3. Review of Literature

3.1 Introduction to the family – Pontederiacea

Introduction to plants:

1. *Parkinsonia aculeata* Linn\(^7\).

*Family*: Leguminosae/Fabaceae.

*Subfamily*: Caesalpiniaceae.

**Part selected for proposed study**: Leaves and Bark

*Division*: Magnoliophyta

*Class*: Magnoliopsida

*Order*: Fabales

*Family*: Fabaceae

*Subfamily*: Caesalpinioideae

*Genus*: *Parkinsonia*

*Species*: *P. aculeata*

**Photo No.3.** Fresh leaves of *P. aculeata*

**Photo No.4.** Fresh flowers of *P. aculeata* in natural habitat
Vernacular Names:

Kannada : Parangi jali,

Hindi : Vilayati kikar,
        vilayati babul

Telugu : Sima tumma

Marathi : Adanti

Nature: A large spinous shrub or a small tree, native of tropical America, found almost throughout the drier parts of India. Bark green or brown, thin, smooth; leaves bipinnate, ending in a stout spine: 15-30 cm long, pinnules ovate or oblanceolate, minute; flowers in ax axillary racemes, yellow, fragrant; pods slender, moniliform, upto 10 cm. Long; seeds usually 4-7, oblong, smooth dark brown.

The plant is frequently grown for its showy flowers and also as a hedge. Analysis of fallen leaves is reported and it is as follows. Protein, 7.5; ether extract, 1.8; N-free extract, 44.8; fiber, 29.0; ash, 16.9; calcium, 4.16; and phosphorus, 0.17% on dry basis.

Ethnobotanical uses\textsuperscript{71,72}: All parts of plant are reported to be used as antipyretic; leaves are considered as diaphoretic and abortifacient.

Distribution: Parkinsonia, a small genus of tress and shrubs distributed in the warmer parts of America and Africa. One species has been introduced and become naturalized in India. They are large shrubs or small trees growing to 5–12 m (16–39 ft) tall, dry season deciduous, with sparse, open, thorny crowns and green bark. The leaves are pinnate, sometimes bipinnate, with numerous small leaflets; they are only borne for a relatively short time after rains, with much of the photosynthesis carried out by the green twigs and branches. The flowers are symmetrical or nearly so, with five yellow or white petals. The fruit is a pod containing several seeds.
Scientific reports:

Green\textsuperscript{73} reported that the composition of the pods of \textit{P. aculeata}. The 73\% of pods consist of hemicellulose, cellulose and lignins. The composition of whole bean is similar to that of alfalfa hay or mesquite beans. The chief proteins of the seed are albumin and glutelin.

Tookey\textsuperscript{74} \textit{et al.} reported that the seeds of 175 species in 26 plant families for water-soluble mucilage content. Those containing over 15\% of mucilage were all from legumes. Out 175 species, seeds of \textit{Parkinsonia aculeata} reported to contain 28\% (Percentage of seed) of mucilage, which was highest.

Bhatia\textsuperscript{60} \textit{et al.} reported that the leaves of \textit{Parkinsonia aculeata} have been found to contain three C-glycosides. Separated two C-glycosides by fractional crystallization after preliminary lead salt purification. But found that preparative paper chromatography was effective for the separation of all three. They reported that the first (epi-orientin) is a C-glycoside of luteolin and resembles orientin in composition, chemical reactions and UV and IR spectra but differs in m.p. and rotation and may be an epimer of orientin. The second (Purkinsonin-A) is a C-glucoside of 5-O-methyluteolin and is closely related to orientin. The third (Parkinsonin-B) is a C-glucoside of 5,7di-O-methyl luteolin and has stereochemistry related to epi-orientin.

Trivedi & Schemes\textsuperscript{61} presented that the Pharmacognostical data on \textit{Parkinsonia aculeata} as well as its use as an antirabies agent based on folklore with clinical data involving 3 patients (ages 14, 28, and 40 yr). The drug was given orally with water in the form of expressed juice or as a fine powder. The dose varied according to the age of the patient and the severity of the disease. The drug residue was used as poultice on the wound. The drug was effective in all 3 cases. Antipyretic, diaphoretic, analgesic, antiseptic and healing activities were also noted.

