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THE ANTIHYPERLIPIDEMIC ROLE OF *PLUCHEA LANCEOLATA*: A NATURAL REMEDY FOR LIPID DISORDERS

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Abstract

Pluchea lanceolata (Asteraceae), commonly known as Rasna, is traditionally used for antipyretic and anti-inflammatory properties. This study investigates the antihyperlipidemic potential of *Pluchea lanceolata*, a medicinal plant known for its rich content of bioactive compounds. Quercetin, Isorhamnetin, β-sitosterol, Daidzein, Hesperidin and β-sterol are present in *Pluchea lanceolata.* These are key phytoconstituents that plays a crucial role in reducing cholesterol levels and maintaining cardiovascular health. These bioactive compounds are believed to exhibit lipid-lowering effects by modulating lipid metabolism, improving the lipid profile, and reducing the risk of atherosclerosis. By stabilizing atherosclerotic plaques, they prevent plaque rupture, which is a significant cause of cardiovascular complications. Due to its promising pharmacological properties, *Pluchea lanceolata* could be explored further as a natural alternative for the management of hyperlipidemia and associated cardiovascular diseases, offering a complementary approach to conventional therapies.

Keywords: *Pluchea lanceolata,* Rasna, Antihyperlipidemic, Atherosclerosis, cardiovascular diseases

Introduction

Fast food consumption and sedentary lifestyles have raised the risk of obesity and obesity-related illnesses [1]. As per the Centres for Disease Control and Prevention report, 26% of boys and 48% of girls do not regularly engage in intense exercise [2]. Along with bad dietary choices made by young people in recent years, the obesity pandemic has been largely attributed to the rising consumption of fast food and considerable changes in eating patterns in recent times [3]. This poses a serious risk to the public's health. Overweight and obesity are the main risk factors for non-communicable diseases linked to years reduced as a result of cardiovascular diseases [4,5]. Because of CVD (Cardio vascular disease), the death rate in the USA has risen from 18.6% to 31.6% over the last ten years [6]. Atherosclerosis, a CVD condition where the arteries thicken due to cholesterol build-up, is a key contributor to rise in incidence of the CVD [7]. Research has shown that body adiposity and HFD (high-fat diet) especially saturated fat is linked with each other [8]. Increased body fat can lead to the formation of ROS (reactive oxygen species), which can then increase the release of hormone like TNF-α (tumor necrosis factor - alpha) and adipokine, ultimately contribute to promote the chronic inflammation [9]. This chronic inflammation, which is induced due to the high-fat diet, is a key contributor for the development of cardiovascular diseases, particularly hyperlipidemia which is a major risk factor to cause

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atherosclerosis. Saturated fats in the diet lead to an increase in LDL (low density lipoprotein), which pierces the arterial walls and gets oxidized. Then these oxidized LDL (ox-LDL) will trigger an inflammatory response, drawing immune cells such as macrophages on the site [10,11]. Then the macrophages will engulf the ox-LDL, convert into foam cells that assemble and pile up fats in the arteries. Over the time, arteries were narrowed by fibrous plaques which are evolved from these deposited fats and ultimately resulting in to restriction of blood flow through arteries.

The chronic inflammatory environment further destabilizes these plaques which increases the risk of rupture [12]. Plaque rupture can further form the blood clots, which can obstruct the flow of blood, strokes, heart attacks and other severe cardiovascular conditions. Thus, a diet which are high in saturated fats generally sets off a cascade of pathological processes that culminate in atherosclerosis and its associated risks **Figure 1** [13].

