MEDICINAL IMPORTANCE OF PLANTS USED FOR TREATING RHEUMATOID ARTHRITIS IN DAKSHINA KANNADA, KARNATAKA, INDIA

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Abstract. Plants and their importance in the field of medicine go hand-in-hand since the ancient Vedic ages when Ayurveda and the other forms of treatment have come into existence. Each and every part of these plants possesses disease curing properties and is used in different forms to treat number of diseases. This paper aims to shed a light on the medicinal value of few of those plants which are used in treatment of Rheumatoid arthritis in traditional system. The plants that are selected for discussion are *Cardiospermum helicacabum, Kiraganelia reticulata, Pongamia pinnata, Scoparia dulcis, Urena Lobata* and *Vitex negundo.* The taxonomic classification along with its ayurvedic properties, ethnobotany, traditional uses that includes medical as well as day to day usage of the plant parts, pharmacognostical studies, phytochemical investigations and the pharmacological evidences along with molecular aspects are discussed in this paper. Each of these selected plants and every parts have various ayurvedic properties and are traditionally valuable, the physicochemical, microscopic and macroscopic factors also have huge importance, Several biochemical compounds, elements, fatty acids, proteins and amino acids are found to be present and pharmaceutically each of these plants have antimicrobial, antioxidant, anti-arthritic, anti-diabetic and various other properties which suggests the medical science can evolve and improve more with these plants in use in different preparations, which can be cost-effective, as well as devoid of side effects and would be beneficial to the medical world.
Keywords: *arthritis, ethnobotany, pharmacology, phytochemistry, taxonomy*

Introduction

Over the years, plants play the biggest role in advancement of medical science around the globe. The concept of curing diseases, be it external or internal have emerged from the usage of plant parts in several forms from ancient times and even today when technology has taken medical science to a different level, the value for plants in medical field remains the same. A good percentage of population believes on Ayurveda which is witnessed to have done miracles to cure a disease when the other modern forms of medicines have failed. Medicinal plants are considered as rich resources of ingredients which can be used in drug development pharmacopoeial, non-pharmacopoeial or synthetic drugs. It is proposed that the developing countries needs to implement policies strategically for cultivation, conservation, processing and marketing of medicinal plants as they can be considered as a possible bridge between sustainable economic development, affordable health care and conservation of vital biodiversity (Srivastava et al., 1996). Ayurveda has been prominent in being one of the oldest yet most dependable form of treatment of several and certain diseases. The emergence of

Ayurveda is known since Indus Valley Civilization around 6000 B.C and the first traces were found in texts in Vedas as Charak Samhit and Sushrut Samhita (Quack, 2012). After Indian independence, there was more focus on Ayurveda and other traditional medical systems. Ayurveda became a part of the Indian National health care system, with state hospitals for Ayurveda established across the country. In Ayurveda, the defoliations, decoctions, pastes and tablets are made of different parts of these plants and are used to treat the diseases. Since these preparations are mostly home-made and do not require any chemical or biochemical additives, they are cost effective and hence a large population of the world can use them easily. More importantly, hence these are purely made from the plant parts itself, they are mostly have no side effects and can be tropically applied, as well can be consumed orally in many cases as and when required unless any individual is allergic to any certain plant or plant part. Thus with less threat to being exposed to side effects and cost effectiveness, usage of these plants for treatment can be recommended more often.

This paper aims to discuss about the traditional as well as pharmaceutical usage of these medically important plants in curing several diseases besides their pharmacognostical and phytochemical valuations and the plants selected for the discussion for their medical importance are, *Cardiospermum helicacabum, Kirganelia reticulata, Pongamia pinnata, Scoparia dulcis, Urena Lobata* and *Vitex negundo* respectively.

Taxanomy of plants

The taxonomic information of the plants selected is represented in *Table 1*.

Table 1. *Taxonomic of the plants.*

S1 no.	Division	Class	Order	Family	Genus	Species	Common names
1	Tracheophyta	Dicotyledonae	Sapindales	Sapindaceae	Cardiospermum	helicacabum	Balloon plant, Kanphuti, Kapalaphuti.
2	Tracheophyta	Magnoliopida	Malpighiales	Phyllanythaceae	Kiraganelia	reticulata	Poir, Krishna-Kamboji, Pancholi.
3	Magnoliophyta	Magnoliopsida	Fabales	Fabaceae	Pongamia	pinnata	Karanj, Indian beech
4	Magnoliophyta	Magnoliopsida	Scrophulariales	Scrophulariaceae	Scoparia	dulcis	Licorice weed, sweet-broom, Vassourinha
5	Tracheophyta	Dicotyledonae	Malvales	Malvaceae	Urena	lobata	Caesarweed, Congo Jute, Lotloti, Kunija.
6	Magnoliophyta	Magnoliopsida	Lamiales	Verbenaceae	Vitex	negundo	Chinese Chase Tree Nishinda Sambalu Nirguri

Cardiospermum helicacabum

Cardiospermum helicacabum is known as balloon plant, belongs to family Sapindaceae. It is a climbing plant widely distributed across tropical and subtropical areas of Africa, Australia and North America (Maiden, 1889). It is regarded as native to South and Central America (Rojo and Pitargue, 1999) and considered as weed and invasive species in Australia, South Africa, Kenya, Tanzania, Uganda, New Caledonia, USA and Cuba (Foxcroft et al., 2003). It is cultivated as ornamental in gardens and once it escapes cultivation and neutralized, it grows over native vegetation, smothering trees, shrubs.

Ethnobotany

The description of the plant is found in Jyautishmati as emetic, laxative, stomachic, and rubefacient and is prescribed in treatment of rheumatism, nervous diseases, piles, etc. The leaves are used in amenorrhoea (*Figure 1*). On the Malabar Coast the leaves are administrated for pulmonic complaints and root is considered aperient (Pettit, 2016). Leaves are administered both externally and internally rubbed up with castor-oil, and applying this paste to reduce swellings and tumors (Maiden, 1889). In Taiwan, leaves are applied to swellings along with salt. In Bangladesh, pills made from a paste of the whole plant are used to treat asthma (Gurib-Fakim and Sewraj, 1992). *C. helicacabum* is also used to treat stiffness of limbs and snakebite. Young leaves can be cooked as vegetables (Gopalakrishnan et al., 1976). The root is diuretic and demulcent and is used to treat rheumatism.The leaves are reported to be used for washing clothes and the head (Rojo and Pitargue, 1999). The seed oil has insect repellent properties and an antifeedant action on insects.