Besson\textsuperscript{62} \textit{et al} reported that isolated the C-glycosylflavones from \textit{Parkinsonia aculeata} leaves. The isolated compounds were identified as orientin, isoorientin, vitexin and isovitexin. They also reported that Orientin was reported to be present in the leavorotatory form.
El-sayed et al reported several known compounds and a new flavone C-glycoside Luteolin (7,4’-Dimethyl Ether 6-C-Glucoside) from the leaf extract of Parkinsonia aculeata collected from Egypt. The known compounds: orientin, iso-orientin, vitexin, iso-vitexin, lucenin-II, vicenin-II, diosmetin 6-C-B-glucoside, apigenin, luteolin, kaempferol and chrysoeriol were identified by standard procedures and are reported for the first time from this plant.

Meera et al reported that Parkinsonia aculeata stems contain glycerol β butanoate α α-dipentanoate, β-Sitostrol, glycerol α-heptanoate α octanoate, β sitosteryl-D glycerol-β-D-glucoside β sucrose. Of these the two glycerides are being reported for the first time.

Leite et al reported that the antidiabetic effect of Parkinsonia aculeata water soluble fraction (WSF) made of aerial parts of the plant (leaves and flowers) was investigated in alloxan diabetic rats. Its effect was compared with that of insulin (positive control). The physico-metabolic parameters measured were: body weight, food and liquid intake, urinary volume, hepatic glycogen, serum glucose, total cholesterol, HDL-cholesterol, triglycerides, urinary glucose and urea, and the weight of epididymal adipose tissue, liver, kidneys and the skeletal muscles (soleus and extensor digitorum longus). Oral administration of WSF (125 or 250 mg/kg) for 16 days exhibited a significant reduction in serum and urinary glucose, urinary urea, total cholesterol, HDL-cholesterol and triglycerides in alloxan diabetic rats. An improvement of hepatic glycogen, a decrease of liquid and food intake, and a significantly positive actions in the weight of skeletal muscles (soleus and extensor digitorum longus) and kidneys were also observed, but just diabetic group treated with WSF at a dose of 125 mg/kg showed significant reduction in urinary volume, body weight, an improvement of epididymal adipose tissue and a positive action in liver weight. The effects of WSF on the physico-metabolic parameters was comparable to those observed in diabetic insulin treated group. The results of this work suggest that P. aculeate may have new clinical significant choice in diabetes mellitus illness, and could explain the basis for its traditional use to manage diabetes-related complications by rural community of northeast of Brazil.
Ali et al\textsuperscript{66} reported that a new flavanone with epoxy-isopentyl moiety named parkintin has been isolated from the methanol soluble part of Parkinsonia aculeata Linn. belonging to the family Caesalpiniaceae. The structure of parkintin has been established with the aid of spectroscopic techniques including COSY and HMBC experiments.

Juan et al\textsuperscript{75} reported that the life cycle of the bruchid beetle \textit{Penthobruchus germaini} (Pic) was studied in the laboratory and some field observations were recorded. Most adults (90.5\%) emerged from the seeds of \textit{Parkinsonia aculeata} L. by making an exit hole at the end of the seed opposite the radicle. Adult longevity with different food types ranged from 11.2 to 59 days and oviposition from 22 to 348 eggs per female. Females laid an average of 2 eggs per day during their life span. The life cycle (oviposition to adult emergence) was completed in 38.7 days at 30 °C in the laboratory, including 8.6 days for the egg stage, 21.8 for the larval stage, and 8.3 for the pupal stage. The larval stage had four instars. Larvae destroyed the seeds by consuming 90–100\% of the cotyledons, preventing germination. They pupated inside the seeds, and only one adult emerged per seed. At three field sites, 48\% of the pods were found to have eggs; the mean number of eggs per seed was 0.37 and per pod was 0.98. Females preferred the swelling of the pod as oviposition site. Mature (purple) and larger pods contained more eggs than immature (green) and smaller pods. Larvae overwintered in the seeds on the ground, began pupating in late winter, and adults emerged in the spring. Depending on plant phenology, two generations per year are possible. Natural parasitism of \textit{P. germaini} was <5\%. \textit{P. germaini} has several attributes as an effective natural enemy of \textit{P. aculeata}.