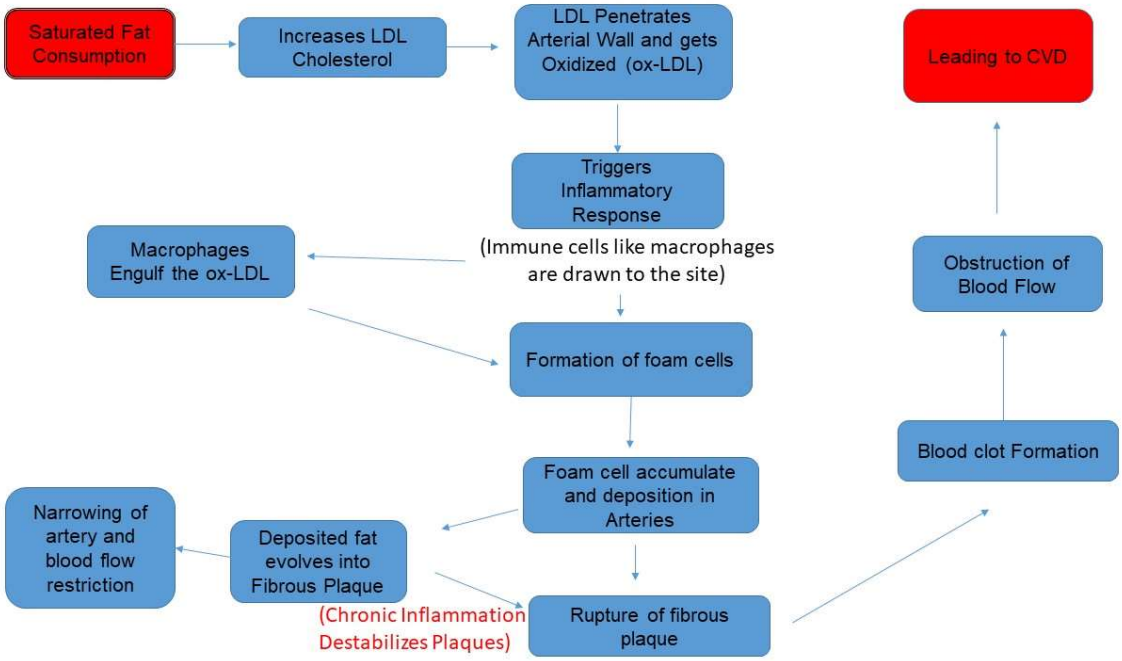

Figure 1: A cascade of pathological processes of saturated fat leads to Cardiovascular risk

India is endowed by a vast abundance of medicinal plants, India is regarded as the global centre for herbal medicine [14,15]. *Pluchea lanceolata*, a member of the Asteraceae family, which is a versatile plant has a wide spectrum of medicinal activities [16]. In Ayurvedic medicine, *Pluchea lanceolata* is commonly used to treat rheumatoid arthritis, fever, inflammation, and discomfort. In addition, it functions as a nerve tonic for conditions like persistent nervous system inflammation, sciatica, and neuritis [17]. The most common places where rasna are found is Punjab, Rajasthan, Upper West Bengal, Uttar Pradesh in India and as well as in neighbouring Asian nations and North Africa [18]. The phytochemicals such as quercetin and isorhamnetin have been identified in *Pluchea lanceolata* [19]. Quercetin (a flavonoid) is reported to inhibit the formation of foam cells induced by oxidised LDL (ox-LDL) and delay senescence [20], whereas isorhamnetin is able to reduce adipogenesis mediated by promoting pancreatic beta cell proliferation and function through moderate level signalling in Wnt signalling pathways and by modulating biological processes involved in obesity by PPAR (peroxisome

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proliferator-activated receptors) [21].

BOTANICAL DESCIRPTION

It is a perennial herb that grows between 30 and 60 cm tall on the Indo-Gangetic plains.

- **Leaves:** The leaves are sessile, oblanceolate or oblong, coriaceous, finely silky, and pubescent on both surfaces. The margins are whole or barely dentate near the apex. The leaves are 2–6 cm in length.
- **Flowers** - Many headed compound corymbs have flowers that are white, purple, yellow, or lilac in colour.
- **Capitulum:** The capitulum has corymbs and is ovoid or campanulate, measuring 6-7 mm in compound pubescence.
- **Involucre:** The outer involucral-scale is 2.5–4.0 mm long, 2 mm broad, 5–3 serrate, obtuse, silky pubescent, and tinged purple outside the apex. The inner involucre is ovoid or broadly campanulate with imbricated scales. The outermost scales are commonly broken into 1-2 shallow lobes, while the interior ones are few, linear, scarious, subacute, slightly longer, and narrower than the outer ones. All of the scales are stiff when dry.
- **Receptacle:** The Receptacle is bare and flat. [22]
- **Stem:** The cylindrical, herbaceous stem has a smooth outer surface that is hairy, branching, and pubescent branches that are terete, ashy, and pubescent.
- **Roots:** The roots are rather twisted and taper progressively over a length of 10 to 20 inches, with a diameter of approximately 3 to 20 mm. [23]