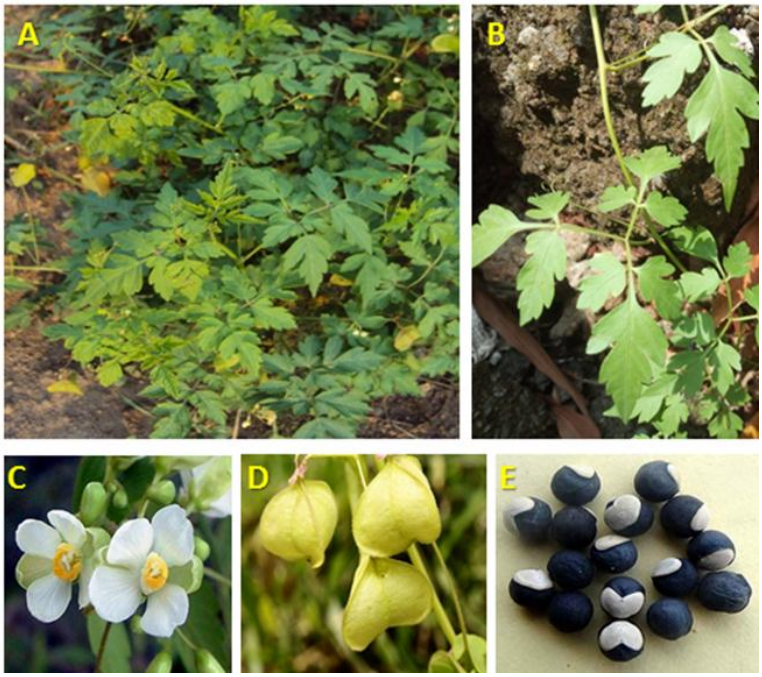

Figure 1. *Cardiospermum helicacabum: (A) whole plant, (B) leaves, (C) flowers, (D) fruits, (E) seeds.*

Pharmacognosy

The pharmacognostical characters of the different parts of the plant are identified which reports the leaves are bi-ternate and length of the leaf is 3-5 cm and breadth 1.5-2 cm. Petiole is 1.5-2.5 cm and midrib 350 µm. The lamina is 60-70 µm thick and stems are 0.2-0.3 cm wide, green in color. Flowers are tetramerous irregular with 2 + 2 sepals, 2 + 2 unequal petals and unequal 8 stamens. Ovary consists of three capillaries with one ovule in each carpel; fruits are globose in shape with winged bloated capsule (Zalke et al., 2013). Seeds are hard and globose in shape, black in color with grayish white colored heart shape spots (Mohaddesi et al., 2013).

Phytochemistry

Alkaloids, flavonoids, saponins, terpenoids, steroids, tannins, glycosides, amino acids and proteins (Kamalakannan et al., 2012) and sugar were present in the crude, alcoholic and aqueous extracts respectively (Deepan et al., 2012). Gas chromatography - mass spectrometry analysis revealed compounds as 1,2,4-trioxolane2-octanic acid, 5-octyl-methyl ester, ethanol, 2-[9-octadecenyloxyl], , 5 octyl methyl ester, ricinolenic acid, [1,1-bicyclopopyl]-2-octanic acid, 2-hexyl-methyl ester, 11-octadecenoic acid, methyl ester, , 9-octadecenoic acid, 1,2,3-propanetriyl ester. (+)- pinitol, βsitosterol, βsitosterol-β-o-glactoside, apigenin-7-o-glucuronide, 1,2,4-Trioxolane-2-octanic acid, arachidic acid, 7-methyl 7tetradecan-1-ol acetate, oleic acid, chryoerior-7-o-glucuronide, linoleic acid, luteolin-7-oglucuronide, and stearic acid (Aishwarya et al., 2014). The LC/MS/MS analysis showed the presence of the anti-inflammatory compounds such as luteolin-7-o-glucoronide, apigenin-7-O- glucoronide and chrysoeriol (Jeyadevi et al., 2013).

Pharmacology

Extract of this plant has proved to have various medicinal properties. Extracts of *C. helicacabum* exhibited therapeutic effects against Freund's complete adjuvant induced arthritis in rat models by decreasing the production of pro-inflammatory cytokines such as TNF-α, interleukin-1 (Kumar et al., 2008) and inhibition of protein denaturation, membrane stabilization and proteinase inhibition (Padmini et al., 2016). λ-Carrageenan hind paw edema model was used for determination of anti-inflammatory activity where the NO level was increased during inflammation. Tumor necrosis factor (TNF-α) increase the secretion of other inflammatory cytokines (Babu et al., 2014; Huang et al., 2011). The ethanolic extract by inhibiting the NO and TNF-α production expressed its anti-inflammatory activity (Babu and Krishnakumari, 2006). Antipyretic activity in rat models from ethanolic and n-hexane extracts have showed significant activity at a higher dose of 400 mg/kg (Raza et al., 2013; Asha and Pushpangadan, 1999).

This extract has showed antibacterial activity against Gram-positive bacteria such as *S. aureus,* (Jayadevi et al., 2013), *Streptococcus pyogenes, Streptococcus fecalis, Bacillus subtilis, etc.* and Gram-negative bacteria *as Shigella dysenterae, Salmonella typhi, Proteus vulgaris, Escherichia coli, Klebsiella pneumonia, etc.* Antifungal activity of plant extract was positive against *Aspergillus niger, Candida albicans* (Raza et al., 2013), *Microsporillum gypsiccus, Trichophyton mentogrophyte*, *Saccharomyces cerevisiae, Penicillium sp*. Methanolic extract of *C. halicacabum* exhibited inhibition of 2,2-diphenyl-1- picrylhydrazyl radical and possessed reducing power, superoxide scavenging ability, nitric oxide scavenging activity (Aishwarya et al., 2014), large quantities of phenolic compounds in *C. halicacabum* extract makes it a strong free radical scavenger (Ponmari et al., 2011).

Ethanolic extract of C. halicacabum leaf was examined against streptozotocin-induced diabetic rats (Veeramani et al., 2008), which showed significant antihyperglyceamic activity at the dose of 200 mg/kg by decreasing the plasma glucose and HbA1 C and increasing the level of insulin and hemoglobin (Naik et al., 2015). Methanolic extract has showed remarkable anticancer potential against the breast cancer cell lines (Sagadevan et al., 2013). Chloroform extract of *C. helicacabum* Linn. showed significant anticancer activity against Ehrlich Ascites carcinoma cell line (Aishwarya et al., 2014). Another study was conducted to investigate the free radical scavenging assay of the ethanol extract of the leaves of *C. helicacabum* to study its anti-rheumatic effects in wistar rats with CFA induced arthritis and to profile the phenolic components thereof

by LC-MS/MS. Ultrasonography and histology images confirmed that the complete cartilage regeneration in the hind limb was visible to those were treated with the ethanolic extract (Jayadevi et al., 2013).

