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Review Article

INTEGRATING *RASAYANA* THERAPY IN CARDIOVASCULAR DISEASE MANAGEMENT: A REVIEW OF PRECLINICAL - CLINICAL EVIDENCES AND POSSIBLE MECHANISM OF ACTION

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ABSTRACT

Cardiovascular diseases are one of the major causes for mortality in the current era. The means and mechanisms to reduce the myocardial damage are known as cardio protection. There is need for pharmacological agents that can activate the repair and regeneration of myocardium. *Rasayanas* of Ayurveda are widely studied for their regenerative and tissue repair potential. The present work focuses on the relevance and scope of *Rasayana* for the management of cardiovascular diseases. The classical Ayurveda textbooks and relevant modern research works were considered. There are *Rasayana* drugs mentioned in Ayurveda which were indicated in *Hridroga* and cardioprotective effect of some were proven through preclinical studies. The antioxidant, adaptogenic and lipid lowering effect of different *Rasayanas* were responsible for its cardioprotective effect. *Rasayana* drugs can contribute significantly for the cardiovascular disease management by virtue of its regeneration and repair potential. Even though there are supportive preclinical evidences, extensive clinical trials are necessary to evaluate its safety and efficacy in humans.

INTRODUCTION

The non-communicable diseases accounts for around 60% of all deaths. Among the aforementioned diseases cardiovascular diseases (CVD) are the leading cause of mortality. Findings of recent studies reveals that approximately 20.5 million people died from cardiovascular disease in the year 2021. Death from CVD accounts for 1/3rd of all deaths.[1] CVD is responsible for 38% of total premature death due to non-communicable diseases. Global burden of disease study state age standardized CVD death rate of 272 per 100000 population in India, which is much higher than global average of 235. [2]

According to the WHO, cardiovascular disease (CVD) includes disorders of the heart and blood vessels, driven by primary risk factors like hypertension, smoking, and obesity, alongside novel markers such as C-reactive protein (CRP) and small dense LDL-C. The process begins with vascular dysfunction caused by high blood pressure or aging, which serves as the critical event in atherosclerosis and myocardial ischemia. This pathogenesis is fueled by inflammation (marked by high CRP and interleukin-6), which causes LDL to accumulate and oxidize within the dysfunctional endothelium. [3] These oxidized lipids attract inflammatory leukocytes, which secrete cytokines and reactive oxygen species, eventually forming foam cells through macrophage activity. Over time, this results in plaque formation and intimal thickening that can occlude coronary vessels. Ultimately, a necrotic plaque breakdown can trigger thrombosis, leading to acute complications like myocardial infarction, stroke, or cardiac death. [4]

Cardio protection encompasses mechanisms that preserve the heart by preventing myocardial damage and reducing necrosis during infarction. [5] The primary goal is to limit cell death by reducing the severity and duration of ischaemia. Research highlights that plant-based bioactive derivatives- including unsaturated fatty acids, vitamins, and polyphenols exert significant protective effects.[6] Phytoconstituents like flavonoids and terpenoids provide antioxidant, anti-inflammatory, and vasorelaxant benefits, preventing endothelial dysfunction and ROS formation. For instance, *Allium sativum* (garlic) manages

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atherosclerosis by reducing LDL and inhibiting smooth muscle proliferation. [7]

Ayurveda manages cardiovascular disease under the term *Hridroga*, identifying *Rasa dushti* (impaired primary nutritive fluid) as the core pathological factor. While secondary prevention traditionally involves *Pathya-apathya* (regimen), *Yoga*, and *Dinacharya*, this article focuses on *Rasayana* (rejuvenation therapy). As one of Ayurveda's eight branches, *Rasayana* aims to qualitatively improve *Rasa dhatu*. Beyond symptomatic relief, it aligns with modern "pre-conditioning" through tissue regeneration and repair. By analyzing preclinical and clinical evidence, this paper explores how *Rasayana* drugs exert antioxidant, anti-inflammatory, anti-apoptotic, and hypolipidaemic effects to manage and prevent CVDs.