Antihyperlipidemic potential of Flavonoids present in *Pluchea lanceolata:*

Anti-inflammatory

Pluchea lanceolata, rich in the phytoconstituent quercetin, demonstrates significant potential for antihyperlipidemic and anti-inflammatory activity. *Quercetin*, a well-known flavonol present in *Pluchea lanceolata*, reported to lower cholesterol, triglycerides, and levels of glucose in animal models. Additionally, it enhances adiponectin secretion, which plays a critical role in improving lipid metabolism. [24]. *Quercetin* stabilizes atherosclerotic plaques by reducing oxidative stress, inhibiting LDL oxidation, and decreasing matrix metalloproteinase 1 expression [25, 26]. It also reduces inflammation by controlling TNF-a, nitric oxide, and IL-6 which helps combat dyslipidemia and insulin resistance [27-31]. It also inhibits the production of inflammation inducing enzymes like LOX (lipoxygenase) and COX (cyclooxygenase) enzyme [32,33]. Although quercetin's effects on oxidative stress in human studies are inconsistent, its ability to lower lipids and improve metabolic health underscores its potential as an antihyperlipidemic agent. This highlights that the quercetin present in *Pluchea lanceolata* performs a significant part in regulating lipid profiles and effectively combating hyperlipidemia [34].

Anti-obesity

Numerous positive health effects of flavonoids have been demonstrated, including the prevention and treatment of obesity, age-related disorders, cancer, cardiovascular disease, and type 2 diabetes mellitus.

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[21,35,36]. The presence of important phytoconstituents such as isorhamnetin, which enhances the plant's therapeutic efficacy and reduces adipogenesis to produce anti-inflammatory, anti-obesity, and diabetic effects, makes *Pluchea lanceolata* a powerful medicinal tool [37].

Research conducted on pre-adipocytes indicates that isorhamnetin inhibits the production of fat by downregulating important adipogenic genes such as PPAR. It also lowers LDL, total, and HDL cholesterol in mice given a high-fat diet, but it has no effect on plasma triglyceride levels. Additionally, it inhibits the production of triglycerides by decreasing the activity of GPDH (glycerol-3-phosphate dehydrogenase). Isorhamnetin inhibits the expression of genes linked to fat storage while influencing Wnt antagonists such as sFRP1 and Dkk1. Its anti-adipogenic activities are mediated through the PPAR and Wnt signalling pathways. This illustrates the ability to reduce hyperlipidemic potential of *pluchea lanceolata* [38].

Cholesterol-lowering Effect

One of the main phytoconstituents found in *pluchea lanceolata* is β-sitosterol, which is well known for its ability to prevent the intestinal absorption of cholesterol. By vying with dietary cholesterol for absorption into micelles, it successfully decreases serum cholesterol levels. Since ancient times, *Pluchea lanceolata* has been used to treat inflammation and hyperlipidaemia. This indicates that β-sitosterol has a significant role in managing cardiovascular diseases linked to high-fat diets. Because of its pharmacologic properties, which include anti-inflammatory, antioxidant, and cholesterol-lowering benefits, it can be considered a promising candidate for additional research on the treatment of hyperlipidaemia [39]. Another phytoconstituent found in *Pluchea lanceolata*, called daidzein, is also said to have anti-inflammatory, antioxidant, and cholesterol-lowering properties. Daidzein is a synthetic oestrogen that works in multiple ways to prevent cancer. It does this by suppressing the activity of matrix metalloproteinase-2, which also helps to prevent cancer, and by encouraging the differentiation of osteoblasts, which helps to prevent osteoporosis. Daidzein improves endothelial function by blocking caveolin-1, which boosts HDL cholesterol, decreases LDL cholesterol, and triglycerides while also increasing nitric oxide generation. Moreover, it alters signalling pathways such as PI3K-PKB/Akt to achieve anti-inflammatory and cardiovascular benefits. To improve its solubility and bioavailability, formulations based on nanotechnology, such as lipid carriers and polymeric nanoparticles, have been investigated [40].

