



**RESEARCH ON: SAFETY AND EFFICACY OF HERBAL FORMULATION IN  
TREATMENT OF CARDIOVASCULAR DISEASE**

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**ABSTRACT**

Herbal medicine has become a popular form of health care, globally. Herbal medicine is a preferred option nowadays even though few contrasts exist between herbal medicines and customary pharmacological medicines. Herbal formulations have been the most effective treatment for various disease conditions. Many studies have proved the efficiency of herb-herb combinations. In comparison with single drugs, drug combinations have shown a more promising effect in the treatment of disease. This drug combinations conception has been well established in many countries and extraordinary success has been reached. But not all the natural treatments are found to be inherently safe. A herbal formulation may carry risk. So, it is essential to know which herbal remedies do better than side effects and for which condition.<sup>[1]</sup> Cardiovascular diseases (CVDs) are a significant health burden with an ever-increasing prevalence. They remain the leading causes of morbidity and mortality worldwide. The use of medicinal herbs continues to be an alternative treatment approach for several diseases including CVDs. Currently, there is an unprecedented drive for the use of herbal preparations in modern medicinal systems.<sup>[2]</sup> Herbs have been used as medical treatments since the beginning of civilization and some derivatives (Eg, aspirin, reserpine, and digitalis) have become mainstays of human pharmacotherapy. For cardiovascular diseases, herbal treatments have been used in patients with congestive heart failure, systolic hypertension, angina pectoris, atherosclerosis, cerebral insufficiency, venous insufficiency, and arrhythmia. However, many herbal remedies used today have not undergone careful scientific assessment, and some have the potential to cause serious toxic effects and major drug-to-drug interactions.<sup>[8]</sup>

**KEYWORDS:** Herbal formulation, cardiovascular diseases, pharmacotherapy, safety & efficacy, etc.

**INTRODUCTION**

Cardiovascular diseases (CVDs) are diseases of the heart or blood vessels. CVDs register a global annual toll of more than 17 million deaths. As a result, CVDs remain the world's most common cause of death and are a major economic and health burden, worldwide. The World Health Organization (WHO) reported that CVDs account for 31% of annual global deaths (World Health Organization, 2017). In Europe, CVDs account for 45% of all deaths according to the European Cardiovascular Disease Statistics 2017 (Martinet et al., 2019). The American Heart Association's current statistics estimate that around half of the population of the USA has a form of CVD.<sup>[2]</sup>

the rate of increase in CVD in developing countries is twice as high as in developed countries.<sup>[3]</sup> CVD also typically occurs at a younger age in developing countries: for example, about 52 per cent of deaths from such disorders in India occur before 70 yr of age, compared with 23 per cent in established-market economies.<sup>[4]</sup>

Cardiovascular diseases (CVD) comprise of a group of diseases of heart and the vascular system. 30.5% of all deaths takes places globally according to the global and regional estimates for 2008. Compared with all other countries, India suffers the highest loss, due to deaths from CVD in people aged 35-64 years. The prevalence of CVD is 2-3 times more in urban than rural.

On the Indian subcontinent and in Africa, it is predominantly due to rheumatic fever, whereas calcific aortic valve disease is the most common problem in developed countries. With over 3 million deaths owing to CVD every year, India is set to be the "HEART DISEASE CAPITAL OF THE WORLD" in few years, said doctors on the eve of WORLD HEART DAY (Sept. 29th 2010).

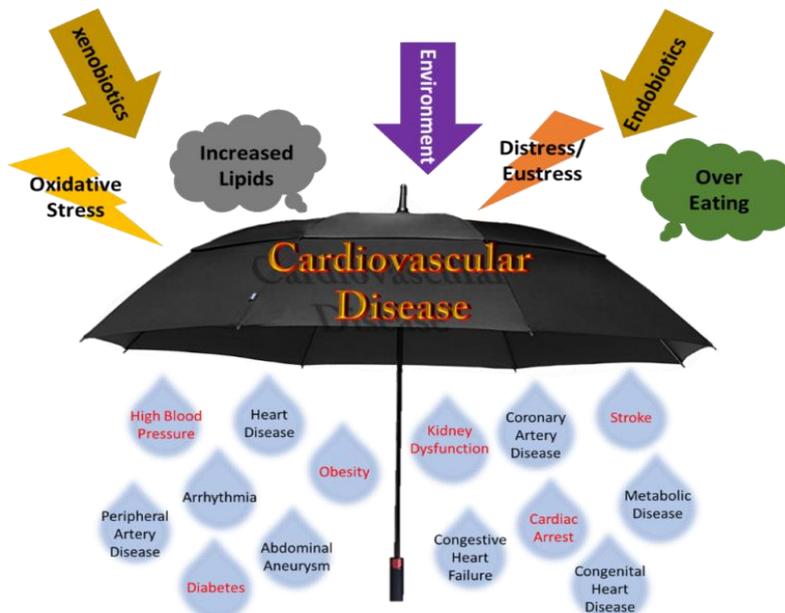
BP regulation, and therefore hypertension, depends on two main factors: cardiac output and systemic vascular resistance. Increased cardiac output or vascular resistance elevate BP. Cardiac output is majorly affected by sodium intake, renal function, and mineralocorticoids. Vascular resistance is affected by the sympathetic

