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Hridya Activities of Hrid Dashemani Dravyas as an Antioxidant Formulation with Special Reference to Charaka - A Review



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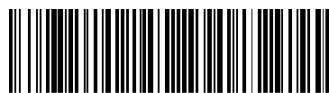
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ABSTRACT

Hridroga is one of those diseases mentioned in Ayurveda where in the description is quite brief. In view of increasing evidence of cardiac disorders presently, this aspect assumes added importance. Majority of present day illness are due to shifts in the balance of pro-oxidant and anti-oxidant haemostatic phenomenon in the body. Pro-oxidant conditions occur either due to increased generation of free radicals caused by excessive oxidative stress or due to poor scavenging of free radicals. Several lines of evidence suggest that free radical mediated oxidative damage may be a contributing factor for the development of coronary artery disease (Hridroga.) Many herbs are listed in Ayurveda as being Hrida, or good for the heart. In his classification, Acharya Charaka mentions the Hridya Mahakashaya. This is a collection of ten medications that are good for the heart. Each of the ten medications is an Amla Rasa Pradhana (sour in flavour) and a good source of vitamin C which is a powerful antioxidant. In this article, the medications listed in Hridya Mahakashaya are briefly described, along with their likely mechanisms of action.



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INTRODUCTION:

Cardiovascular diseases (CVD) remain among the 2 leading causes of death since 1975 with 633,842 deaths or 1 in every 4 deaths, heart disease occupied the leading cause of death in 2015 followed by 595,930 deaths related to cancer. CVD is also the number 1 cause of death globally with an estimated 17.7 million deaths in 2015¹.

Cardiovascular disease risk factors are categorized into -Modifiable and non-modifiable. Modifiable risk factors include – Hypertension, Diabetes, Hyperlipidemia, Obesity, Tobacco and physical inactivity, whereas non-modifiable risk factors include- Age (Male > 45 years, Female >55 years), Gender and family history².

Oxidative stress is an imbalance between production and manifestation of reactive oxygen species (ROS) and a biological systems ability to readily detoxify the reactive intermediates or to repair the resulting damage. CVD and atherosclerosis could be partly induced by oxidative stress pathways of ROS production are upregulated and oxidative damage to phospholipids and proteins has been consistently reported³.

Lipids, proteins, carbohydrates and DNA are all potential targets for chaotic oxidative attack of radicals. Polyunsaturated fatty acids (PUFA) residue (Fatty acids with more than 1 carbon-carbon double bond) lipoproteins make them particularly vulnerable targets for free radical oxidation, which may lead to Artherogenesis.

Oxidative modification hypothesis on Atherosclerosis⁴ :

Cholesterol that is present in the plaque is usually circulating Low density Lipoprotein (LDL) particles. which have been ingested by sub-endothelial macrophages. So when there is lot of exposure to high concentrations of native LDL Macrophages, they do not accumulate cholesterol after they reach to a point due to down regulation of LDL receptor mediated uptake in the cholesterol replete state. In contrast, these are oxidatively are modified forms of LDL are much more avidly taken up by cultured macrophages which become converted to cholesterol laden cells called 'foam cells'.

These LDL will not be down-regulated by cholesterol replete and this is taken up by a new receptor known as “Scavenger receptor”. LDL can be oxidized by all of the cell types found in arterial wall. Oxidized forms of LDL may also be atherogenic, as these Oxidized forms of LDL are chaemoattractant for Macrophages us smooth muscle cells, and this facilitates

monocyte adhesion to endothelium and entry into the subendothelial space. They are also cytotoxic towards arterial endothelial cells and inhibit the release of NO and the resulting endothelium dependent Vasodilation.