Other therapeutic effect of *pluchea lanceolata*

Antimalarial Effect:

The activation of significant pro-inflammatory immune responses is closely associated with the clinical symptoms of severe malaria. In vitro antiplasmodial activity against the chloroquine-sensitive Plasmodium falciparum NF54 strain was demonstrated by the aerial portions of *Pluchea lanceolata*. With IC50 values of 4.97 and 4.77 mg/ml, respectively, the hexane extract and TxAc (taraxasterol acetate) showed notable activity among the other extracts. Pentacyclic triterpene TxAc also showed anti-inflammatory properties by blocking pro-inflammatory cytokines TNF-α and IFN-γ in mouse malaria produced by Plasmodium berghei. TxAc was not harmful to peritoneal macrophages, according to in vitro cytotoxicity experiments. These results demonstrate the superiority of *Pluchea lanceolata* as

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a source of anti-inflammatory and antimalarial chemicals. [41]

Neuroprotective

The hippocampal region is implicated in memory and learning, and it is one of the brain's most susceptible regions to ischaemic injury and stroke. Severe inflammation and oxidative stress from stroke can result in neurodegeneration and cellular death [42, 43]. When HAPL (hydroalcoholic extract of *Pluchea lanceolata*) was administered to rats in a model of ischaemic hippocampus injury, significant neuroprotective benefits were seen. Better performance in the Morris water maze demonstrated the improvements in locomotor activity, exploratory behaviour, and cognitive skills brought about by HAPL therapy. Moreover, it maintained dendritic branching, especially in CA1 neurones, and shielded pyramidal cells in the hippocampal CA1 and CA3 areas. Because *Pluchea lanceolata* has antioxidant qualities that are linked to its neuroprotective benefits, it may be useful in the treatment of brain damage caused by ischaemic stroke. [44]

Anti-neurinflammatory

Astrocytes are immunocompetent cells that present antigens and secrete immunomodulatory cytokines, which contribute significantly to nervous system inflammation [45]. By blocking pro-inflammatory cytokines such as TNF-α, IFN-γ, and IL-6, bioactives derived from *Pluchea lanceolata*, tartascosterol (Tx) and its derivative TxAc, successfully decreased lipopolysaccharide (LPS) induced neuroinflammation in rat glial cells (C6). While TxAc only demonstrated substantial suppression at higher dosages, Tx was more powerful against all cytokines. These results were corroborated by molecular docking experiments, which showed that TxAc modifies inflammation via the TNF-α pathway, whereas Tx operates largely through the NF-κB pathway. Strong binding affinities between the two drugs and important inflammatory proteins increased their anti-inflammatory effects. Crucially, neither substance showed signs of harm to cells. These findings support the long-standing Ayurvedic practice of using *Pluchea lanceolata* to treat neuroinflammation, especially when it comes to immune response pathway modification. They also point to the plant's potential as a therapeutic agent for neurodegenerative diseases. [46]

Immunosuppressive

Pluchea lanceolata 50% ethanolic extract and its bioactive chloroform fraction (PLC) both have immunosuppressive properties. In mice, PL dramatically decreased delayed-type hypersensitivity (DTH); at 600 mg/kg, the highest reduction was observed. At larger doses, it also postponed skin allograft rejection and reduced primary and secondary antibody responses. Studies conducted in vitro and in vivo revealed that PLC inhibited CD4+ and CD8+ T-cells and decreased phagocytic activity. According to these findings, P. lanceolata may be used as an immunosuppressive drug because of its impact on humoral and cell-mediated immune responses. [47]