nervous system (SNS), rennin–angiotensin system (RAS), humoral factors, and local autoregulation.<sup>[2-3]</sup>

**CARDIOVASCULAR DISEASE**

✓ Cardiovascular disease (CVD) is a general term for conditions affecting the heart or blood vessels.

- ✓ It's usually associated with a build-up of fatty deposits inside the arteries (atherosclerosis) and an increased risk of blood clots.
- ✓ It can also be associated with damage to arteries in organs such as the brain, heart, kidneys and eyes.
- ✓ CVD is one of the main causes of death and disability in the UK, but it can often largely be prevented by leading a healthy lifestyle.



**Fig.No. 1: Cardiovascular Diseases.**

**TYPE OF CARDIOVASCULAR DISEASE**

There are many different types CVD. Four of the main types are.

- ❖ Coronary Heart Disease
- ❖ Strokes And Transient Ischemic Attack (TIA'S)
- ❖ Peripheral Arterial Diseases
- ❖ Aortic Disease

**CAUSE OF CVD**

- high blood pressure,
- high low-density lipoprotein (LDL) cholesterol
- diabetes
- smoking and secondhand smoke exposure
- obesity
- unhealthy diet and physical inactivity.



**Fig. No: 2- Cause of Cvd.**

**HISTORY OF CARDIOVASCULAR DISEASE**

The cardiovascular history is obtained to identify evidence of organic heart disease or symptoms that suggest the presence, or possible presence, of cardiovascular abnormalities.

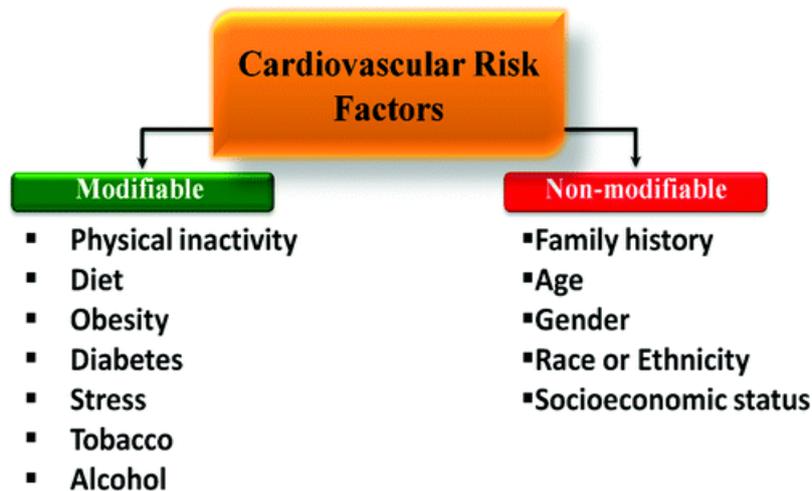
**HISTORY OF SPECIFIC CARDIOVASCULAR DISEASE**

Heart attack. The term heart attack means different things to different people. A history of heart attacks as a child, or "ten heart attacks since 1970," should be.

1. viewed with some skepticism unless documentation has been obtained. Today, the majority of patients with myocardial infarction experience a hospital stay of at least a week. Patients who state they were hospitalized for only a day or two, or were discharged from the emergency room, usually were not suffering from acute infarction. Further documentation is needed.
2. Coronary artery disease. Again, details concerning the diagnosis are needed.
3. Valvular disease. A history of a "leaky valve," or mitral prolapse, is obtained frequently. As some patients are told that they have mitral prolapse based solely on personality type, symptoms (usually chest pain or palpitations), and a systolic murmur (frequently an innocent flow murmur), further support for this diagnosis is needed.