Also, Endothelial dysfunction is defined as a decreased production and availability of NO, with or without an imbalance between endothelium-derived contracting and relaxing factors associated with a pro-inflammatory and prothrombotic status. Under oxidative stress, ROS are able to mediate endothelial dysfunction and vascular abnormalities by disrupting the vasoprotective NO signaling pathway, leading to NO synthase (NOS) uncoupling. NOS are the enzymes responsible for the synthesis of NO from L-arginine in the presence of cofactors and dioxygen, but they are also able to produce superoxide anions. Three NOS have been identified: type I or neuronal NOS (NOS1 or nNOS), type II or inducible NOS (NOS2 or iNOS), and type III or endothelial NOS (NOS3 or eNOS). NOS1 and NOS3 isoforms are constitutively expressed in the heart, more particularly in striated muscle and endothelial cells, and possess calcium-dependent activity. The NOS2 isoform has calcium-independent activity. It is not constitutively expressed in the healthy heart but it is expressed in pathological conditions such as inflammation. When NOS are uncoupled, they switch from NO to superoxide anion production ($\bullet\text{O}_2^-$) and peroxynitrite (ONOO^-) by the association of the two preceding, leading to reduced bioavailability of NO and vasoconstriction. Peroxynitrite is involved in atherosclerosis progression by inhibition of vasorelaxation, decrease in the beneficial effects of NO on platelet aggregation and vascular smooth muscle cell proliferation, and oxidation of DNA and lipids⁵.

In Ayurvedic text word “Hridya” is generally used for the drug which is beneficial for the heart “Hridya Hitam Hridyam”. (Charak Su. 4/10). Thus Hridya means Cardiac tonic, the drugs which are helpful in maintaining the cardiac health Hridya Mahakashya -Group of Cardio Tonics Drugs are called as Hridya. Acharya Charak classified the drugs based on their pharmacological action in fifty Mahakashaya (class). One of them is Hridya mahakashaya the group of ten drugs that are beneficial for heart.

HRIDYA MAHAKASHAYA⁶ :

Amra, Amrataka, Lakucha, Karamarda, Vrikshamla, Amlavetas, Kuvala, Badar, Dadima and Matulunga these drugs come under Hridya mahakashaya.

SR.NO.	SANSKRIT NAME	LATIN NAME	FAMILY
1.	AMRA	<i>Mangifera indica</i>	Anacardiaceae
2.	AMRATAKA	<i>Spondias Mangifera/pinnata</i>	Anacardiaceae
3.	LAKUCHA	<i>Artocarpus lacucha</i>	Moraceae
4.	KARAMARDA	<i>Carissa carandas Linn.</i>	Apocynaceae
5.	VRIKSHAMLA	<i>Garcinia indica chois</i>	Guttiferae
6.	AMLAVETAS	<i>Garcinia pedunculata Roxb.</i>	Guttiferae
7.	KUVALA	<i>Ziziphus mauritiana Lam.</i>	Rhamnaceae
8.	BADAR	<i>Ziziphus jujuba Mill & Lamk</i>	Rhamnaceae
9.	DADIMA	<i>Punica granatum</i>	Pnicaceae
10.	MATULUNGA	<i>Citrus medica Linn.</i>	Rutaceae

Hridya Mahakashaya enlists fruits that contain Amla rasa and are rich in antioxidants which help in secondary prevention of heart diseases and vitamin C. According to Ayurveda, the Amla rasa is one of the six primary tastes, and it is believed to have specific qualities and effects on the body. In the context of the heart, it is said that Amla rasa nourishes or rejuvenates the heart, as indicated by the statement "Hridyam Tarpayati"⁷ (Charak Su. 26/42/2), which means "nourishes the heart."

OBJECTIVE OF THE STUDY:

To review the literature of Hridya Mahakashaya and Hridya karma.

MATERIALS AND METHODS:

Information on Hridya Mahakashay and Hridya Karma has been gathered through systematic research of possible Ayurvedic scriptures and other verifiable texts.