Antioxidant and Anticlastogenic activity

It has been reported that *Pluchea lanceolata* possesses antioxidant and anticlastogenic properties. Pre-treatment with Pluchea lanceolata restored the glutathione redox cycle enzymes and glutathione levels in the kidneys, which were depleted by B(a)P (Benzo(a)pyrene). Additionally, *pluchea lanceolata* decreased xanthine oxidase activity and lipid peroxidation while enhancing the activities of renal antioxidant enzymes such as glutathione peroxidase and catalase. In mouse bone marrow cells, *pluchea*

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lanceolata dramatically prevented the development of B(a)P-induced micronuclei and decreased DNA fragmentation, suggesting protective effects on DNA integrity. It amply demonstrates *Pluchea lanceolata's* solid backing as a viable antioxidant choice for preventative research. [48]

Antimutagenic and antigenotoxic properties

The well-known environmental pollutant cadmium (49) is a nonessential transition metal with the ability to cause cancer (50) and impact reproductive systems, leading to sterility, growth retardation, and teratogenic effects (51). According to the study, cadmium chloride ($CdCl_2$)-induced oxidative stress and genotoxicity are successfully reduced by *Pluchea lanceolata*. Lipid peroxidation and oxidative damage are caused by cadmium exposure; however, malondialdehyde levels and xanthine oxidase activity were dramatically decreased ($P < 0.001$) after seven days of pre-treatment with PL extract at doses of 100 and 200 mg/kg. Furthermore, PL reduced lipid peroxidation and reinstated the activity of antioxidant enzymes such as glutathione peroxidase and catalase.

Quercetin and isorhamnetin, two of PL's flavonoid contents, are thought to be responsible for its chemopreventive properties. Micronuclei production and chromosomal abnormalities decreased as a result of this treatment, indicating the potent antimutagenic and antigenotoxic qualities of PL against damage caused by $CdCl_2$. [52]

Oxidative stress, Hyperproliferation, and Renal carcinogenesis

Reactive oxygen species (ROS) have a major role in the pathophysiology of various diseases, including ischemia-reperfusion injury, pulmonary oxygen toxicity, atherosclerosis, mutagenesis, carcinogenesis, radiation and chemotherapy effects, and ageing [53]. Oxidative stress is produced in the tissues by Fe-NTA [54]. According to the study, ferric nitrilotriacetate (Fe-NTA)-induced kidney carcinogenesis, hyperproliferation, and oxidative stress in rats are all considerably reduced by *Pluchea lanceolata* (PL). Treatment with 100 and 200 mg/kg of PL extract restored glutathione and antioxidant enzyme activities while lowering lipid peroxidation, xanthine oxidase activity, hydrogen peroxide levels, blood urea nitrogen, serum creatinine, and renal DNA synthesis. [55]

Phytoconstituents present in *Pluchea lanceolata*

Different secondary metabolites of the plant *Pluchea lanceolata* have been identified utilising a variety of isolation techniques, such as column chromatography and successive extraction. GC-MS, HPTLC, gas liquid chromatography, thin layer chromatography, paper chromatography, etc. Their structures were determined using a variety of spectroscopic and physicochemical techniques. Table 1: lists the different phytochemical components that were extracted from *Pluchea lanceolata*. **[56.57]**

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Table 1: List of several phytochemical elements that were isolated from *Pluchea lanceolata*

Plant parts	**Phytoconstituents**	**Reference**
Flowers	Pluchine, Moretenol acetate, moretenol, neolupinol, Nonacosane, Heptacosane, Hentriacontane.	58, 59,60,61
Leaves	Quercetin, Quercitrin, Isorhamnetin, Monoacetylpleuchioside, Indole alkaloids, 3-Oxo-pleuchiol, Moretenol, Neolupenol, Pleuchioside, 3-Oxo-pleuchioside, Monoacetyl pleuchiol, Pleuchiol.	58, 62 - 68
Stem	Diadzein, Stem powder - 47 Compounds representing various functional groups like COOH, alkenes, OH, CO-, R-O-R, alkanes and oxygen atom**.**	69
Root	Formononetin-7-Oglucoside, Sorghumol, Sorghumol acetate, Boehmerol, Phloroglucinol, Chlorogenic acid, Methylated coumarins, Plucheasterolide, Pluchea chromenone [2, 2-Dimethyl-7-acetyl-8-hydroxychromenone], Monoterpene ester [4- Isopropyl-cyclohex-1-en7-(2'-ox)-2'-methyl butyl) oate].	59, 70 - 75
Aerial	Quercetin, 5,7-dihydroxy-8- isobutylflavone, β-Sitosterol, β-Sitosterol glucoside, β –Amryrin, β-Amyrin acetate, β –Amyrin, β-Amyrin caproate, ψ-Taraxasterol acetate, Taraxasterol acetate, Neolupeol, Phenol, Ascorbic acid, n-Tridecanyl-n-octadecanoate, n-Nonadecanol, Two aliphatic hydrocarbons, Plucheasesquiterpenyl ester, Plucheaursenyl acetate, Plucheasesterpenyl ester, Pluchealactone, Plucheasequiterpenyl hexa-decanoate.	59, 60, 76 - 83
Weeds	Hesperidin, Formononetin-7-O-glucoside , Taxifolin-3-arabinoside.	71,72, 84