4. Heart murmur. The age at which the murmur was first discovered is an important piece of historical data. In addition, a history of any physical restrictions placed on the patient at the time of diagnosis should be sought.
5. Rheumatic fever. This is a frequently misused diagnosis and must be interpreted with caution. Details of the illness must be explored. Many patients state that their parents told them they had rheumatic fever, or give a history of fever, sore throat, and a heart murmur.
6. Enlarged heart. This is usually a radiologic diagnosis and is extremely nonspecific. Since "enlarged heart" can mean dilatation, hypertrophy, or poor x-ray technique, this history is of limited value.
7. Heart failure. Commonly, a history of shortness of breath with exertion, especially in the elderly, is translated as due to congestive heart failure. Because congestive failure is more a symptom complex (similar to fever) than a true diagnosis, this claim must be investigated further.
8. History of other vascular disease:- Because there is an association between peripheral artery and coronary artery disease, this can be helpful. Since many adults complain of "cold feet," "poor circulation," and leg cramps, these symptoms alone do not confirm a diagnosis.

**Risk Factors**

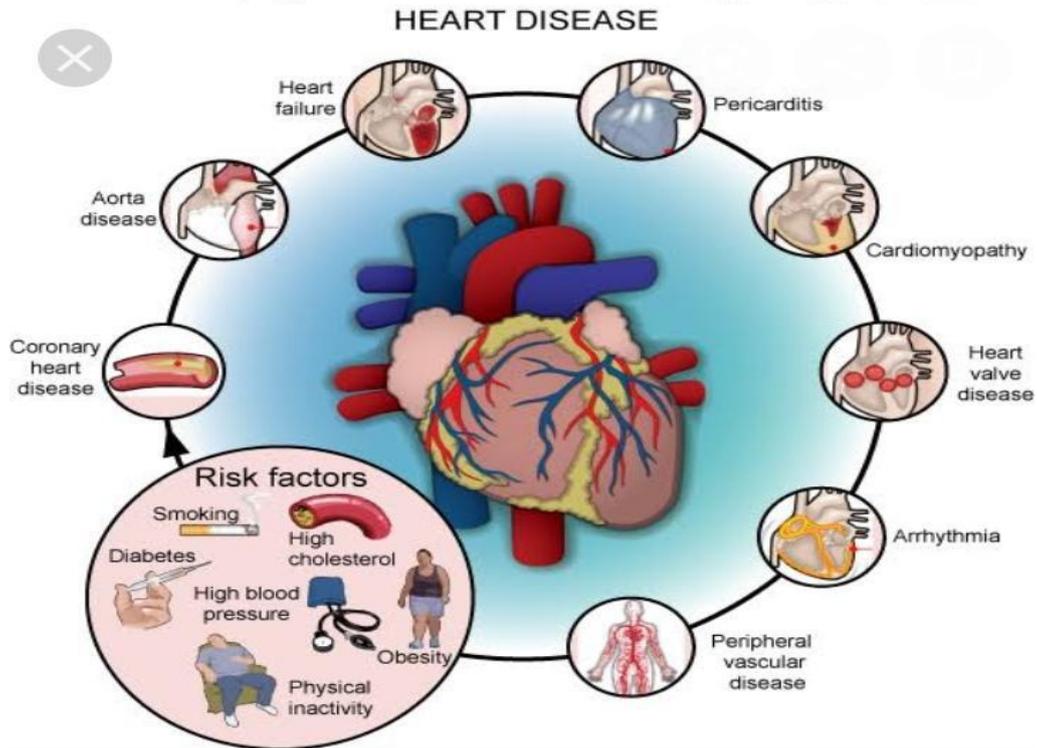


There are many risk factors for heart diseases.

- ❖ Age
- ❖ Sex
- ❖ Tobacco Use
- ❖ Physical Inactivity
- ❖ Excessive Alcohol Consumption
- ❖ Unhealthy Diet
- ❖ Obesity
- ❖ Genetic Predisposition And Family History Of Cardiovascular Disease
- ❖ Raised Blood Pressure (Hypertension)
- ❖ Raised Blood Sugar (Diabetes Mellitus)

- ❖ Raised Blood Cholesterol (Hyperlipidemia)
- ❖ Undiagnosed Celiac Disease
- ❖ Psychosocial Factors
- ❖ Poverty And Low Educational Status
- ❖ Air Pollution.

