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REVIEW ARTICLE

An Insight into the cardioprotective properties of *Prisniparni* (*Desmodium gangeticum* (L)DC) through its secondary metabolites.

Mridula. M.K [1], P.Y. Ansary [2], Sara Monsy Oommen[3].

[1]PhD Scholar, Dept. of Dravyaguna vijnana, Govt. Ayurveda College, Tripunithura.
[2]Professor&HOD, Dept. of Dravyaguna vijnana, Govt. Ayurveda College, Tripunithura.
[3]Professor&HOD, Dept. of Dravyaguna vijnana, Govt. Ayurveda College, Kannur.

*Email: drmridulamk@yahoo.com

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Abstract

Prisniparni is a medicinal plant that is often used in the formulation of many Ayurvedic medicines. Even though some controversy exists about the botanical source of the plant, Kerala physicians generally use *Desmodium gangeticum* (Linn.) DC. of the Leguminosae family as *Prisniparni*. Specific usage of the drug in *hridroga* is emphasized in traditional Ayurvedic textbooks and regional books of Kerala. The results of recent preclinical studies support *Prisniparni*'s traditional use in *hridroga.* However, their clinical and scientific validation is lacking, especially in terms of their mechanism of action. The therapeutic potential of medicinal plants depends on their secondary metabolites. The plant's pharmacological activity may be due to the combined activity of its secondary metabolites. Based on this, a literature search on secondary metabolites of *Desmodium gangeticum* (Linn.) DC was done by electronic and hand search. Results of this review revealed the richness of alkaloids and polyphenols in *Desmodium gangeticum* (Linn.) DC which are antioxidant and anti-inflammatory in nature. The findings support the plant's cardioprotective potential and its traditional use since inflammation and oxidative stress are reported to be major contributors to cardiovascular diseases.

Introduction

Prisniparni is a plant with various uses in Ayurveda dating back to the Vedic period. It's listed as a part of *dasamoola*[1] and a member of the *amsuumatidwaya*[2] in the Samhita period. Roots are the most useful part of the plant[3], but seeds and leaves are also useful[4]. It is used by Ayurvedic physicians in vitiated conditions of *vata*, *Jwara (*fever)[5], *kasa* (cough), *swasa* (Bronchitis and asthma)[6],*hridroga*(cardiopathy)[7,8] etc. But some controversy exists regarding the botanical identity of the drug *Prisniparni* in southern and northern part of India. It is described that the controversy arises due to regional variation. However, the Physicians of Kerala generally uses the plant *Desmodium gangeticum* (Linn.) DC. of Leguminosae family as *Prisniparni.* It is commonly known as *orila* in Malayalam[9].

Specific usage of the plant in the management of *Hridroga*[10]is emphasized in *Ayurveda classical text books and some regional Ayurveda books of Kerala.* Acharya Charaka has listed it under *ghrita* preparations

advocated orally in curing *hridroga* and *Paithikahridroga in trimarmeeya chikitsa adhyaya*[11]. He referred it as the best of the *sangrahika* (astringent), *vatahara* (alleviates vata), *deepaneeya* (promotes digestion), and *vrishya* (increases virility) medications[12]. It has been identified by Acharya Susrutha as a component of the *rodradhi basthi*, a panchakarma therapy formulation used to treat *hridroga*[13]. Acharya Vagbhata mentioned *Prisniparni* under *Vidaryadi gana* having *hridya karma* in Ashtanga Hridaya[14]. The drug serves as an ingredient of medicated ghee, *Amritaprasha ghrita,* which is *hridayamayapaham*[15]. *Prishniparni* is included in the preparation of *Mahasneha* (mixture of all the four fats, ghee, oil, muscle fat and marrow) which is administered orally for curing *vatika hridroga*[16]. *Ksheerapaka* made up of *prisniparni* root is recommended for oral administration in *hridayagata vata*, according to *vatavyadhi chikitsa*.[17,18] It is evident from all of these formulations that *Prisniparni* plays a crucial role in *hridroga chikitsa*. Therefore, an in-depth understanding of the plant's pharmacological, biochemical, and biomolecular properties will improve its rational application in the avoidance and control of *hridroga*. Recent preclinical investigations significantly indicate the efficacy of *Desmodium gangeticum* (L) DC in cardiac hypertrophy,[19,20] myocardial reperfusion injury[21,22,23]and myocardial infarction[24].In a clinical study, *ksheerapaka* made up of *prisniparni* root was found to reduce symptoms of stable angina in patients[25].In vitro experimental studies *ksheerapaka* of *Prisniparni* revealed its cardiotonic[26,27]and antioxidant properties[28].These findings support the traditional use of *Prisniparni* in *Hridroga.*