Joaquin et al\textsuperscript{76} reported that N-Acylamino acid amidohydrolase (EC 3.5.1.14), or aminoacylase, was isolated from the seeds of Palo Verde (\textit{Parkinsonia aculeata} L.). The enzyme was localized within the cotyledons and embryo of the seed. An acetone powder preparation from the combined cotyledons and embryo furnished an active extract which was purified greater than 75-fold. Fractionation consisted of treatment with (NH\textsubscript{4})\textsubscript{2}SO\textsubscript{4}, cold acetone, freeze-thaw (which removed a cold-labile, inhibitory protein), and chromatography on DEAE-Sephadex A-25. The specific activity was 2650 μmoles/h per mg protein nitrogen. 2. \textsuperscript{2} Co\textsuperscript{2+} was shown to enhance activity and also to provide
stability to the enzyme during the (NH₄)₂SO₄ fractionation. 3. 3. N-Formyl-l-methionine was the best substrate and exhibited a \( v_{\text{max}}/K_m = 2.9 \cdot 10^5 \) at pH 7.2. The acetyl derivatives of l-methionine, l-valine, and l-leucine inhibited the enzyme at concentrations above 10 mM. The hydrolyses of N-acetyl-l-leucine and N-acetyl-l-valine exhibited non-Michaelis-Menten kinetics with an indication of two possible binding sites. 4. 4. The molecular weight was estimated by gel filtration to be 79 500.

Shweta et al⁵⁵ reported that Two medicinally important seed oils *viz. Mimusops elengi* and *Parkinsonia aculeata* were analyzed for fatty acids distribution pattern in triacylglycerols using pancreatic lipase hydrolysis method. The seed oils contain high percentage of unsaturated acids (*M. elengi* 64.8% and *P. aculeata* 82.7%). The lipolytic data revealed that linoleic acid dominates at 2-position of triacylglycerols of all seed oils. *M. elengi* contain erucic acid in small amount (0.3%).

Singh et al⁴⁹ reported that the present study states the phytochemical investigation and the therapeutic importance of *Parkinsonia aculeata* Linn. (Family-Leguminoseae). It can be proved that plant possess potent medicinal value. Worldwide trend towards the utilization of natural plant remedies has created an enormous need for the use of medicinal plants. This study involves the preliminary phytochemical screening of the methanolic crude extract of *P. aculeata* leaves. Phytochemical analysis of the methanolic extract prepared from *P. aculeata* leaves revealed the presence of alkaloids, flavonoids, C-glycosides, terpenoids and saponins. The results showed that the phytochemical properties of the leaves can be used for curing various diseases. Out of seven fractions fraction-2, 4, 5, 6 and 7 were screened for DPPH antioxidant activity again. The crude CHCl₃ fraction showed 71.7% inhibition and fr-4 showed 85. 4 % inhibition which is more potent than standard gallic acid which was measured 83.5%. IC50 of 0.41, 0.29, 0.38 and 0.33 mg/ml were recorded for CHCl₃, EtOH, Aqueous and EtOAc extract. For CHCl₃ fractions IC50 reported were 0.32, 0.36, 0.37 and 0.37 mg/ml for fraction F2, F4, F5 and F7. The *P. aculeata* leaves is a potential source of various types of bioactive compounds with diverse chemical structures as well as pharmacological activities.
Singh et al\textsuperscript{50} reported that the present study evaluation the qualitative analysis of phytochemical and antibacterial activity of chloroform leaves extract of Parkinsonia aculeata L family (Leguminoseae) leaves against some bacteria causing Urinary tract infection in human. The preliminary phytochemical screening show the presence of flavonoids, alkaloids, C-glycoside and Saponins. The crude extract show maximum antibacterial activity against E- Coli with zone inhibition 23±0.2 at concentration of 500 mg/ml.