**HEART DISEASES**



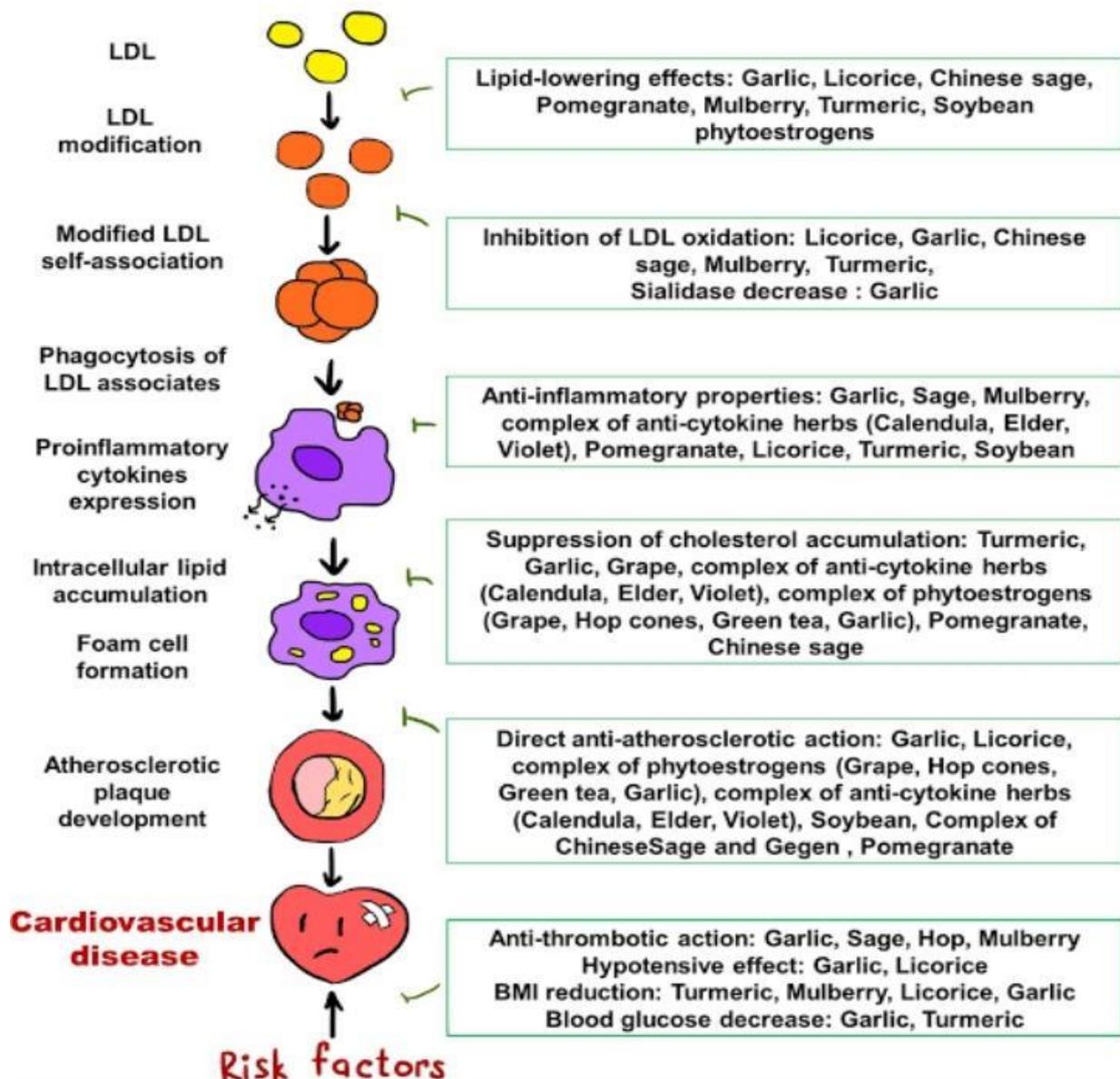
**Fig No. 3: Heart Diseases.**

**CONCERNS ABOUT USING HERBAL FORMULATIONS FOR CARDIOVASCULAR DISEASES<sup>[14]</sup>**

Concern	Description
Lack of proof of efficacy and safety	Differently from conventional medications, herbal medications do not need proof of efficacy and safety before they enter the market.
Children and pregnant women	Most herbal medications are not tested in pregnant women or children. Their use in children and in pregnant, attempting to become pregnant, or breastfeeding women should be avoided because of the increased risk of side effects, including cardiovascular events.
Contamination and substitution	Substitution of the plants listed on the labels with alternative plant species has been often reported. Contamination with conventional medications has also been described.
Active ingredient	Active ingredients for many herbal medications have not been ascertained, and if ascertained their level might vary considerably in different preparations.
Lack of antidotes	Severe side effects and organ damage might derive from the inappropriate use of herbal medications (i.e., prolonged use or overdose). No antidotes are available to counteract the effect of herbal medications.