Molecuar aspects

A collection of *C. helicacabum* plants were taken from five different regions of Kerala and the genetic variability was determined by RAPD analysis. UPGMA dendrogram analysis resulted in two clusters, one having plants collected from the Trivandam, Kanyakymari and Kollam districts and the other containing plants from the Palakkad and Alappuzha districts (Sheeb et al., 2014). Results showed that all plants showed low polymorphism. Total polymorphism was only 38% and number of polymorphic fragments range from 125 bp to 3.5 kb.

Kirganelia reticulata

Kirganelia reticulata is also known as *Phyllanthus reticulatus* (Poir) (Unander et al., 1990) belongs to family Euphorbiaceae (Youngken, 1950) (*Figure 2*). It is a shrub or small tree to 5-10 m tall, found all over India and is cultivated worldwide in dry forest upto 800-meter height. It is indigenous to Africa and it has reached temperate and tropical area of Asia also (Agrawal and Paridhavi, 2013; Datta and Datta, 1980). *Kirganelia* is a large Genus comprising about 750 species in tropical and subtropical regions (Gokhale and Kokate, 2008) with about 150 species in mainland tropical Africa and the Indian Ocean islands (Soni et al., 2013).

Figure 2. *Kirganelia reticulata: (A) whole plant, (B) leaves, (C) flowers, (D) fruits.*

Ethnobotany

The leaf decoction is orally consumed to treat sore throat, snakebites, mental problems and diarrhoea. In Ghana a soup is made of *K. reticulata* leaves boiled with palm oil for women after childbirth (Pullaiah, 2006). The whole plant is an astringent,

diuretic and alternant. It can be used as attenuant and against burning sensation, gastropathy, ophthalmodynia, burns, diarrhea, skin eruption and obesity (Balakrishnan and Chakrabarty, 2007), bleeding gums, smallpox, and asthma. Powdered root is sprinkled on infected wounds and chancre. The stem and leaves are rubbed on the chest against asthma (Unander et al., 1990). Leaves are also crushed and rubbed on body of a malaria patient. Fruits are useful to treat problems related to bowels, and are also useful in inflammations and diseases of the blood. Stem is used to cure eyes, the juice as eye drops from them being blown into eyes to cure conjunctivitis and soreness. In Ayurvedic system of Indian medicine recognized its activity against jaundice, fever, liver disorders, syphilis and many other diseases (Soni et al., 2013). In few countries, red or black dye is extracted from fruit, bark, roots is used for tanning and dyeing fishing lines and nets (Jain et al., 1998; Manimegalai and Umavathi, 2010).

Pharmacognosy

Pharmacognostical investigation noted that palisade ratio ranged from 9-13, lower surface stomata number ranged from 59-84. Stomata index of lower surface ranges from 26.3-35.7. Vein islet number ranges from 20-25, vein termination number ranged from 35-39. Leaf powder was studied under UV light with reagents like alcohol, 10% Sodium hyrdoxide, 50% Sulphuric acid, and 50% Nitric acid and water. In daylight they showed different colours as pale green, brownish green, olive green, blood red, orangish yellow and orangish green (Soni et al., 2013).

Phytochemistry

Phytochemical investigation of stem bark revealed presence of pentacosane, 21 α-hydroxyfriedelan3-one, taraxerol, 1 up-20(29)-en-3 β-24-diol, β-sitosterol, β - sitosterol-β-D-glucoside etc (Shruthi et al., 2012; Joshi et al., 1981). The methanolic extract of the leaves consisted of eight compounds (β-Sitosterol-3-O-β-glucoside, stigmasterol-3-O-β-glucoside, , methyl brevifolincarboxylate, kaempfero methyl gallate, ellagic acid, corilagin l and astragalin) (Anjenenlu et al., 1973), including flavonoid glycosides rutin (quercetin 3-rutinoside) and quercetin 3- O- β –Dglucopyranoside (isoquercitrin) (Yoshida et al., 1992; Aswal et al., 1996), were isolated. Besides, it contains lignans, flavanoids, triterpenoids, alkaloids, and Polyphenolic compounds as lupeol acetate, stigmasterol and lupeol (Satyanarayana et al., 1988).

Pharmacology

Researches done on this plant depicts its various pharmacological properties. A study was conducted to investigate the possible interactions using herbal medicine under Rheumatoid arthritis between plant isolates and synthetic drugs. *K.reticulata*, traditionally used to treat rheumatism was found to have bioactive compounds such as Scopoletin, Methyl brevifolin, Methyl gallate, Ellagic acid, Kaempferol, Quercetin etc (Jamal et al., 2008). Ellagic acid isolated from this plant was showed to be efficient in comparison with Naproxen (Khatun et al., 2012). Anti-arthritic activities on methanol and chloroform extracts of dried leaves of *K. reticulata* at 100µg/ml and 250µg/ml showed maximum effect (Rahmatullah et al., 2010). Production of auto-antigens in certain rheumatic diseases was found may be due to in vivo denaturation of proteins. Ethyl acetate and methanol extracts are reported with analgesic and anti-inflammatory

activity in the acetic acid-induced writhing test (Kumar et al., 2012; Kumar and Ciiaturvedi, 2005; Jaya and Rashmi, 2011).

In another study using carrageenan-induced rat paw edema model, the methanol extract showed 40.03% inhibition of edema at the end of 4 hours (Satyavati et al., 1987) showing anti-inflammatory and analgesic properties. The plant is seen to have antibacterial activity to some gram-negative strains such as *Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella typhi* (Shruthi et al., 2012) and gram-positive organisms such as *Staphylococcus aureus* (Das et al., 2011). The petroleum ether and ethanolic extracts of roots were orally tested in alloxan induces diabetic mice and proved to possess good hypoglycemic activity (Ram et al., 2009). Methanolic extract of fruits contained major flavanoids classes like flavones, isoflavones, flavonones which showed major antioxidant activity. Anthocyanin pigments shows many therapeutic benefits including vasoprotective, anti-inflammatory, anticancer properties and reversing age related deficits (Shruthi and Ramachandra, 2011). A study was conducted to evaluate of anti-helminthic activity of polyprenol at different concentrations using *Pheretima posthuma* as a test worm. The bioassay consists of the determination of paralysis time and death time of the worm used.