Plants have been used as a source of biologically active compounds for centuries. Increasingly, people are turning to plant-herbal remedies to avoid synthetic drugs' long-term side effects. Researchers are still investigating medicinal plants for potential drug applications. *Prisniparni* is one of several plant drugs available for the treatment of heart disease. They can be used alone or in combination with chemical drugs to prevent cardiovascular problems[29]. However, their clinical and scientific validation is lacking, especially in terms of their mechanism of action[30].The secondary metabolites of medicinal plants determine their therapeutic potential. Most secondary metabolites have pharmacological, toxicological, or biological consequences. There is scientific evidence that mixing various defensive compounds results in a synergistic potentiation of biological activities. As a result, the plant's pharmacological effects may be due to the combined action of its secondary metabolites[31].Evaluation *Desmodium gangeticum* (L) DC of revealed the richness of alkaloids and polyphenols, which may be reason of its high therapeutic potential. Considering all these factors, this review is an attempt to explain the cardioprotective activity of the plant DG based on its reported secondary metabolites. Thereby providing a possible explanation on the use of *Prisniparni* in the management of heart disease.

Materials and Methods

All available information on secondary metabolites of *Desmodium gangeticum* (L) DC was gathered through an electronic search and a library search of peer-reviewed academic articles. Hand search of Ayurveda classical text books, unpublished PG thesis and other relevant text books were also conducted.

Results

Desmodium gangeticum (L) DC is reported to be rich in alkaloids, flavonoids, terpenoids, and steroids. The abundance of alkaloid and phenolic groups in *Desmodium* species may explain their diverse biological functions, including *Desmodium gangeticum* (L) DC.[32] The table below lists the key classes of phytoconstituents of the plant, which include alkaloids, flavonoids, steroids, and terpenoids.[33,34,35]

Table: 1 - Alkaloids

Sl no	Aerial part	Root
1	Indole-3-alkylamines	Berberine
2	N, N-dimethyl tryptamine	Pilocarpine
3	5-methoxymethyl tryptamine	Kopsinine
4	5-methoxy amine oxide	Galanthamine
5	Hordenine	Atropine
6	Candicine	Carboline
7	ß-phenylethylamine,	Gangenoid
8	Hypaphorine	N,Ndimethyltryptamine,
9	N-methyl tyramine	N,Ndimethyltryptamine N_b,-oxide
10		Hypaphorine
11		Hordenine
12		Candicine
13		N-methyltyramine,
14		Beta phenylethylamine.
15		Halostachine

Table: 2 - Polyphenols

	Aerial part	Root	Leaves
Pterocarpans	-	Gangetial Gangetin Desmocarpine Desmodin Gangetinine	-
Flavones	-	4-O-alfha-L rhamnopyranosyl (1–6)-ß-d glucopyranoside	-
Phenolic acid	1.salicylic acid 2.caffeic acid 3. chlorogenic acid 4. Protocatechuic acid (3,4-dihydro benzoic acid) 5. gallic acid	-	-
Flavonoid glycoside	Rutin Quercetin-7-O-ß-D glycopyranoside, kaempferol-7-O-ß-D glycopyranoside 4,5,7 trihydroxy 8-prenyl favone 4-O-L-rhamnopyranosyl (1–6) D glycopyranoside 8-C-prenyl-5,7,5, trimethoxy-3,4- methylene dioxy flavones	-	-
Isoflavone			Genistein 2'-hydroxygenistein
Isoflavanone			Dalbergioidin Diphysolone kievitone. desmocarpin