**Regulation of herbal medicines.**

- 1) Herbal medications do not need to be approved by the FDA before they enter the market, and they do not have to be proven safe or effective in the treatment of a given disease or condition.
- 2) The FDA's role in regard to these medications relates mainly to monitoring their safety by reviewing serious adverse events reported by the manufacturer, consumers, or health care professionals through the Safety Reporting Portal.
- 3) The FDA is responsible for taking action against any adulterated or misbranded dietary supplement product after it reaches the market.
- 4) If the FDA finds a product to be unsafe, it can take action against the manufacturer and may issue a warning or request that the product be removed from the market.



### Marked Differences Between Synthetic Drugs And Natural Drugs.

- The active principles are frequently un-known.
- Standardization, stability and quality control are feasible but not easy.
- The availability and quality of raw materials are frequently problematic.
- Well-controlled double-blind clinical and toxicological studies to prove their efficacy and safety are rare.
- Empirical use in folk medicine is a very important characteristic.
- They have a wide range of therapeutic use and are suitable for chronic treat-
- Ments.
- The occurrence of undesirable side effects seems to be less frequent with herbal medicines, but well-controlled randomized clinical trials have revealed that they also exist.
- They usually cost less than synthetic drugs.

### Rationale behind the growth of phototherapeutic market

- ❖ Preference of consumers for natural therapies.
- ❖ Concern regarding undesirable side effects of modern medicines and the belief that Herbal drugs are free from side effects, since millions of people all over the world
- ❖ Have been using herbal medicines for thousands of years.
- ❖ Great interest in alternative medicines.
- ❖ Preference of populations for preventive medicine due to increasing population age.
- ❖ The belief that herbal medicines might be of effective benefit in the treatment of certain diseases where conventional therapies and medicines have proven to be inadequate.
- ❖ Tendency towards self-medication.
- ❖ Improvement in quality, proof of efficacy and safety of herbal medicines.
- ❖ High cost of synthetic medicines.<sup>[15]</sup>

**USING HERBAL MEDICINES TREATMENT ON CARDIOVASCULAR DISEASE.**

Plant name	Family	Action
Agaricus alboluteus Zeller	Agaricaceae	Cardioprotection
Antiaris toxicaria Lesch.	Moraceae	Circulatory stimulant
Arnebia benthami	Boraginaceae	Heart ailments
Camellia sinensis	Theaceae	Cardioprotection
Ginkgo biloba	Ginkgoaceae	Anti-ischemic action
Ipomoea digitata Linn.	Convolvulaceae	Hypertension and heart diseases
Ocimum sanctum	Lamiaceae	Hypotensive, cardiac depressant activity
Urtica dioica	Urticaceae	Antihypertensive
Solanum nigrum	Solanaceae	Heart ailments
Portulaca oleraceae	Portulacaceae	Strengthen arteries and heart problems
Valeriana officinalis	Valarianaceae	Against heart disease and hypertension
Viscum album	Viscaceae	Antihypertensive, Heart problem
Oroxylum indicum	Bignoniaceae	Cardioprotection
Digitalis ambigua Murray	Plantaginaceae	Against heart disease
Coronilla varia	Fabaceae	Against heart disease
Coronilla varia	Fabaceae	Against heart disease

**List of herbal plants used for prevention of cardiac diseases**

**HERBAL MEDICINES**

- 1) Astragalus (Astragalus membranaceus),
- 2) Asian Ginseng (Panax Ginseng)
- 3) Flaxseed oil (Linum usitatissimum),
- 4) Garlic (Allium sativum),
- 5) Ginkgo (Ginkgo biloba),
- 6) Grape (Vitis vinifera) seeds,
- 7) Green tea (Camellia sinensis),
- 8) Hawthorn (Crataegus).
- 9) Milk thistle (Silybum marianum).
- 10) Soy (Glycine max).

**CENTRAL ILLUSTRATION: An Evidence-Based Review of Herbal Medications Used in Cardiovascular (CV) Medicine**

Clear evidence of benefit	Limited evidence of benefit (to be confirmed in large studies)		No or conflicting evidence of benefit	
	Limited side effects		Limited side effects	Potentially severe side effects
	 Flaxseed oil  Milk-thistle  Grape seeds  Green tea  Hawthorn  Garlic  Soy		 Astragalus  Asian ginseng	 Ginkgo biloba

 High risk of interactions with CV medications

**Liperoti, R. et al. J Am Coll Cardiol. 2017;69(9):1188-99.**

For each herb, we described possible indications, biological and clear data, and safety concerns.