Conclusion

Despite the fact that antihyperlipidemic properties of *Pluchea lanceolata* have not been well explored, the information which is highlighted on its bioactive constituents—quercetin, isorhamnetin, β-sitosterol, hesperidine, and daidzein, in particular—indicates a great potential for treating hyperlipidaemia. *Pluchea lanceolata* may be a useful natural remedy for lowering cholesterol and averting cardiovascular issues because of its anti-inflammatory, antioxidant, and lipid-lowering qualities. Further studies are

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required to elucidate the specific molecular mechanisms and authenticate its therapeutic efficacy in clinical scenario.

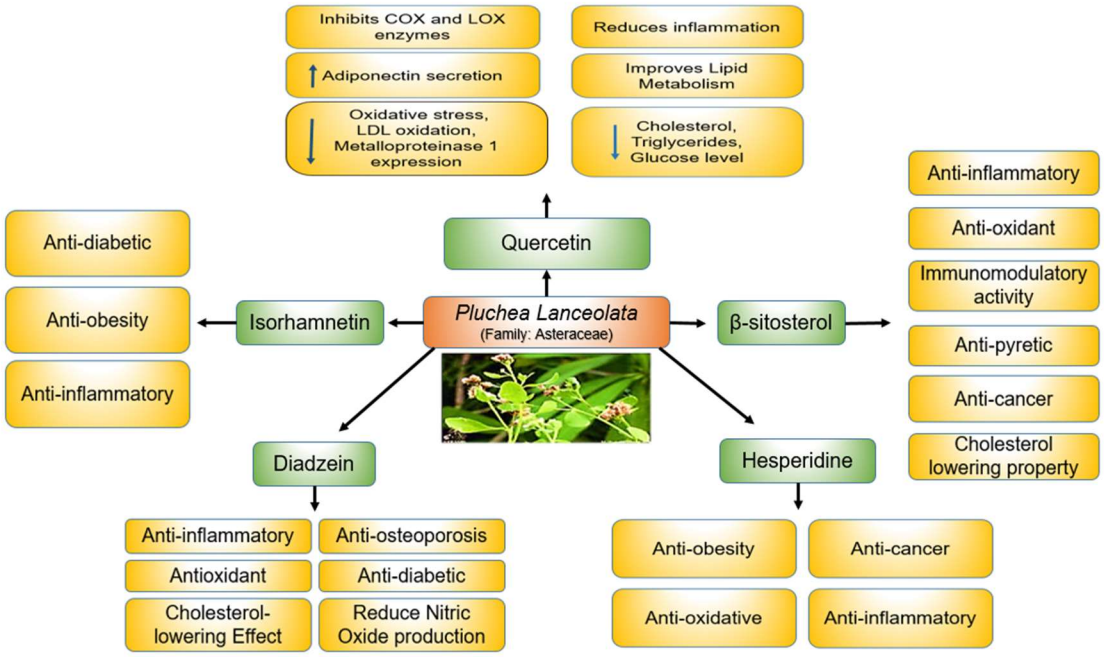

Figure 2: Therapeutic uses of phytoconstituents present in *Pluchea lanceolata*

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