MATERIALS AND METHODS

A comprehensive literature search was conducted to collect focused information on the role of *Rasayana* in cardiovascular diseases. A comprehensive review of *Brihat trayis* and other relevant Ayurveda classical text books were carried out. Systematic search of databases such as PubMed, Google scholar was done to gather relevant articles related to the topic. The key words used were cardiovascular disease, *Rasayana*, herbal products, cardio protection, antioxidant. The relevant invitro-in vivo studies, clinical trials and review articles were selected. Studies focusing on the effects of *Rasayana* on biological systems other than cardiovascular system were excluded. Selected studies were critically evaluated and consolidated to provide clear understanding of existing knowledge.

OBSERVATIONS AND DISCUSSION

Hridroga and *Rasadusthi:* The Ayurvedic view of cardiovascular pathology

Hridaya is considered as one of the *Trimarma* (three vital spots) of the body[8] and principle seat of *Ojas*.[9] *Hridaya* is the place of origin of two vital channels of the body *Rasavaha (*channels carrying nutrition) and the *Pranavaha srotas*.[10] Therefore, any pathology affecting the *Hridaya* directly impairs the body's essential nutrition and vitality. *Hridroga* refers to any disease condition affecting *Hridaya.* The classical textbooks further classify the *Hridroga* into five types based on the predominant *Dosha- Vataja, Pittaja, Kaphaja, Sannipataja* and *Krimija* (parasitic origin).[11]

The etiological factors of *Hridroga* can be classified into *Aharaja* (related to food*), Viharaja* (related to lifestyle) and *Manasika* (mental factors). *Aharaja* factors involve excess consumption of *Ushna* (hot*), Guru* (heavy*), Kashaya* (astringent taste*), Tikta rasa* (bitter taste*)* and *Adyasana* (consumption of food before the digestion of previous meal*)*. *Viharas* like *Ativyayama* (excess exercise), *Vegadharana* (suppressing natural urges*)* and *Manasika vikaras* such as *Chinta* (stress), *Bhaya* (fear) are known to cause *Hridroga*.[18] *Aharaja nidanas* like consumption of *Guru* and dietary practices like *Adyasana* may be correlated with high cholesterol diet which is a major risk factor for CVD. The *Manasika nidana* like *Chinta, Bhaya* can be correlated with persistent psychological stress, which is now considered as the predominant risk factor for coronary artery disease. [12]

The crucial event in the pathogenesis of *Hridroga* is *Rasa dusthi (*vitiation of *Rasa dhatu)* occurring due to *Tridosha dusthi* (vitiation of 3 *Doshas*).[13] This *Rasadusthi* eventually leads to *Agnimandya* (impairment of digestion) and formation of *Ama* (unprocessed metabolic byproduct). The *Ama* will lead to *Srotorodha* (blockage of channels) leads to *Hridroga*. Since *Rasayana* in general aims to correct the *Agnimandya,* removes *Ama* and improves the quality of *Rasa*, it is a logical intervention for *Hridroga* where *Rasa dusthi* (vitiation of *Rasa*) is major contributing factor.

Concept of *Rasayana* and its significance in cardiovascular disease

Rasayanatantra (geriatrics/*Jara chikitsa*) is the Ayurvedic branch dedicated to immunomodulation and healthy aging. Its primary function is to optimize the quality of *Rasa* (nutritive essence), which subsequently vitalizes all *Dhatus* (tissues). By correcting *Agni* (metabolic fire) and clearing *Srotas* (circulatory channels), *Rasayana* ensures that nutrients reach tissues competently. When preceded by *Panchakarma* to eliminate metabolic waste, these therapies ensure the peak functional integrity of *Doshas* and *Dhatus.* [14] In managing *Hridroga, Rasayana* offers a unique dual action: protecting the heart from further injury while simultaneously promoting the restoration of function.