Shah et al\textsuperscript{51} reported that Free radicals are generated during the metabolism of synthetic chemical substances/drugs by liver can cause hepatotoxicity. Supplementation with exogenous antioxidants, including alkaloid compounds from plant sources, may useful for protecting liver against free radical induced hepatotoxicity. P. aculeata has been reported to have potent anti oxidant activity. With this background the present study has been undertaken to explore the in vivo hepatoprotective action of P. aculeata leaves. In the present work leaf extracts of P. aculeata (Fabaceae) was selected to determine its in vitro and in vivo hepatoprotective activity, where hepatotoxicity was induced by CCl4 (20 mM) for in vitro study and by oral administration of Paracetamol (2 gm/kg) for in vivo study. Extract was administered orally at a daily dose of 200 mg/kg and 300 mg/kg, for 7 days (in vivo). In vitro hepatoprotective activity was assessed by checking the viability of the cells by using Trypan blue dye and by measuring release of cytosolic enzymes in the medium and In vivo hepatoprotective activity was assessed by measuring serum biochemical parameters and endogenous anti oxidant enzymes. The levels of cytosolic enzymes, serum enzymes and endogenous antioxidant enzymes, used as a marker of oxidative damage to hepatocytes, was reversed to the same level as in Normal group in does dependent manner. No obvious signs of toxicity were observed 300 mg/kg treatment dose.

Kamba et al\textsuperscript{52} reported that preliminarily phytochemical and antimicrobial investigation of the crude extract of the leaves of parkinsonia aculeata leaves showed the presence tannin, alkoloids, glycoside, terpenoids flavonoid, terpenes, steriods volatile oil and saponin. The presence of these secondary metabolites indicates the pharmacological
property of the plant leaves. The crude ethanolic extract, petroleum ether and chloroform extracts were also found to inhibit pseudomonas aeruginosa, streprococcus faecalis staphylococcus aureus, escherichia coli, and salmonella typhimurium and klebsiella sp. The tin layer chromatography(TLC) revealed four spots, three spots and two spots for ethanol, petroleum ether and chloroform extract respectively using ethyl acetate: hexane solvent mixture. The minimum inhibitory concentrations (MIC) of the crude extracts were determined for the various organisms which ranged between 35 and 50 mg/ml while the minimum bactericidal concentration (MBC) ranged between 45 and 60 mg/ml. parkinsonia aculeata could be a potential source of antimicrobial agents.

Hundekari et al\textsuperscript{53} reported that liver is a vital organ performing wide range of functions, oxidative damage is implicated in the pathogenesis of various liver disorders. Present study was aimed at evaluating protective ability of Parkinsonia aculeata Linn against CCl4-induced hepatotoxicity in rats. Seven experimental groups of six rats each were made. Petroleum ether, methanolic, chloroform, and aqueous leaves extract were used for evaluation of hepatoprotective activity administered orally in a daily dose of 500 mg/kg for 10 days. In vivo hepatoprotective activity was assessed by measuring biochemical parameters like various enzymes, triglycerides and thiopental induced sleeping time potentiation. Results were also confirmed histopathologically. Petroleum ether and methanol extracts showed the strongest hepatoprotective effect comparable with standard drug Liv 52. No signs of toxicity was observed at 500 mg/kg daily dose. The hepatoprotective effects of P. aculeata may be due to both the inhibition of lipid peroxidation and the increase of antioxidant activity.
3.2. *Rotula aquatica* lour\textsuperscript{77}.

**Synonym:** Carmona viminea (Wallich), Ehretia viminea Wallich, Rhabdia viminea (Wallich) D.

**Family:** Boraginaceae.

**Part Used:** Root

*Fig No. 5* Fresh leaves and flower of *Rotula aquatica*

**Vernacular Names:**

Kannada: Paashaanabheda,

Hindi: Pashanabhed

Telugu: Pashanabhedi

Marathi: Machim

Tamil: Ceppunerinji

Malayalam: Kalluranci

Sanskrit: Ashmahabhedah

Division: Angiosperms

Class: Asterids

Order: (unplaced)

Family: Boraginaceae

Subfamily: Ehretioideae

Genus: *Rotula*

Species: *R. aquatica*
**Nature**: A small much branched shrub, 60-180 cm high with numerous short lateral arrested branchlets off ten rooting; leaves simple, nearly sessile, spatulate, rouded at the apex, more or less hairy, crowded on the branches; flowers pink or reddish, shortly pedicellate, single or 2-3 together on short lateral branches, stamens exerted beyond the corolla tube; fruits subglobose, orange red drupes, tipped with the remains of the style.