DISCUSSION:

Literary review of the drugs in Hridya mahakashaya :

1) Amra (*Mangifera indica Linn*) :

Rasa – Madhur, amla, kashaya

Guna - Laghu, ruksha (seed pulp), snigdha (fruit)

Veerya - Sheeta
Vipaka - Katu/ amla
Gana - Hridya, chardinigrahan, purishsamgrahaniya,mutrasamgrahaniya
mahakashaya (Charak)
Nyagrodhadi gana (Sushruta) (Vagbhat)

Useful Parts - Fruit, seed pulp, leaves, bark

Active principles - Vitamin A, B, citric acid, and gallic acid

High-performance liquid chromatography coupled to electrospray ionization and quadrupole time-of-flight mass spectrometry (HPLC-ESI- qTOF-MS/MS) analysis of MLS extract had been identified. neomangiferin, mangiferin, kaempferol-3-0-rutinoside, isoquercitrin, and quercetin as the main compounds and also reported that these compounds contributed directly to the antioxidant activity of MLS⁷.

2) Aamratak (*Spondias mangifera* (Linn. F. Kurz.) :

Rasa – Amla
Guna - Guru
Veerya - Ushna
Vipaka - Katu
Gana - Amla skandha, Hridya mahakashaya (Charaka)
aamradi Varga (Bhavaprakash, Raj, and Dhanvantari nighantu)

Useful Parts - Fruit, bark, leaves

Active principles - Beta-amyrin, oleanolic acid, beta-sitosterol

In an study conducted, Plant extracts of *Spondias mangifera* showed high antioxidant potential. Among all extracts, maximum antioxidant potential was observed in methanolic extracts of both callus (51.11%) and in vitro Significant free radical scavenging activity was observed in all extracts of callus and in vitro leaf through Beta-carotene bleaching assay. In the docking study, the main phytoconstituents of *S. mangifera* fruit, such as oleanolic acid, beta-sitosterol, and beta amyrin, show strong affinity for pancreatic α -amylase. These results

imply that *S. Mangifera* has α -amylase and α -glucosidase inhibitory properties and may be used as an antidiabetic with antioxidant characteristics⁸.

3) Lakucha (*Artocarpus lakoocha*) :

Rasa – Madhur, Amla, Kashaya

Guna - Guru, Vistambhi

Veerya - Ushna

Vipaka - Madhura

Gana - Phalavarga (Sushruta)

Aamradi phala varga (Bhavprakash nighantu)

Aushadhi varga (Kaiyyadeva nighantu)

Useful Parts - Fruit, seeds, bark

Active principles - Tannins, flavanoids, triterpenoides, saponins, glycosides

Phytochemical screening of the major fractions revealed that the methanol fraction of *A. lakoocha* contained the highest amount of phenols, flavonoids, and tannins as compared to other fractions. The fraction also showed the highest antioxidant activity⁹.

4) Karamarda (*Carissa carandas* Linn.) :

Rasa – Amla

Guna - Guru

Veerya - Ushna

Vipaka - Katu

Useful Parts - Root, fruit

Active principles - Vitamin C, Glycosides -Cardiac Glycosides.

The 95% of ethanol with 1% hydrochloric acid *C. carandas* extract yielded the antioxidant-enriched extracts with highest amount of anthocyanin. Cyanidin-3-O- β -glucoside increases endothelial nitric oxide synthase phosphorylation and preserves nitric oxide availability [171], which promotes endothelial cell migration and survival. Anthocyanins help to suppress

the endothelial cell activation promoted by the retention of apoB-containing lipoproteins (LDL, very low-density lipoprotein (VLDL), and apoE remnants) in the subendothelial space. Lipoprotein accumulation leads to an increase in proinflammatory receptors (Toll-like receptor 2) and cytokines (MCP-1 and interleukins, IL)¹⁰.

