine would some day be equated to evidence based medicine. Alternative therapies give hope to the sufferers and ethnopharmacological research should play a pivotal role in heart diseases. The phytotherapy of various heart diseases has gone a long way from folklore to the present era of evidence based medicine.

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