Molecular studies

The polyprenol was seen to have antibacterial activity against different bacterial strains and exhibited better glucosamine-6-phosphate synthase inhibition in molecular docking studies under minimum docking energy and better ligand efficiency conditions when compared to the standard (Shruthi et al., 2013). RBP-J is a protein involved in both molecular pathways Notch and Toll-like receptor, was selected as a therapeutic target to Rheumatoid arthritis in molecular docking studies against ellagic acid. Like this, few isolated compounds is suggestive of being a good antiarthritic, antibacterial and antihelminthic agent. Nuclear ribosomal internal transcribed spacer (ITS1 - 5.8S rRNA-ITS2), internal transcribed spacer 2, and chloroplasts such as *rbc*L, *mat*K, *psb*A-*trn*H, *trn*L, and *trn*L-*trn*F were carried forward for screening their potential as DNA barcodes for the identification of 48 *Phyllanthus* taxa in Brazilian medicinal plant germplasm banks and in "living pharmacies". The markers were also tested for their ability to validate four commercial herbal teas labelled as *quebra-pedra*. High clade posterior probability in Bayesian phylogenetic analysis denoted the internal transcribed spacer, internal transcribed spacer 2, and chloroplast *mat*K, *psb*A-*trn*H, *trn*L, and *trn*L-*trn*F markers all reliably differentiated the four *Phyllanthus* species, with the internal transcribed spacer and *mat*K possessing the additional advantage that the genus is well represented for these markers in the Genbank database (Inglis et al., 2018).

Pongamia pinnata

Pongamia pinnata belongs to the pea family Fabaceae, also known as *Millettia pinnata* (Panigrahi and Murti, 1989). It is a legume tree that grows to about 15-25 metres and plays a part in nitrogen fixation by its root nodules known as “Bradyrhizobium”. It is naturally distributed in tropical and temperate Asia, from India to Japan to Thailand to Malaysia to north and north-eastern Australia to some Pacific islands (Panigrahi and Murti, 1989).

Ethnobotany

Dried and powdered flower is taken orally to reduce blood sugar. Juice extracted from the green fruits is mixed with mustard oil and applied for rheumatic pain. The decoction of the leaves taken orally cures the asthma. The seed oil applied on wounds is reported to cure wounds. The stem can be used as a toothbrush in toothache. Different parts of the plant have been used in traditional medicine for bronchitis and cold conditions like whooping cough, rheumatic joints and to quench dipsia in diabetes (Kirtikar and Basu, 1935), leucoderma, leprosy, lumbago, muscular and articular rheumatism. The leaves are laxative, anthelminitic and cure piles, wounds and other inflammations, rheumatic pain and for cleaning ulcer in gonorrhoea and scrofulous enlargement (Satyavati et al., 1987; Chopra and Chopra, 1994). The seed oil is used in treatment of skin itchyness and other skin diseases (Pritee et al., 2007). The bark is used internally for bleeding piles (Mumcuoglu et al., 1990), beriberi and diabetes (Akhtar et al., 1996). Roots are used for cleaning gums, teeth and ulcers.

Pharmacognosy

Pharmcagonostical characters show that the pods are compressed, woody, indehiscent, yellowish gray when ripe, varying in size and shape, elliptic to obliquely oblong, 4.0-7.5 cm long and 1.7-3.2 cm broad with short curved beak. Number of seed usually found 1 rarely 2, elliptical or reniform in shape and size 1.7-2.0 cm long and 1.2-1.8 cm broad, wrinkled with reddish brown leathery testa (Meera et al., 2003) (*Figure 3*). A brown to yellowish brown powder with a faint characteristic odour and bitter unpleasant taste. The epidermis is composed of a layer of conical and thick walled palisade cells with a thick cuticle. The epidermal cells appeared more regular, polygonal and yellowish-brown (Kumar et al., 2013).

Figure 3. *Pongamia pinnata: (A) whole plant, (B) leaves, (C) flowers, (D) fruits, (E) seeds.*

Phytochemistry

Six compounds viz., two sterols, three sterol derivatives and one disaccharide along with eight fatty acids (three saturated and five unsaturated) were isolated from the seeds. Other compounds detected were Oleic acid, stearic and palmitic acids, Hiragonic and octadecatrienoic acids ß avone and chalcone derivatives such as Pongone, Pongalabol, pongagallone A and B and Galbone. The new structures were determined to be (2S)-3′,4′-dimethoxy-6″, 6″-dimethylpyrano[2″,3″:7,8]-flavanon, (2S)-6,3′,4′-trimethoxy-6″, 6″ dimethylpyrano [2″,3″7,8]-ß avanone and few more. Alkaloids, Carbohydrates, Steroids, glycosides, Proteins, saponins and flavonoids were present in petroleum ether, Chloroform and methanol extracts. Phenols were present in Petroleum ether and methanol extracts. Tannins were found in methanol extract (Menpara and Chanda, 2014).

Pharmacology

The *P. pinnata* hydroalcoholic extract tested against Carrageenan-induced paw edema with inflammation and Freund's s Complete Adjuvant (FCA) induced arthritic rats with standard drugs, doses given orally at 250 and 500 mg/kg showed significant inhibition of edema and decreased arthritis which was evident with arthritis index, paw volume and joint diameter. It also significantly increased mechanical hyperalgesias and nociceptive threshold. The hematological parameters also revealed the control in arthritis with these extracts. It is reported that the 70% ethanolic extract of *P. pinnata* leaves has potent anti-inflammatory activity against different phases such as acute, subacute and chronic phases of inflammation without side effect on gastric mucosa (Srinivasan et al., 2001). It is also reported that the oil obtained *P. pinnata* shows antimicrobial activity against *Aspergillus niger*, *Staphylococcus aureus* and *Pseudomonas aeruginosa* (Ahmad et al., 2004). Effect of *P. pinnata* leaf extract on circulatory lipid peroxidation and antioxidant status was evaluated in ammonium chloride-induced hyperammonium rats accompanied by a significant decrease in the levels of vitamin A, vitamin C, vitamin E-reduced glutathione, glutathione preoxidase, superoxide dismutase and catalase. It showed that extracts undergoes these changes by altering the oxidant-antioxidant imbalance during hyperammonemia and this could be due to its anti-hyperammonemic effect to detoxify excess ammonia, urea and creatinine and antioxidant property (Mohamed Essa and Subramanian, 2006).

Molecular studies

10 systematically characterized candidate plus trees (CPTs) of *P. pinnata* from North Guwahati was compared for genetic diversity by PCR with RAPD, ISSR and AFLP. Results showed that polymorphism rates of 10.48, 10.08 and 100 % were achieved using 18 RAPD, 12 ISSR and 4 AFLP primer combinations, respectively. Polymorphic information content (PIC) varied in the range 0.33-0.49, 0.18-0.49 and 0.26-0.34 for RAPD, ISSR and AFLP markers, respectively. Clustering of individuals was not similar when RAPD- and ISSR-derived dendrogram analyses were compared with that of AFLP (Vigya Kesari et.al, 2010). The Mantel test cophenetic correlation coefficient was higher for AFLP (r = 0.98) than for ISSR (r = 0.73) and RAPD (r = 0.84). Salinity tolerance of *Pongamia pinnata* along with physiological and molecular responses were examined with a reduction in net photosynthetic rate without affecting leaf water potentials even at 500 mM NaCl for 15 days with no visible stress symptoms. Na + localization analysis using CoroNa-Green AM revealed effective Na + sequestration in

the roots when compared to leaves. Elementally Na + accumulation was more than K + content in leaves. At the molecular level, salt stress significantly induced the expression levels of salt overly sensitive 1 marked as SOS1, SOS2, SOS3, high affinity K + transporter (HKT1), ABA biosynthetic and receptor genes (NCED and PYL4), guaiacol peroxidase (POD) exclusively in roots and tonoplast localized Na + /H + exchanger (NHX1) in leaves (Marriboina et al., 2017). The results indicated that leaves and roots of *P. pinnata* exhibit differential responses under salt stress although roots are more efficient in sequestering the Na + ions.