5) Vrikshamla (*Garcinia indica*) :

Rasa	– Amla, Madhura
Guna	- Guru, Ruksha
Veerya	- Ushna
Vipaka	- Amla
Gana	- Hridya mahakashaya, amla skanda (Charaka) Aamradiphala varga (Bhavaprakash nighantu)
Useful Parts	- Fruit, root bark, seed oil
Active principles	- Cuxanthone, isogarcinol, garcinol, and comboginol, morelloflavone, volksensiflovone

6) Amlavetasa (*Garcinia pedunculata Roxb.*) :

Rasa	– Amla
Guna	- Laghu, Ruksha
Veerya	- Ushna
Vipaka	- Amla
Gana	- hridya mahakashaya, amla skanda, dipaniya, and swasahara mahakashaya (Charaka)
Useful Parts	- Fruit
Active principles	- Pedunculol, garcinol, and combogenn, Flavonoids

The physiological effects of flavonoids include possible antioxidant activity, therefore, suggesting their role in the prevention of coronary heart diseases including atherosclerosis.

7) Kuvala (*Ziziphus mauritiana Lam*) :

Rasa – Kashaya, Madhura, Amla

Guna - Laghu, Snigdha

Veerya - Seeta

Vipaka - Madhura

Useful Parts - Fruits

Active principles – Flavonoids, triterpenes

A review of the literature shows that ZM is rich in biologically active compounds such as triterpenes, cyclopeptide alkaloids and flavonoids that have been shown to exhibit inhibitory effects on histamine release, COX-1&2, activation activity of choline acetyl transeferase, cytotoxic activity and immunological adjuvant activity.¹¹

8) Badar (*Ziziphus sativa Gaertn*) :

Rasa – Madhura, Amla

Guna - Guru, Snigdha

Veerya - Sheeta

Vipaka - Madhura

Gana - chardi nigrahana, swedopaga, virechanopaga, and hridya
mahakashay (Charaka)

Nyagrodhadi gana (Sushruta)

Useful Parts - Bark, leaves, fruits

Active principles - Leucocyanidine, mauritines, zizogegin, zeatin

Some studies have indicated that jujube contains a large number of active substances, such as polyphenol, flavonoid, triterpene, polysaccharide, ascorbic acid, cyclic adenosine monophosphate (cAMP). These active ingredients

have antioxidant, anti-inflammatory, antibacterial, liver protection, gastrointestinal protection, blood glucose reduction and anticancer effects.¹²

9) Dadima (*Punica granatum Linn.*) :

Rasa	– Kashaya, Madhura, Amla
Guna	- Laghu, Snigdha
Veerya	- Ushna
Vipaka	- Madhura, Amla
Gana	- Hridya and chardinigrahana mahakashaya (Charaka) Parushakadi gana (Sushruta)(Vagbhat)
Useful Parts	- fruit, fruit rind, and root bark, floral bud
Active principles	- Tannins, punicalin, punicic acid

Dadima is rich in flavonoids phenolic compounds which acts as a natural anti-oxidant.

10) Matulunga (*Citrus medica Linn.*) :

Rasa	– Amla, Madhura
Guna	- Laghu, Snigdha
Veerya	- Ushna
Vipaka	- Amla
Gana	- Hridya and chardinigrahan mahakashaya (Charaka) Phala Varga (Sushruta)(Ashtanga hridaya)
Useful Parts	- fruit, and root
Active principles	- Absciscic acid, abscisin, limonin, limocitrol

Phenolic compounds and ascorbic acid were identified as possible antioxidants which helps in free radical and nitric oxide scavenging activity.

HRIDYA ACTION:

Drugs of Hridya Mahakashaya comprise of Amla and Madhura rasa dravyas along with ushna veerya, Madhura vipaka and laghu snigdha gunas.

Amla rasa, due to its composition of agni (fire) and prithvi (earth) mahabhuta (elements), and qualities of snigdha, ushna and laghu guna plays a curative role in hrdroga (heart disease) by interrupting the progression of samprapti (pathogenesis). It accomplishes this through various actions:

Jataragni and Rasadhatwagni Deepana: Amla rasa stimulates jataragni (digestive fire) and rasadhatwagni (metabolic fire), promoting proper digestion and metabolism.

Vatanulomana: Amla rasa possesses the property of vatanulomana, which helps normalize samana vata (a subtype of Vata dosha) and facilitates the proper functioning of agni.