**SAFETY OF HERBAL MEDICINE**

Herbal medicines are generally regarded as safe based on their long-standing use in various cultures. However, there are case reports of serious adverse events after administration of herbal products. In a lot of cases, the toxicity has been traced to contaminants and

adulteration. However, some of the plants used in herbal medicines can also be highly toxic.

Assessment of the safety of herbal products, therefore, is the first priority in herbal research. There are various approaches to the evaluation of safety of herbal medicines. The toxic effects of herbal preparation may be attributed mainly to the following.

- Inherent toxicity of plant constituents and ingredients.

- Manufacturing malpractice and contamination.
- ❖ Experience of safety
- Requirements for pharmaceutical assessment that cover the safety assessment of herbal products are as follows:
- ❖ Toxicological studies, where vindicated

The risks associated with the use of herbal substances, which has unfortunately resulted in a number of fatalities, are considered highly significant and are related to problems associated with the failure of good handling and manufacturing of certain products.

Herb	Possible Cardiovascular Indications
Hawthorn ( <i>Crataegus</i> species)	Heart failure, angina, hyperlipidemia
Garlic ( <i>Allium sativum</i> )	Hypertension, hyperlipidemia, antithrombotic
Danshen ( <i>Salvia miltiorrhiza</i> )	Angina, ischemic stroke, hyperlipidemia, antithrombotic
Lingzhi ( <i>Ganoderma lucidum</i> )	Hyperlipidemia, hypertension, diabetes
Ginkgo ( <i>Ginkgo biloba</i> )	Cerebral insufficiency, peripheral vascular disease, antithrombotic
Foxglove ( <i>Digitalis</i> species)	Heart failure, atrial fibrillation
Ginseng ( <i>Panax</i> species)	Angina, hypertension, diabetes

**EFFICACY OF HERBAL MEDICINE**

The efficacy of medicine is the measure of its ability to improve health and well-being. This is a central issue in the modern debate about herbal medicine. The use of herbal remedies is often justified by their long history of usage—from prehistoric time in some cases. The term “efficacious”, however, has a relative meaning as it may be interpreted differently by the practitioners of traditional medicine and the proponents of so-called modern medicine (conventional medicine). Traditional medicine usually takes a “holistic” approach where the physical, spiritual (which includes mental), and most often social well-being of an individual are treated.

**Case I**

Garlic (*Allium sativum* L.) is known to have multifold properties such as lowering of total serum cholesterol levels, anti-platelet activation, and anti-bacterial, -

hypertensive, and -thrombotic activities. There are numerous products of garlic available on the market. Rigorous clinical trials have been conducted on garlic preparations, mainly for lipidlowering properties. The outcome of these trials has been largely supportive of its regular use to prevent cardiovascular diseases. Epidemiological data indicate a protective effect of garlic against arteriosclerosis and various forms of malignancies.

**Case II**

Ginkgo (*Ginkgo biloba* L.) is among the most popular medicinal herbs of the world. Double-blind clinical studies on ginkgo preparations indicate a significant but modest increase in pain-free walking distance as compared to the placebo. Clinical studies also suggest that it can delay the clinical deterioration in dementia patients.