Scoparia dulcis

Scoparia dulcis is a flowering herb which grow upto 1 m tall plant belonging to plantain family, also known as "sweet broom" (Chittenden, 1951). It is found as a weed in Florida citrus groves, a common weed of lowland tropical and subtropical areas, found in areas where it rains all year round and also where there is a prolonged dry season (Jain and Singh, 1989).

Ethnobotany

In Siddha medicine it is used for treatment of kidney stones and decoction of this plant is drunk to treat remittent fever, gonorrhoea, to induce labour etc. (Standley and Steyermark, 1958) (*Figure 4*). The fresh or dried plants were reported to externally treat a wide range of skin problems including pimples, impetigo, ulcers, eczema, bruises and contusions. An infusion is used as a mouthwash for infected gums and leaves are chewed to treat cough. Bunches of the branches are kept in containers of drinking water keeps the water cool as ice (Standley and Steyermark, 1958). *S. dulcis* is used to treat diabetes in India and hypertension in Taiwan (Pari and Latha, 2004). In Brazil it is used to treat hemorrhoids and wounds (Freire et al., 1996), sickle-cell disease in Nigeria. It protects stomach from ulcers caused by indomethacin. The fresh or dried plant kills fleas, lice and intestinal worms (Standley and Steyermark, 1958).

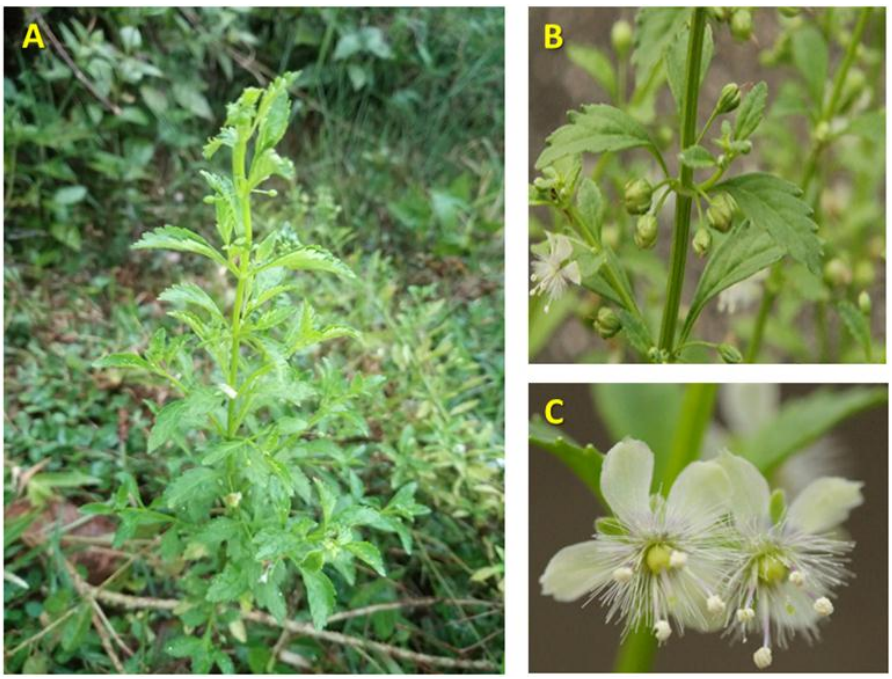

Figure 4. *Scoparia dulcis: (A) whole plant, (B) leaves, (C) flowers*.

Pharmacognosy

Fluorescence analysis of the powdered samples of each part reveals that root and shoot upon treatment with powder with water under ordinary light gives dull white and light green colour and white and light green colours under UV light. With 1N NaOH both appears light brown under ordinary light and appears dark and yellowish brown under UV light; with 50% H_2SO_4 it appears light and dark green; whereas with 1N HCl they appeared to be light yellow and light green respectively (Binu and Vijayakumari, 2015). In the leaf, the vein islet number (11.5-14.6), veinlet termination number (16.1-20.4), stomatal number (76-79 in upper surface, 82-86 in lower surface), number of epidermal cells (477-532 in upper surface and 435-491 in lower surface), stomatal index (12.5 ± 2 in upper surface and 14.3 ± 2 in lower surface) and palisade ratio (6-9) respectively (Mishra et al., 2012).

Phytochemistry

It comprises of mainly terpenoids, flavonoids, carbohydrates and steroids and some miscellaneous compounds (14 compounds) and Two aetylated flavonoid glycosides Apigenin7-O-alphaL-3-Oacetylrhamnopyranosyl-(1—>6)-beta D glucopyranoside and apigenin 7-O-alpha-L-2, 3-di-O-acetylrhamnopyranosyl-(1—>6)- beta-D glucopyranoside. Chemicals found were scopadulcic acids A and B, scoparic acids A – C, betulinic acid scopadiol, scopadulciol, scopadulin, (Jose and Adikay, 2015), acacetin, amyrin, apigenin, , cirsimarin, cirsitakaoside, coixol, coumaric acid, cynaroside, daucosterol, dulcinol, dulcioic acid, gentisic acid, benzoxazin, benzoxazolin, benzoxazolinone, glutinol, hymenoxin, linarin, luteolin, mannitol, , taraxerol, vicenin, scoparinol, scutellarein, scutellarin, sitosterol, stigmasterol and vitexin (Saikia et al., 2011).

Pharmacology

Plant is reported to possess cytotoxic, anti-cancerous, antimicrobial, anti-malarial, anti-ulcer, antacid, anti-cholesterol and antioxidant actions (Christi and Senthamarai, 2015). The ethanolic extract and cream based formulation exhibited significant antimicrobial activity against gram positive organism and antifungal activity against *Staphylococcus aureus* and *Escherichia coli* (Valsalakumari et al., 2014), and fungal strains such as *Candida albicans* and *Aspergillus niger* (Wankhar, 2015) compared with respective reference drugs Gentamicin and Clotrimazole. The analgesic, anti-inflammatory and antipyretic activities of the water and ethanolic extracts of *Scoparia dulcis* L. were tested in mice and rats (De Farias Freire et al., 1993) which showed that the extract is endowed with analgesic effects probably related to the anti-inflammatory activity of the plant in presence of glutinol and flavonoids, which exert their action on the early phase of the acute inflammatory process through central and peripheral mechanism (Zulfiker, 2010).