Formation of Ahara Rasa: The normal functioning of agni ensures the proper formation of ahara rasa (nutrient essence).

Improved Quality of Rasa Dhatu: With the correct functioning of agni and the formation of ahara rasa, the quality of rasa dhatu (plasma tissue) improves.

In the context of Hridayaroga (heart disease), the mentioned factors contribute to the formation of Aam (toxic metabolic waste), contamination of Rasa (nutrient plasma), and vitiation in Doshas (bioenergetic forces) that result in obstructions in the Rasavaha srotas (channels responsible for transporting nutrient plasma). This obstruction leads to the aggravation of Vata (the air and ether element), which in turn reduces the supply of Pranavayu (vital air) and nutrition to the heart (Hridaya).

Amla ras (sour taste) helps restore Vata to its normal state and proper channel due to its specific action known as Vatanulomana (balancing Vata). Additionally, Amla rasa aids in opening the channels through its ushna veerya (hot potency). The clear channels facilitate Dhatu Poshana (tissue nourishment) and promote the production of Ojas (a factor that enhances immunity). Amla rasa acts as an antioxidant, helping to restore the vitiated Vayu (air element) to a healthy state and pacify Ama (toxicity). As a result, drugs belonging to the Hridya Mahakashay (a group of herbs beneficial for the heart), which are predominantly rich in Amla rasa, play a significant role in maintaining a healthy heart.

MODERN ASPECT OF HRIDYA:

Most of the drugs that are present in Hridya mahakashaya are rich in phenol compounds such as flavonoids, glycosides etc. Antioxidants play a crucial role in protecting cells from damage caused by reactive oxygen species (ROS). ROS are highly reactive molecules that can be

generated as byproducts of normal cellular processes or as a result of exposure to environmental factors such as pollution, radiation, and certain chemicals.

Oxidative stress occurs when there is an imbalance between the production of ROS and the body's antioxidant defenses. This imbalance can lead to cellular damage and has been associated with various health conditions including diabetes, cancer, cardiovascular diseases (CVD), neurodegenerative disorders, and the aging process.

Flavonoids are a class of naturally occurring compounds found in various fruits, vegetables, and other plant-based foods. They have been extensively studied for their antioxidant properties and have shown effectiveness in preventing lipid peroxidation. Lipid peroxidation is a process where free radicals attack and damage lipids (fats) in cell membranes, leading to various diseases such as atherosclerosis, diabetes, hepatotoxicity, inflammation, and even accelerating the aging process. Flavonoids act as exogenous antioxidants, meaning they can be consumed through the diet or as supplements. They directly interact with free radicals, undergoing oxidation themselves and forming less reactive species. Flavonoids employ several mechanisms to exert their antioxidant effects. These mechanisms include inhibiting the activity of nitric-oxide synthase and xanthine oxidase, modulating channel pathways, and interacting with other enzyme systems¹³. The antioxidant potential of flavonoids has been found to be stronger than that of vitamin C in certain cases. However, it's important to note that the antioxidant effects of flavonoids can vary depending on the specific compound and its concentration, as well as factors such as bioavailability and interactions with other substances in the body. In addition to their antioxidant properties, flavonoids have been associated with other health benefits, including anti-inflammatory, anti-cancer, and cardiovascular protective effects. Including a variety of fruits, vegetables, and other plant-based foods in your diet can help ensure an adequate intake of flavonoids and other beneficial compounds that support overall health. As citrus fruits are rich in vitamin C, vitamin c is also a potent anti-oxidant, Vitamin C is an electron donor and therefore a reducing agent. All known physiological and biochemical actions of vitamin C are due to its action as an electron donor. Ascorbic acid donates two electrons from a double bond between the second and third carbons of the 6-carbon molecule. Vitamin C is called an antioxidant because, by donating its electrons, it prevents other compounds from being oxidized¹⁴. These are the possible mechanisms in which the hridya mahakashaya helps in preventing heart disease.

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