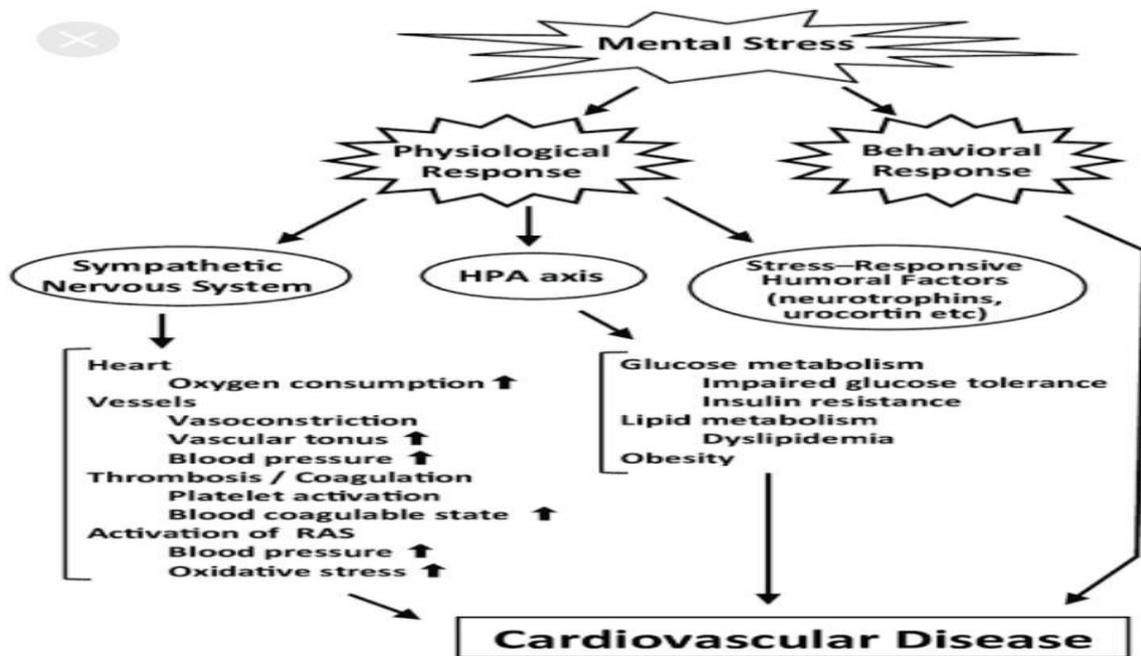


Fig. No.4 Efficacy of Herbal Medicine.

## LITERATURE REVIEW

Sr.No	Author	Topic	Year
1	Sarojini k Laxminarayan avivarasu, sumiline Ginja	A review on safety, efficacy and regulations	2020
2	Abdullah A shaito	Herbal medicine for cardiovascular disease. Efficacy, mechanism and safety	2020
3	Shadrach micheales	Heart attacks for the risk of young peoples	2019
4	Jillian levy	Pericardities:six natural ways to help recovery	2018
5	Villy kyto, matti nimela	Acute pericardities in national library of medicine	2017
6	Panniyammakal jeemon, K S reddy	Social determinants of cardiovascular disease outcomes in indians	2011

## MATERIALS AND METHODS

In this review, we performed a literature search for information on the bioactive components of medicinal plants and their effect on oxidative stress.

The Institute for Scientific Information (ISI) Web of Knowledge, MEDLINE, PubMed, Scopus, Google Scholar, and the China National Knowledge Infrastructure (CNKI) databases were searched using relevant keywords and phrases, including “natural drugs and oxidative stress”, “natural active ingredients and oxidative stress”, “traditional Chinese medicine and oxidative stress”, “photochemistry/medicinal plant extracts and oxidative stress”, “medicinal plants and cardiovascular diseases”, and “natural active ingredients and cardiovascular diseases”.<sup>[19]</sup>

From the search results, we manually selected original articles discussing natural medicines or their active ingredients and their effect(s) on oxidative stress or CVDs. Our search selection criteria were mainly based on the following.

- ❖ Different Mechanisms Used by Natural Medicines and Active Ingredients to Treat Cardiovascular Diseases.
- For example, total flavonoids of matsuba can dilate the coronary artery, increase blood flow, and reduce abnormal electron transfer of the myocardial cell membrane and the production of oxygen free radicals, thereby improving myocardial ischemia and treating coronary heart disease.<sup>[17]</sup> Orientin can protect red blood cells from oxidative damage by reducing oxidative stress, increasing the activity of antioxidant enzymes, and maintaining the structural integrity of red blood cells .

- ❖ Different Categories of Natural Medicines and Active Ingredients with Therapeutic Efficacy in Cardiovascular Diseases.
- The active ingredients of natural medicines including flavonoids, saponins, polyphenols, polysaccharides, and anthraquinones can exert different therapeutic effects. For example, saponin-based active ingredients have multiple functions such as antiviral activity, scavenging oxygen free radicals, expanding blood vessels, strengthening the heart, and reducing the synthesis of reactive oxygen species (ROS) and malondialdehyde (MDA). Polyphenols inhibit the formation of hydroxyl free radicals, increase endogenous superoxide dismutase (SOD) activity, inhibit lipid peroxidation, and increase cellular energy metabolism.
- ❖ Different Therapeutic Targets of Natural Medicines and Active Ingredients.
- For example, berberine can regulate adenosine 5-monophosphate- (AMP-) activated protein kinase (AMPK) and mammalian target of rapamycin (mTOR) signaling pathways. Curcumin can inhibit phosphatidylinositol 3-kinase- (PI3K-) serine/threonine protein kinase- (AKT-) mTOR signal transduction. Further, some active ingredients can regulate multiple signal pathways and can also regulate the growth, proliferation, differentiation, migration, and apoptosis of a variety of cells.