Stems gray or black-gray, glabrous. Petiole 0.5-4 mm; leaf blade oblong or oblanceolate, 0.5-2.5 cm × 2-10 mm, ± leathery, strigose, base rounded, cuneate to broadly cuneate, margin entire, apex obtuse, mucronate. Corolla 6-7 × 6-7 mm. Fruit yellow- to brownish red, ca. 4 mm in diam., nearly dry.

**Distribution**: *Rotula aquatica* is a species of aromatic flowering shrub in the borage family, Boraginaceae. It is a rare *rheophyte* native to India, where it is a member of the lotic ecosystem of streams.

**Ethnobotanical uses:**

**Sivarajan and Indira Balachandran** (Ayurvedic Drugs and Their Plant Sources.) reported that the plant is a mandatory component of many ayurvedic drug preparations and is an important traditional medicine for kidney and bladder stones. The root tuber is astringent, bitter, diuretic and also useful in treating coughs, heart diseases, dysuria, blood disorders, fever, poisonings, ulcers and uterine diseases.

**Christiana et al.** reported that Root decoctions are both diuretic and laxative and are used to treat bladder stones and sexually transmitted diseases.

**Patil et al.** reported that plant was extensively used by vaidyas (Ayurvedic practioners) in holistic treatment of cancer.

In another **Website**, the ethnobotanical uses of *Rotula aquatica* were reported. Those are as follows.

- **Indian-herbs-exporters** reported that the roots are bitter, astringent. cooling, diuretic and laxative and are useful in hemorrhoids, renal and vesicle calculi, diabetes and venereal diseases.

**Scientific reports:**
Christina et al.\textsuperscript{81} reported that the decoction of \textit{Rotula aquatica} lour was screened for antilithic activity in male Wistar rats and the results were summarized based on the ionic changes in both urine and serum. Nephrolithiasis was induced in rats by feeding them 3\% glycolic acid mixed feed for 45 days, which resulted in high urinary calcium, oxalate and high serum potassium. Simultaneous treatment with the decoction reduced calcium and oxalate ion concentration in urine, confirming the stone inhibitory effect. Histopathological studies of kidney tissue samples further substantiated the findings. The decoction was found to be nontoxic over the 45-day treatment period.

Patil et al.\textsuperscript{55} reported that plant was extensively used by vaidyas (Ayurvedic practitioners) in holistic treatment of cancer. In the present study, an attempt has been made to evaluate the antimitotic activity of \textit{R. aquatica}. Preliminary antimitotic screening was done using \textit{Allium cepa} root tip assay. The mitotic index of the root tips markedly decreased with increasing concentration of the aqueous extract. The different fractions obtained by successive extraction of \textit{R. aquatica} using solvents of increasing polarity were also evaluated for their antimitotic activity. Tannins were isolated which showed a better activity than the non-tannin fraction. Experiments were also carried out with incorporation of folic acid in the aqueous extract. Folic acid inhibited the antimitotic activity of aqueous extract of \textit{R. aquatica} in a dose dependent manner. The results obtained were compared with methotrexate a known drug available in market as anti-cancer agent. The studies were extended to human cells using 3 pancreatic cancer cell lines, \textit{viz}: HPAF-II, BxPC-3, and CAPAN-2. Extract of \textit{R. aquatica} was found to be extremely effective in the prevention of cell proliferation of the pancreatic cancer cell lines. The phytochemical evaluation revealed presence of polyphenols (tannins) and steroids. A HPTLC fingerprinting was developed and studied. Two compounds were isolated and subjected to spectral studies like UV, IR and mass spectrums. The empirical formula was derived by considering this data with elemental analysis of the compounds.

Mengi et al.\textsuperscript{56} reported that the aqueous extract of \textit{Rotula aquatica} Lour (Boraginaceae) roots was investigated for its anti-inflammatory potential in acute and chronic inflammatory conditions in rats. The aqueous extract of the plant at doses 50,
100, and 200mg kg$^{-1}$, p.o., were screened against carrageenan-induced rat paw edema, cotton pellet-induced granuloma as well as crystal-induced inflammation in rats. The IL-6 levels in the exudates formed due to crystal-induced inflammation were also determined. The extract exhibited a statistically significant (p<0.05) inhibition of rat paw edema as compared to the control group. With respect to crystal-induced inflammation, the extract demonstrated a statistically significant (p<0.05) reduction in the neutrophil and monocyte count in the inflammatory exudates compared to the control group. The extract at a dose of 200mg kg$^{-1}$ also effectively inhibited IL-6 levels. The extract exhibited a statistically significant (p<0.05) reduction in the weight of cotton pellet-induced granuloma at the doses of 100 and 200mg kg$^{-1}$ employed in the study compared to the control group.