Table 3: Terpenoid and steroids

	Aerial part	Seed
Terpenoid	ß-Amyrone	
Steroids	Stigmasterol lupeol ß-sitosterol	Amino glucosylglycero-lipid

Gino A Kurian et.al [36,37] used GC-MS to identify 4-[2-(dimethyl amino) ethyl] phenol, a G protein agonist and alpha-asarone, a potent antioxidant and 2,5-bis (1,1-dimethyl ethyl) phenol from the root of the plant DG. These constituents are well-known for their effects on cardiac tissues.

Table 4: Secondary metabolite and biological activity.

Secondary metabolite	Biological activity
Salicylic acid.	Blocks HMGB1, a protein that causes inflammation in injured tissues.
Caffeic Acid	Antioxidant and anti-inflammatory properties. Prevents oxidative stress and thus DNA damage caused by free radicals.
Chlorogenic acid	anti-oxidant, scavenges free radicals, which inhibits DNA damage. Anti-inflammatory, antilipidemic, and antioxidant. Protects vascular health by inhibiting ED.
Protocatechuic acid (3,4-dihydro benzoic acid)	Anti-inflammatory Anti-oxidant promotes the expression of antioxidant enzymes by activating Nrf2 signalling pathways, which reduces oxidative stress and its accompanying issues like endothelial dysfunction.
Gallic acid	Antioxidant anti-inflammatory Improves cardiac dysfunction, reduces cardiac fibrosis
Rutin	Anti-inflammatory and antioxidant activity. Through ROS-scavenging processes, they lower the degree of oxidative stress. alleviated cardiac dysfunction and decreased cardiomyocyte apoptosis in septic mice ERK, JNK, and MAPK pathway are suppressed to prevent heart hypertrophy. protects the heart by activating SIRT1/NRF2 pathway. By lowering growth factor and MMP expressions, rutin reduces heart fibrosis. Reduces pathological cardiac remodelling.
Quercetin	antioxidant.studies have reported that quercetin may be applied to cardiovascular diseases, including atherosclerosis, ischemia-reperfusion injury, cardiotoxicity, and hypertension.
Pterocarpans	Could be protein tyrosine phosphate kinase inhibitors Which can significantly contribute to cardiovascular disease and endothelial dysfunction.
Gangetin	In the exudative and proliferative stages of inflammation, showed significant anti-inflammatory effect. In the hot plate method and acetic acid-induced writhing, analgesic effect was observed in a dose-dependent manner.
Desmodin	a potential inhibitor of cyclin-dependent kinase 5.Cyclin-dependent kinase inhibitor drugs have emerged as potential anti-inflammatory agents that can influence the resolution of inflammation.
kaempferol-7-O-ß-D glycopyranoside	free radical scavenger
Gangenoid	Anti-inflammatory
(17Z,20Z)-hexacosa-17,20-dien-9-one (HCDO)	Anti-inflammatory
Berberine	Recent researches reported biological activities including the reduction of blood sugar, regulation of lipids, as well as anti-arrhythmic and cardio-protective effects
Asarone	Anti-inflammatory
Hordenine	Positive inotropic effect upon the heart, increases systolic and diastolic blood pressure, peripheral blood flow volume
Atropine	provides potential clinical use in the targeted therapy of an abnormally low heartbeat since it increases cardiac rate and the force of cardiac contraction.
Beriberine	Due to its effects on potassium channels prevents ventricular fibrillation. Antiplatetic activity, lipid lowering activity, antiarrhythmic effect
Pilocarpine	maybe by activating K+ current mediated by M3 receptors, helps to change the cellular electrical properties of the hearts.
Galanthamine	Alleviate inflammation, In myocardial I/R rats, activating the AMPK/Nrf2 pathway reduced ERS -associated apoptosis, myocardial fibrosis, and cardiac dysfunction.
Carboline	Antioxidant, Cardioprotective

Discussion

Cardiovascular disease is caused by several factors, such as reactive oxygen species formation, oxidative stress, immune cells, and inflammatory signalling. And among the multiple pathologies, atheroma formation leading to atherosclerosis is considered as the beginning of CVDs. So, the drugs having lipid lowering, antiplatelet, thrombolytic, antioxidant, anti-inflammatory and free radical scavenging activities will be beneficial in the management.