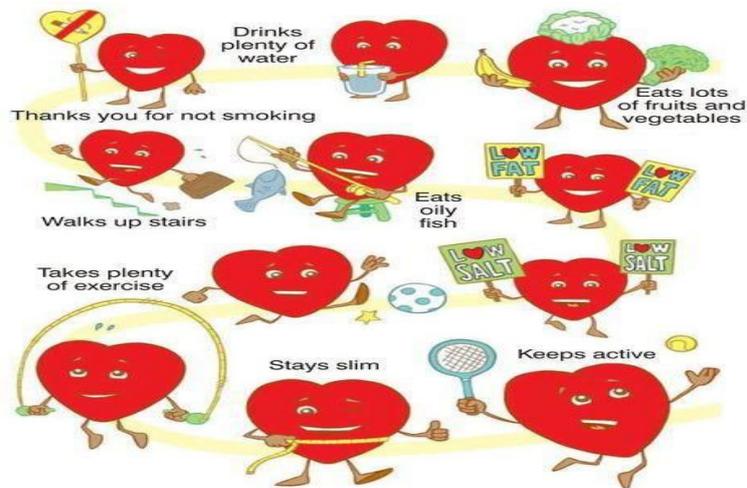
Patients were categorized into two groups: those taking no supplements (Group 1) and those are taking vitamin, mineral, or herbal supplements in various combinations (Group 2). Patient demographic (age, gender, ethnicity) and clinical (coronary artery disease, heart failure, and left ventricular ejection fraction; diabetes; hypertension; dyslipidemia; cerebrovascular and peripheral vascular disease; and smoking) characteristics were recorded.

Variable	Group I	Group II
All patients (%)	81	106
Female (%)	23 (28)	44 (42)
Male (%)	58 (72)	61 (56)
Angina Pectoris (%)	15 (19)	35 (33)
Hypertension (%)	81 (76)	81 (76)
Smoking (%)	28 (35)	27 (26)
Hyperlipidemia (%)	52 (64)	85 (80)
Family history of premature coronary disease (%)	22 (27)	45 (43)

Consecutive patients attending a preventive cardiology clinic were interviewed, examined, and followed for up to 1 year. The physician collected the information by

direct questioning and recorded it on forms prepared for this study.

**Helthy Heart Tips**



**Marketed Herbal formulation used in treatment of Cardiovascular Disease:-**



➤ Three powerful herbs makes ArjunGuna a highly well rounded herbal medicine for cardiovascular diseases. ArjunGuna is a best heart blockage treatment.



- Himalaya HeartCare:- supports your blood pressure and cholesterol levels already within normal range
- Supports your peripheral circulation, heart rate, and gives you support during physical exertion\*
- Non-GMO Project verified with Arjuna, Ashwagandha, Holy Basil and other herbal ingredients

### RESULTS AND DISCUSSION

Herbal remedies are generally derived from leaves, flowers, fruits, stems, roots, bark, tubers of plants-consumed raw or prepared as extracts (by boiling with water) to drink, bathe, or apply to lesions. Different types of herbs are taken by a person or as a family or group to maintain well-being, prevent sickness, reduce symptoms, and sometimes cure.

### SUMMARY AND CONCLUSION

Use of herbal medications for the treatment of cardiovascular diseases is not supported by scientific evidence. Although most of the herbs demonstrate an effect on biological mechanisms associated with cardiovascular disease, available clinical studies are limited in sample size and do not show any impact on relevant clinical outcomes.

A recent increase in the popularity of alternative medicine and natural products has revived interest in traditional remedies that have been used for the treatment of cardiovascular diseases. This article highlights the cardiovascular effects of four potent traditional botanicals viz. Garlic (*A. sativum*), Guggul (*C. wightii*), Hawthorn (*C. oxyacantha*) and Arjuna (*T. arjuna*). Although these plants have been used in the treatment of heart disease for hundreds of years, current research methods show us they can be utilized effectively in the treatment of CVDs including ischemic heart disease, congestive heart failure,

Therefore, to date, available data do not provide enough evidence to recommend the use of herbal medications in clinical practice. In addition, potential relevant side effects, including increased risk of drug interactions, have been described, and the possibility of contamination or substitution with other medications is a concern. Physicians should improve their knowledge of herbal

medications to adequately weigh the clinical implications related to their use, and be able to discuss with patients their possible benefits and side effects, and explain that natural does not always mean safe.

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