Normal glucose loaded and streptozotocin induced diabetic rats were investigated were treated with methanolic extract of aerial parts of *Scoparia dulcis* leaves which exhibited significant hypoglycemic activity when compared with a standard antidiabetic agent Glibenclamide (Mishra et al., 2013). The antioxidant efficacy of *S. dulcis* in STZ diabetic rats when compared with Glibenclamide showed increase in the activities of

plasma insulin, superoxide dismutase, catalase, glutathione peroxidase, glutathione-S-transferase and reduced glutathione in brain of 200 mg/kg body weight upon treatment for 6 weeks (Mishra et al., 2013). Both the treated groups showed significant decrease in thiobarbituric acid reactive substances (TBARS) and hydroperoxides formation in brain suggesting its role in protection against lipid peroxidation induced membrane damage (Patra, 2014).

The hydro-ethanolic extract of *Scoparia dulcis* exhibited mast cell stabilizing and anti-anaphylactic effects in murine models upon exposure to a known allergen. It was noted that the hydro-ethanolic extract of *S. dulcis* has significant mast cell stabilizing as well as anti-anaphylactic activities, making it a better adjunct in case of asthma management (Ofori-Amoah et al., 2016). The aqueous extract of leaves was investigated for its anti-ulcer activity against pylorus ligation and ethanol induced ulcer models in experimental rats at doses of 250 and 500 mg/kg body weight and showed significant reduction in gastric volume, free acidity and ulcer index (Girish, 2011).

Scoparia dulcis when was orally administered, the effect on Trypanosoma brucei showed changes in serum total protein, albumin and globulin were investigated in rabbits over a period of twenty eight days. Results showed that infection resulted in hyperproteinaemia, hyperglobulinaemia and hypoalbuminaemia (Orhue et.al, 2005). The study speculates that the herb may be involved in modulating the severity of these trypanosome associated lesions by some yet undefined mechanisms. Investigation of the anti-inflammatory activity of betulinic acid was examined by detecting the levels of cyclooxygenase-2 (COX-2), nitric oxide (NO), tumor necrosis factor (TNF-α), interleukin-1β (IL-1β) and malondialdehyde (MDA) in the edema paw tissue and the activities of superoxide dismutase (SOD), glutathione peroxidase (GPx) and glutathione reductase (GRd) in the liver by HPLC. The activities of SOD, GPx and GRd in the liver tissue were increased and the MDA levels in the edema paws were decreased (Tsai et al., 2011).

Urena lobata

Urena lobata is a tender perennial, erect shrub or subshrub belonging to the family Malviceae. It will be usually 0.5 meters to 2.5 meters tall plant containing about 243 genera and 4225 species of herbs, shrubs and trees (Stevens, 2001). This family is largely tropical but can also grow in subtropical and temperate regions. The genus Urena consists of 4 species (Liogier and Martorell, 1982). Considered as weed, it is widely distributed in the tropics, including in Brazil and Southeast Asia.

Ethnobotany

The root decoction of the plant is used to treat colic. Infusions of the root are used internally as emollient. Externally it is used for Rheumatism, Lumbago and skin diseases associated with pain and inflammation. Decoction of dried root also treats Rheumatic pain. Boiled and crushed leaves are used to treat bladder and intestinal inflammation. A poultice of fresh leaves is used for snake bite, sprains and bruises (Wagner et al., 1999) (*Figure 5*). Besides being a weed, the plant is used environmentally in soil conservation, rituals and as an emergency (famine) food for human consumption. Essential oil and fibres extracted from the plants are used as materials. The root is a popular diuretic and used externally for lumbago and rheumatism. The flowers are used as a pectoral and expectorant in dry coughs and its

infusion is used as a gargle for sore-throat. Leaves are used as abscess in Rema-Kalenga (Islam et al., 2018). Extracts of leaf, root and barks are used to treat malaria, gonorrhea, leucorrhea, hematemesis, carbuncle, trauma, bleeding, cold, fever, inflammation and rheumatism.

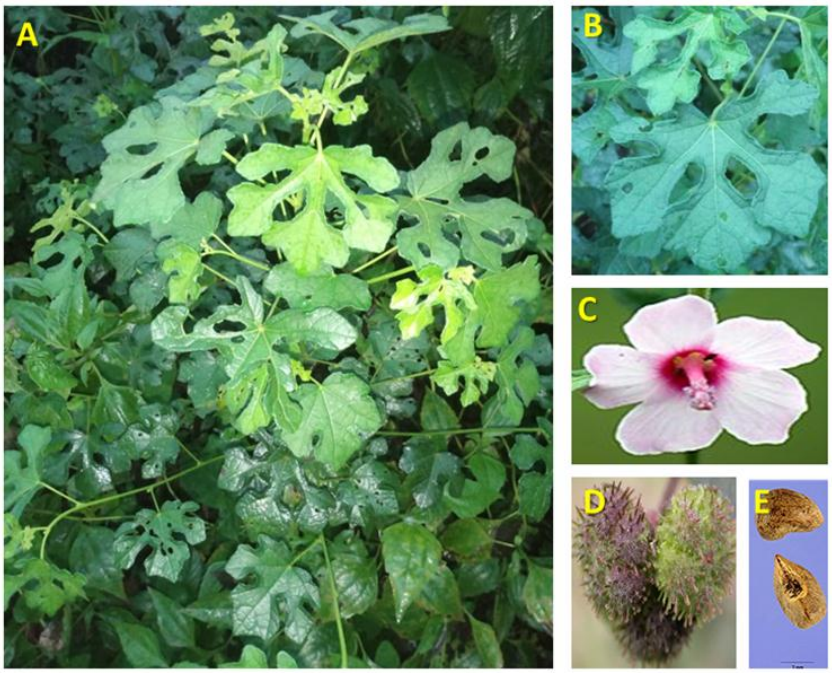

Figure 5. *Urena lobata: (A) whole plant, (B) leaves, (C) flowers, (D) fruits, (E) seeds.*

Pharmacognosy

Microscopic characters reveal that the leaf is palmately lobed; Stem, leaves and fruits have tiny hairs or fur on them. Flowers of the plant are pink-violet and grow upto one centimeter. Ash values determined for powdered samples and fluorescence analysis of leaf, leaf powder and stem powder done under with different chemical reagents at 254 nm and 366 nm which gave different colours at different stages as Green, dark green, faint green, light green, yellow, yellowish green, brown, dark brown, light brown, blue, black etc. (Mane et al., 2016).