These therapies are enriched with anti-inflammatory, antioxidant, and immunomodulating constituents that counteract the oxidative stress associated with cardiovascular disease pathology. Preclinical studies indicate that *Rasayana* drugs work by suppressing inflammatory cascades and strengthening endogenous antioxidant defense mechanisms. This limiting of initial damage is crucial, as cardiac aging leads to pathological changes such as hypertrophy, increased arterial stiffness, and impaired endothelial function. While existing medical modalities improve symptoms and reduce mortality, they often fail to replace damaged cardiomyocytes.[15] However, research suggests that plant-derived compounds can play a vital role in activating cardiac stem cells to facilitate myocardial regeneration.[16]

Specific *Rasayana* drugs have demonstrated a direct role in cardiomyocyte and vascular health. For example, curcumin found in *Haridra* slows endothelial senescence by reducing ROS formation, enhancing eNOS activity, and restoring NO bioavailability. This improves vasodilation and reduces arterial stiffness through the activation of SIRT1/NRF2 pathways and the suppression of the p53/p21 senescence axis.[17] Similarly, long-term administration of *Amalaki Rasayana* has been shown to reverse fibrotic remodeling in cases of left ventricular hypertrophy. By enhancing mitochondrial energy production and ATP use, it enables the heart to recover its optimal geometry and mechanical efficiency.[18]

Preclinical evidence

There are many preclinical and clinical studies done to explore the cardioprotective effect of different *Rasayana* drugs.

Table 1: Preclinical evidence for cardioprotective effects of selected *Rasayana* drugs

***Rasayana* Drug**	**Animal Model**	**Key mechanism**	**Specific Finding**
Shilajatu[19]	Wistar rats, myocardial injury was experimentally induced using Isoproterenol.	Mild positive effect on total antioxidant capacity and lipid peroxidation index.	Improvement in hemodynamic, attenuated cardiac troponin levels, reduced cardiac lesions.
Brahma rasayana and *Chyavana prasha*[20]	Doxorubicity induced cardiotoxicity model of swiss albino mice.	Reinforcement of antioxidant activity.	Both formulation at higher dose, reduced lipid peroxidation. Pre-administration of *Brahma rasayana* and *Chyavanaprasha* maintained the reduced glutathione, SOD levels near to normal.
Amalaki Rasayana[18]	Aging wistar albino rats/rats with pressure overload left ventricular hypertrophy induced by aortic constriction.	Enhancement of myocardial energetics and muscle contractile function. Modulation of signalling pathways	*Amalaki rasayana* increased the expression of proteins related to calcium handling and muscle contraction, antioxidant activity, oxidative phosphorylation, TCA cycle. Increased expression of ADRB1/2 and pCREB. Decreased expression of pAMPK and NF-kB.
Ashwagandha [21]	In-vivo experimental mode of Ischemia and reperfusion injury (adult male wistar rats).	Antioxidant activity and anti-apoptotic effect	Upregulation of ant-apoptotic protein, decrease in pro-apoptotic protein, reduced lipid peroxidation, prevented the decline in glutathione.
Arjuna[22]	ISO induced model of rats	Maintaining antioxidant enzyme activity, inhibiting lipid peroxidation, anti-inflammatory action.	Reduced the decline in fall of left ventricular pressure and cardiac output. Reduced the levels of inflammatory markers, restored fall in SOD and reduced glutathione level. Protective effect was comparable to standard drug.
Hridayarnava rasa[23]	Male New Zealand white rabbits in which atherosclerosis was induced by administration of high fat diet.	Anti-hyperlipidaemic and antioxidant activity.	Reduced the dyslipidaemia markers, reversed the atherosclerotic changes in the artery.
Curcumin from *Haridra*[24]	ISO induced animal model, doxorubicin induced rat model, high fat rat model different models.	Anti-inflammatory, anti-oxidant, lipid-regulation	Targets NF-kb and MAPK pathway, inhibition of pro-inflammatory markers, improvement of endothelial function.