Oxidative stress has a significant impact on the pathophysiology and development of cardiovascular disease. And one of the main causes of oxidative stress is the production of reactive oxygen species (ROS). In addition, both are associated with endothelial damage linked to cardiovascular disease, atherosclerosis progression, and myocardium injuries caused by sustained myocardial infarction and ischemia reperfusion. It is well known that a lack of nitric oxide (NO)-dependent vasorelaxation poses a serious threat to the development of cardiovascular disease, and ROS degradation is one factor contributing to the reduction in NO bioavailability. Therefore, antioxidants are becoming increasingly popular strategies for reducing ROS in the vasculature. Polyphenols are plant metabolites that have antioxidant properties and regulate various cellular antioxidant defence mechanisms. They change a wide range of targets involved in the pathogenesis of cardiovascular disease, such as eNOS and NO, inflammatory cytokines including TNF, IL-6 and IL-8, VCAM-1 and ICAM-1, as well as SIRT1, MAP38 kinase, NF-B, and AP-1, among many others[70].

A diet high in flavonoids may lower the chance of developing cardiovascular disease, according to epidemiological studies. Quercetin in particular helps to alleviate endothelial dysfunction and lower blood pressure. This may be accomplished by enhancing the strong vasodilator NO's bioavailability[71]. *Desmodium gangeticum* (L) DC is rich in polyphenols and that may be the reason behind its antioxidant capacity and cardio protection. Recently, there is growing consensus on the hypothesis that the specific intake of food and drinks with high concentrations of flavonoids may reduce CVD risk[72]. In *Ashtanga hridaya Uttara sthana*, it is advised to give cow's milk or goat's milk medicated with roots of *Sthira (Prisniparni)* for children who were not receiving enough breast milk from mother. This points out its nutritional value as well[73].

The second-largest class of natural isoflavonoids is called pterocarpans[74] which is most frequently found in the Fabaceae family[75]. Pterocarpans can lower total and low-density lipoprotein cholesterol levels, which lowers the chance of developing a number of ailments, according to scientific research[76]. They also have platelet aggregation inhibition activity, anti-oxidant activity and can modulate inflammation[77,78]. *Desmodium gangeticum* (L) DC is a rich source of pterocarpans like Gangetial,Gangetin, Desmocarpine, Desmodin, and Gangetinine. A recent in silico molecular docking investigation suggested that *Desmodium gangeticum* (L) DC pterocarpans might act as PTP kinase inhibitors. This enzyme significantly contributes to cardiovascular disorders[79]. Researches also reported the promising activities of alkaloids of *Desmodium gangeticum* (L) DC especially anti-inflammatory and anti-oxidant activity that supports cardio protection.

When it comes to endothelial cell activation and dysfunction, which are linked to CVDs, the inflammatory response is quite important[80]. Various inflammatory cells have been shown to contribute to vascular oxidative stress, according to recent studies. Researchers demonstrated the protective effect of classical therapies for inflammatory disorders in CVDs, which have a feature of normalization of oxidative stress[81]. *Desmodium gangeticum* (L) DC contains many phytochemicals with anti-oxidant and anti-inflammatory activity and this may make it a potent drug candidate for the management of cardiovascular diseases.

Conclusion

This review reveals the pharmacological activity of several secondary metabolites of *Desmodium gangeticum*(L)DC, contributing insight into its cardioprotective potential and substantiating its traditional use. Through the study of secondary metabolites in medicinal plants, we can better explain how drugs work to the scientific community. Furthermore, it is necessary to conduct computational system biology studies on Ayurvedic medicinal plants using their secondary metabolites. This will help to understand the action of drugs in various disease pathways and help drug discovery process.

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