Phytochemistry

Roots contain carbohydrate 33%, protein 1.9%, fat 1.8%, fiber 51.7%, moisture 6.6%, and ash 5% (Babu et al., 2016). Leaves in methanol extract contained alkaloids, flavonoids, saponins, and tannins. Ethyl acetate portion and n-butanol portion of a 95% ethanol extract of branches and leaves found ten flavonoid compounds, viz. kaempferol, rutin, quercetin, afzelin, astragalin, tiliroside, crenuloside etc. Raw leaves are reported to contain 81.8% moisture, 54 cal, 3.2 g of 57 protein, 0.1 g fat, 12.8 g carbohydrates, 1.8 g fiber, and 2.1 g ash, 558 mg calcium, and 67 mg of phosphorous per every 100 g. Several primary and secondary metabolites are also found along with carbohydrates, phytosterols, flavonoids, saponins, tannins, terpenoids and mucilage (Gupta et al., 2010). Elements found are Potassium, Sodium, Calcium, Magnesium, Iron, Zinc, Manganese, Copper, and compounds like Quercetin, Kaempferol are isolated by TLC (Bhatt and Rawat, 2001).

Pharmacology

Urena being a weed is used widely in pharmacology world-wide in various aspects of treatment. Aqueous extract of the leaves of *Urena lobata* were investigated for anti-arthritic activity by protein denaturation method using acetyl salicylic acid as standard. The maximum antiarthritic activity was observed in the concentration 1000µg/ml and minimum in the concentration 100 µg/ml (Rajagopal et al., 2019; 2018). Significant anti-inflammatory activity was exhibited by the aqueous extracts of the leaves which were directly proportional to the concentration. Kaempferol, quercetin, and tiliroside extracted from leaves shows strong antimicrobial activity against *Escherichia coli*, *Bacillus subtilis*, and *Klebsiella pneumonia*.

Methanolic extract of root along with standard herbal formulation shows antibacterial activity on *Shigella dysenteriae* and *Vibrio cholera* (Yadav and Tangpu, 2007; Mazumder et al., 2001) and a significant anti-fungal activity against *Aspergillus niger* (strain: ATCC 16404) *Saccharomyces cerevisiae* (strains: AY529515.1, AJ746340.1, JX103178.1, KG254081.1 and ATCC 204508 (Gao et al., 2015) are also noted. The plant showed significant inhibitory activity against castor oil-induced diarrhea and prostaglandin E2 (PGE2)-induced intrafluid accumulation. It showed a significant reduction in gastrointestinal motility with no signs of toxicity (Rinku et al, 2008). Aqueous extracts of *U. lobata* (roots and leaves) in STZ-induced diabetic rats showed recognizable hypoglycemic/antidiabetic and anti-hyperlipidemic effects (Onoagbe et al., 2010). The Methanolic extract of roots were found to inhibit lipid peroxidation scavenge hydroxyl and superoxide radicals in vitro (Lissy et al., 2006). *U. lobata* roots in adult male Wistar albino rats reciprocally inhibited spermatogenesis and steroidogenesis which indicated reversible antifertility activity (Dhanapal et al., 2012).

Molecular studies

In a study conducted four new lignan glycosides; urenalignosides A–D (**1–4**), along with 12 known ones (**5–16**) were isolated from *Urena lobata* (Luo et al., 2019). Their structures were determined on the basis of extensive spectroscopic and spectrometric data by using 1D and 2D NMR; IR; CD; and HRESIMS. Compounds **2–4; 6; 7; 10;** and **11** showed inhibition of nitric oxide production in lipopolysaccharide-induced RAW 264.7 macrophage cells with IC_{50} values in the range of 25.5–98.4 µM (positive control; quercetin; IC_{50} = 7.2 ± 0.2 µM). Another study revealed that two new compounds isolated from the aerial parts of *Urena lobata* L., ceplignan-4-O-β-d-glucoside and 2,5-dihydroxy benzoic acid-7-(2,6-dimethyl-6-hydroxy-2,7-octadienoic acid) anhydride-5-O-β-d-apiofuranosyl(1 → 2)-β-d-glucoside (urenoside A), on the basis of chemical and spectral evidence, including 1D and 2D NMR spectroscopic data as well as mass spectrometry (HR-ESI-MS) (Jia et al., 2010).

Vitex negundo

Vitex negundo is a large aromatic shrub which grows upto 2-8 m in height, commonly found near water bed, disturbed land, grasslands, and mixed open forests (*Figure 6*). It is a popular traditional medicine which yields edible seed and provides various other values. It is cultivated as hedge and medicinal plant in entire central, eastern and south Eastern Asia. It is native to tropical Eastern and Southern Africa and Asia.

Figure 6. *Vitex negundo: (A) whole plant, (B) leaves, (C) flowers, (D) fruits, (E) seeds.*

Ethnobotany

Vitex negundo is been used since ancient times as a female remedy and also for pains in Ayurveda and also in Roman medicine (Ladda and Magdum, 2012). In India, it is used widely as an ayurvedic remedy to pain, inflammation and female diseases. A mixture of 20 ml decoction with 1gm Pippali and 250 mg Vacha can cure cold and pneumonitis (Khare, 2008). Leaves are stuffed in pillows to dispel catarrh and headache. Crushed leaf poultice is applied to diminish headaches, neck gland sores, tubercular neck swellings and sinusitis. Essential oil from leaves cures venereal diseases and other syphilitic skin disorders (Sharma et al., 2000). A tincture of root-bark provides relief from irritability of bladder, rheumatism and dysmenorrhea. It is used in bath for women in perpetual state and in case of new born babies and used as an antidote for snake-bite (Alam and Gomes, 2003). Traditional uses include the usage of the plant as toothbrushes, tonic and carminative, as vermifuge. It is used in treatment of Asthma and cancer, Jaundice, Urticarua, Cellulitis, Abcesses, Carbuncles, Eczema and liver disorders, bodyache as well as kwashiorkor aches and pains, catarrehal, and rheumatic afflictions as well as migraine, joint pain as Refrigerant for cattles.

Pharmacognosy

Roots are woody, fairly thick and 8-10 cm in diameter. Stem Barks are 0.3- 0.5 cm thick. Leaves are palmately compound, petiole is 2.5-3.8 cm long. Middle leaflet is 5-10 cm long and 1.6-3.2 cm broad, with 1-1.3 cm long petiolule. Vein-islet and vein termination number of leaf are 23-25 and 5-7 respectively in lamina. Physical constituents such as total ash, acid insoluble ash, water soluble ash, petroleum ether extract, benzene extract, chloroform extract, alcohol extract, carbohydrate, crude fibre, fat, alkaloids and proteins are determined (Singh et al., 1999).