Table 2: Clinical evidence for cardioprotective effects of selected *Rasayana* drugs

***Rasayana* Drug**	**Study design**	**Disease condition**	**Key outcome**
Arjuna [25]	Double-blind randomised control trial	Chronic heart failure	Found beneficial effects on exercise tolerance, quality of life and antioxidant status in participants. Significant change was not seen in LVEF.
Ashwagandha[26]	Double blind, randomised and placebo-controlled study	Cardiorespiratory endurance in healthy athletic adults	Enhanced the cardio-respiratory endurance evident from increase in maximum oxygen consumption.
Curcumin from *Haridra* [27]	Randomised controlled trial	Patients with diabetes and atherosclerotic cardiovascular drugs	Significant reduction in systolic and diastolic BP, Decreased levels of oxidative stress marker MDA, Decreased LDL levels, Decreased TNF-α.

Cardioprotective and Regenerative Mechanisms of *Rasayana*

The cardioprotective effect of *Rasayana* lies in its ability to act on multiple biological targets offering a distinct advantage over the single-target pharmacological therapy. Since CVD develops through several interconnected factors like sustained inflammation, oxidative stress and dyslipidaemia, *Rasayana* drugs offer a broader and more coordinated protective effect. Current evidences show these *Rasayana* drugs support cardiomyocyte survival through anti-oxidant, anti-apoptotic actions, counter atherosclerotic process through hypolipidemic and anti-inflammatory effects.

Antioxidant activity

Modern chronic diseases often arise from an imbalance between excessive free radical generation and deficient dietary antioxidant scavenging.[28] In the cardiovascular system, Reactive Oxygen Species (ROS) are primarily generated by mitochondria, xanthine oxidase, and NADPH oxidase. These species, such as superoxide anions and hydroxyl radicals, causing oxidative modification of lipids, proteins, and DNA. Pathological ROS levels damage the sarcolemma and mitochondria, specifically oxidizing endoplasmic reticulum Ca^{2+} ATPase and contractile proteins. This leads to contractile dysfunction, myocardial infarction, and heart failure. To counter this, the body relies on enzymatic (SOD, catalase, glutathione-s-transferase) and non-enzymatic (alpha-tocopherol, bilirubin) defenses.[29,30] *Rasayana* formulations, rich in polyphenols and vitamins, either directly neutralize ROS or augment these endogenous defenses. *Brahma rasayana* and *Chyavanaprasha* protect against doxorubicin-induced cardiotoxicity by replenishing antioxidant levels and safeguarding mitochondria. Similarly, *Arjuna* stem bark, containing arjunolic and gallic acids, stabilizes free radicals and prevents lipid peroxidation (evidenced by reduced TBARS and MDA). Continuous administration of *Arjuna* significantly increases SOD and catalase levels, demonstrating a dual action of direct scavenging and potentiating the heart's natural defense mechanisms.

Bioenergetics preservation and Anti-apoptotic effect

Maintaining viable myocardium is critical in CVD, particularly during ischemia-reperfusion were oxidative stress triggers apoptosis. As a regulated, energy-dependent process, apoptosis is a modifiable target that prevents the replacement of contractile units with fibrotic tissue [39]. *Ashwagandha* supports this by restoring a favorable Bcl-2/Bax ratio, inhibiting the caspase cascade and mitochondrial dysfunction to conserve cardiomyocytes. Beyond antioxidant effects, *Rasayana* herbs optimize mitochondrial energy metabolism. Mitochondrial dysfunction, characterized by disrupted oxidative phosphorylation (Ox Phos), is central to heart failure.[31] Evidence shows *Amalaki Rasayana* (AR) enhances mitochondrial performance by improving TCA cycle activity and Ox Phos efficiency, increasing ATP production to mitigate pathological remodeling and cardiac hypertrophy.

Anti-inflammatory activity

Anti-inflammatory mechanisms are essential for cardio protection because atherosclerosis is now recognized as a chronic inflammatory condition rather than mere lipid accumulation. Inflammation promotes endothelial dysfunction, enabling LDL infiltration and foam-cell formation which drive plaque development. Persistent inflammatory activity also weakens the fibrous cap, increasing the risk of plaque rupture and subsequent thrombosis, ultimately leading to events such as MI.[32] Curcumin found in *Haridra* also reduces inflammation by preventing the activation of NF-κB, and downregulation of transcription factor inflammatory pathways. These mechanisms decrease the infiltration of inflammatory cells into ischemic heart and reduce cardiomyocyte injury.

Modulation of key signalling pathways

The cardioprotective effect of *Rasayana* stem from their capacity to influence multiple molecular signaling pathways, substantiating the multi-target action. Drugs like *Arjuna* and *Ashwagandha* enhance the cellular survival by modulating the caspase cascade pathway. The *Amalaka rasayana* positively influenced the ADRB1/2 and pCREB. This improves the heart's response to stress, cell survival and protection. At the same time, it slows down the NF-kB, and pAMPK pathway. This reduced the inflammation, prevented the pathological remodelling.

Hypolipidemic effect

Dyslipidaemia is one of the major risk factors for cardiovascular diseases. Low density lipoprotein transports the cholesterol to the artery wall. It will subsequently lead to atherosclerotic cardiovascular disease. [32,33] The *Hridayarnava rasa* found to reduce the lipid level by decline the expression of HMG-CoA reductase gene and inhibition of CETP. By this the reverse cholesterol transport mechanism is enhanced and internal cholesterol synthesis has been reduced. A randomized controlled trial conducted on patients with coronary artery disease with *Arjuna* stem bark proved that consumption of bark powder significantly reduced the cholesterol levels.[34] The reduction in LDL levels will prevent the further progression of atherosclerosis.

These are the different mechanisms by which a *Rasayana* exert cardioprotective effect. The multi-targeted mode of action is one of the key strengths of *Rasayana* in cardio protection. CVD is inherently multi-factorial arising not from a single cause but from the convergence of multiple causes like oxidative stress, chronic inflammation, dyslipidaemia. This multi-target strategy is beneficial because by administration a single *Rasayana* can lower lipid levels, attenuate the inflammation and oxidative stress thereby providing cardio protection through multiple complementary mechanisms.

Limitations and Suggestions

Rasayana therapy offers a promising framework for CVD management, supported by preclinical studies that clearly define its molecular mechanisms. However, clinical research remains limited, with most studies focused on the rehabilitation phase rather than prevention. To advance this field, an integrated medical approach is essential. Future efforts must prioritize extensive clinical trials targeting the preventive phases of CVD and adopt novel drug delivery systems to enhance the bioavailability and therapeutic efficacy of *Rasayana* formulations.

Future Perspective

Clinical trials of *Rasayana* drugs which has significant cardioprotective effect supported by preclinical studies. Developing criteria for the selection of appropriate *Rasayana* drug according to the clinical condition of the patient. More detailed studies on drug-herb interactions and novel drug delivery systems.

CONCLUSION

This scoping review highlights the preclinical and clinical evidences supporting the vital role of *Rasayana* on the prevention and management of cardiovascular disease. The *Rasayana* exhibit cardioprotective effect through anti-oxidant, anti-apoptotic effect, anti-inflammatory effect, hypolipidemic effect or by modulation of cellular signalling pathways. A *Rasayana* drug mostly has multi-targeted action that mostly they act by more than one of above-said mechanisms. In addition to the protective effect *Rasayana* can provide an internal environment for cardiomyocyte regeneration and stimulate the repair mechanism of body. There is a necessity for the well-designed extensive clinical trials to ensure the safety and efficacy of *Rasayana* drugs in management of cardiovascular disease. As the medical world is in search for pharmacological agents for the regeneration and repair of myocardium, *Rasayana* either in the form of single drug or polyherbal formulation can be a solution.

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