Phytochemistry

Leaves are said to have 6′-p-hydroxybenzoyl mussaenosidic acid; 2′-p-hydroxybenzoyl mussaenosidic acid viridiflorol; β-caryophyllene; sabinene; 1-oceten-3-ol; globulol (Singh et al., 1999); betulinic acid, ursolic acid, n-hentriacontanol; β-sitosterol; p-hydroxybenzoic acid; protocatechuic acid; oleanolic acid etc. (Mallavarapu et al., 1994). Seeds contain vitedoin-A; vitedoin-B (Singh et al., 1999), 6-hydroxy-4-(4-hydroxy-3- methoxy-phenyl)-; 5-oxyisophthalic acid (Subramanian and Misra, 1979). Roots have vitexin; isovitexin, negundin-A; negundin-B; (+)-diasyringaresino, 3-hydroxymethyl-7-methoxy-3,4-dihydro-2-naphthaldehyde, β-sitosterol; p-hydroxybenzoic acid l; (+)- lyoniresinol (Vishwanathan and Basavaraju, 2010); vitrofolal-E; vitrofolal-F (Gautam et al., 2008). Essential oil of fresh leaves, flowers and dried fruits has δ-guaiene;; ethyl-hexadecenoate; α-selinene; germacren-4-ol; caryophyllene epoxide (Singh et al., 1999); Viridiflorol (19.55%), β-caryophyllene (16.59%), sabinene (12.07%), 4-terpineol (9.65%), γ-terpinene (2.21%), caryophyllene oxide (1.75%), 1-oceten-3-ol (1.59%) and globulol (1.05%) Viridiflorol (Meena et al., 2010).

Pharmacology

The seeds are known to be effective in rheumatism and joint inflammation. Total lignin content in the seeds inhibit the paw edema and decreases arthritis index, with no influence on the body weight and the indices of thymus and spleen of CIA rats (Jing et al., 2019), spleen index, and reversed the weight loss of CFA-injected rats (Zheng et al., 2014). Same actions were visible in case of Freund's complete adjuvant (FCA) induced arthritis injected in male albino rats when treated with indomethacin (Lad et al., 2015). Phenylbutazone and ibuprofen by *Vitex negundo* Linn. indicates that it is anuseful adjuvant therapy along with standard anti-inflammatory drugs. Some researchers stated in their studies, established anti-inflammatory properties of Vitex negundo Linn. extracts in acute and sub-acute inflammation are attributed to prostaglandin synthesis inhibition (Mahalakshmi et al., 2010; Tandon and Gupta, 2006).

Methanolic extract of the leaves was found to significantly potentiate the sleeping time induced by pentobarbitone sodium, diazepam and chlorpromazine in mice depicting CNS depressant activity (Gupta and Tandon, 2005). Essential oils and successive ethyl acetate and ethanol extracts has showed antibacterial activity against *Staphylococcus aureus, Bacillus subtilis, Escherichia coli* and *Pseudomonas aeruginosa bacterial strains.* Antifungal activity was found against *Trichophyton mentagrophytes* and *Cryptococcus neoformans* (Sathiamoorthy et al., 2007). The plant exhibits a potent scavenging activity for (2, 2′-azino-bis 3-ethyl benzothiazoline-6-sulfuric acid) ABTS radical cations in a concentration dependent manner, showing a direct role in trapping free radicals and also in rats, by using ethanol induced oxidative stress model (Prabhu and Rajan, 2010; Devi et al., 2007). The methanolic root extracts showed anti-snake venom activity (Tandon and Gupta, 2004). Leaf extracts also showed hypoglycemic activities (Villaseñor and Lamadrid, 2006).

Molecular studies

A novel compound Tris (2,4-di-*tert*-butylphenyl) phosphate (TDTBPP) was isolated from the leaves of *Vitex negundo*. Molecular docking studies were carried out with the X-ray crystal structures of *Daboia russelli pulchella's* (*Vipera russelli*, Indian Russell's

viper) venom $sPLA_2$ and Human non-pancreatic secretory PLA_2 (*Hnps* PLA_2) as targets. Docking results showed hydrogen bond (H-bond) interaction with Lys69 residue lying in the anti-coagulant loop of *D. Russelli's* venom PLA_2, Docking of TDTBPP with *Hnps* PLA_2 structure showed coordination with calcium ion directly and also through the catalytically important water molecule (HOH1260) located at the binding site (Vinuchakkaravarthy et al., 2011). Another study evaluated a few selected phytochemicals (5,3′-dihydroxy-7,8,4′-trimethoxyflavanone; 5,3′-dihydroxy - 6,7,4′trimethoxyflavanone; 5-hydroxy-7,4'dimethoxyflavone; 5,3'-dihydroxy-7,8,4'-trimethoxyflavanone; betulinic acid, ursolic acid; n-hentriacontanol; β-sitosterol) present in *V. negundo* plant leaves based on their capacity to bind and inhibit Adenosine A1 receptor of CVD using computational methods. Simultaneously, Molecular docking was performed using the GOLD (Genetic Optimization of Ligand Docking) software, to study the binding orientation of compounds to the Adenosine receptor (Prasad et al., 2015). All docked compounds were found to have interaction between an oxygen atom of the compounds and Adenosine receptor. A study reporting successful application of DNA barcoding in the authentication of five *V. negundo* herbal products sold in Philippines were done. Samples were authenticated using 42 gene accessions of ITS, *psbA-trnH* and *matK* barcoding loci, following the BLASTn and maximum-likelihood tree construction criterion (Olivar et al., 2016).

Conclusion

This paper was mainly aimed towards discussing the medicinal importance of few chosen plants. The overall data compiled will help the modern day treatment procedure as well as drug designing more efficient and powerful. It is noticeable that all the previous reports about these plants have actually tried to give scientific validation for its importance in Ayurveda. Ethnobotanical evidences stated the traditional knowledge about these plants, pharmacognostic studies depicts their macroscopic and microscopic details and phytochemical investigations has revealed the presence of useful secondary metabolites as well as numerous phytochemicals having drug likely property. Pharmacological studies done highlights the properties in different extracts such as anti-inflammatory, anti-arthritic and anti-pyretic properties which absolutely supports the traditional claim of using these plants for treating rheumatoid arthritis. Other properties reported included the antioxidant, anticancer, anti-ulcer, anti-diabetic and few others as well. A few molecular level studies including genetic variability analysis, in silico docking studies are also reported on these plants. Hence, we can conclude that these plants have huge medicinal values especially relating to rheumatoid arthritis, giving scientific validation to it can improve and pave way for new inventions in medical sciences.

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Conflict of interest

The author confirm there are no conflict of interest involve with any parties in this research study.

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