Supportive studies included determination of in vitro antioxidant potential of the extract by DPPH free radical scavenging method. The results revealed that the extract possesses appreciable anti-oxidant activity (IC$_{50}$=11.07μg mL$^{-1}$). Collectively, the results indicated the extract of *R. aquatica* to have a potentially beneficial effect in relieving inflammation and providing a platform for the development of plant drugs for crystal-induced arthropathy.

Martin et al.$^{82}$ reported that Single medium-based efficient protocols for large-scale multiplication of the rare woody aromatic medicinal plant *Rotula aquatica* Lour. by means of axillary bud multiplication and indirect organogenesis were established using Murashige and Skoog (MS) medium. There were no significant differences with respect to the induction of shoots per node or callus and roots per shoot on media prepared either with tap water and commercial sugar or those prepared with double distilled water and tissue culture-grade sucrose. The most effective medium for axillary bud proliferation was MS medium fortified with 1.0 mg l$^{-1}$ N$^6$-benzylaminopurine (BAP) and 0.5 mg l$^{-1}$ indole-3-butyric acid (IBA), on which shoots were induced at the rate of 15 per node. The excision of node segments from the in vitro-derived shoots and their subsequent culture on medium supplemented with same concentrations of BAP and IBA facilitated enhanced axillary bud proliferation. Callus that developed from the lower cut end of the node explants induced shoots during subculture on half-strength MS medium with 1.0 mg l$^{-1}$ BAP and 0.5 mg l$^{-1}$ kinetin. The shoots developed rooted best on half-strength MS
medium supplemented with 0.5 mg l\(^{-1}\) naphthaleneacetic acid (NAA). Rooted shoots, following acclimation in the greenhouse, were successfully transferred to field conditions, and 80% of the plantlets survived. When the basal ends of shoots harvested from multiplication medium were dipped in an NAA (0.5 mg l\(^{-1}\)) solution for 25 days, a mean of 5.6 roots per shoot developed; the transfer to small pots facilitated the survival of 75% of the rooted shoots. Ex vitro rooting by direct transfer of the shoots from the multiplication medium to the greenhouse resulted in a 65% survival. Commercial sugar and tap water and ex vitro rooting make the protocol economically advantageous. About 750 plantlets were procured in a 3-month period starting from a single node explant.

Raut et al.\(^{83}\) reported that several Ayurvedic plants are known to have activity against diverse urinary crystals. The traditional knowledge of Ayurveda, collective clinical experience in arthritis and the earlier experimental studies on urinary crystals led to the selection of three plants, viz. *Rotula aquatica*, *Commiphora wightii* Bhandari syn. *C.mukul*. and *Boerhaavia diffusa* for screening anticrystal activity against basic calcium phosphate (BCP), calcium pyrophosphate (CPPD) and monosodium urate monohydrate (MSUM). The effects of each plant were assayed on microcrystals in 24-well microplates in vitro. Our results show that the aqueous extracts of only *R. aquatica* and *C. wightii* have shown crystal dissolving activity against MSUM.

Singh et al\(^{84}\) reported that *Aerva lanata* and *Rotula aquatica* Lour both plants widely distributed throughout India. This study was undertaken to in-vitro comparative study for anthelmintic effect of aqueous extract of Rotula aquatica Lour and Areva Lanata on adult earth worm’s pheritma posthuma, using piperazine citrate 15 mg/ml as standard drug. The study involved the determination of the time of paralysis and time taken for death of the worms. Dose dependent activity was observed in different concentration (25, 50, 75 mg/ml) of aqueous extract of *Rotula aquatica* lour and Aerva lanata. The result shows that the aqueous extract of Aerva Lanata is more effective from aqueous extract of Rotula aquatica when compared to standard drug piperazine citrate (15mg/ml).
3.3 Review of literature for Analgesic-Antipyretic-Anti-inflammatory activity:

Kittipong et al\textsuperscript{85} reported that \textit{Tacca chantrieri} Andre is an indigenous perennial of the tropics which is used by local healers to relieve pains of the body and stomach, and as an antidote for food poisoning. The present study was undertaken to investigate the analgesic, antipyretic and anti-inflammatory activities of \textit{T. chantrieri} as claimed in traditional medicine. The ethanolic extract of the plant’s rhizome was prepared and tested in experimental animals. It was found that the extract significantly inhibited pain caused by acetic acid injection in the writhing response test in mice and the tail flick test in rats. This finding suggests that the extract exerts analgesic effect through both peripheral and central mechanisms. The analgesic effect was not antagonized by pretreatment with naloxone, an opioid antagonist and this signifies a mechanism other than that of the opioid system was utilized. The extract also significantly decreased the yeast-induced hyperthermia in rats. Anti-inflammatory effect of \textit{T. chantrieri} extract was demonstrated in ethylphenylpropiololate-induced ear edema and formalin tests in mice. These findings indicate that the ethanol extract of \textit{T. chantrieri} possesses analgesic, antipyretic and anti-inflammatory effects, which is in accord with its use in traditional medicine.

Esther et al\textsuperscript{86} reported that despite the progress made in medical research in the past decades, the treatment of many diseases including inflammatory diseases is still problematic. Conventional drugs used to ameliorate these conditions are either too expensive or toxic, there is therefore an urgent need to search for newer, cheaper and safer medications. \textit{Strophanthus sarmentosus} (SMS) is an indigenous plant used in traditional medicine in West Africa for the treatment of inflammatory diseases among other uses. The present study was designed to explore its therapeutic benefits in inflammation, nociception and pyrexia. Analgesic effect of the ethanolic extract of dried SMS root (50, 100 and 200 mg kg\textsuperscript{-1}) was evaluated in mice using acetic acid-induced writhing and hot plate models, while the efficacy of the herbal drug was compared with 150 mg kg\textsuperscript{-1} acetylsalicylic acid, 0.5 mg kg\textsuperscript{-1} piroxicam and 5 mg kg\textsuperscript{-1} morphine respectively. Anti-inflammatory activity of SMS was also investigated using groups of
oedema-induced rats separately treated with 1 % w/v carrageenan in normal saline and xylene. The effects of 10 mg kg-1 indomethacin and 1 mg kg-1 dexamethasone were also evaluated as respective standard drugs for the two models. The antipyretic effect of SMS was lastly studied using d-amphetamine and Klebsiella-induced pyretic tests with 150 mg kg -1 acetaminophen serving as the comparative agent. Acute toxicity test was conducted on the herbal decoction via both oral and intraperitoneal routes to obtain its LD50. The extract dose-dependently and significantly (p<0.05) inhibited writhing in the acetic acid test group. The effect produced by 200 mg kg-1 extract (72.8 % inhibition), compared well with acetylsalicylic acid (66.6 %), but was much less than piroxicam (90.9 %). A prolongation in reaction time in the hot plate model produced by SMS recorded 68.9 % inhibition with the highest dose and 98.4 % with morphine. The extract produced dose-dependent and significant inhibition (p<0.05) of oedema, which was comparable to indomethacin in the caraageenan-induced paw oedema model. Similarly, SMS demonstrated a significant effect(p<0.05), compared to dexamethasone on the xylene-induced mouse ear oedema test. The extract significantly decreased the hyperthermic temperature in both d-amphetamine and Klebsiella-induced pyrexia as indicated by the percentage reduction in fever recorded. Findings from the present study showed SMS to possess central and peripheral analgesic activity, anti-inflammatory property similar to steroidal and non-steroidal agents as well as antipyretic effect. The presence of diverse secondary metabolites including flavonoids, glycosides, tannins, alkaloids and saponins could account for the wide therapeutic spectrum of SMS. LD50 for oral.

Venkataraman et al87 reported that the pharmacological and chemical constituents of plants from the plant Pergularia daemia Forsk which is widely used in folk medicine. In the present study, the analgesic, antipyretic, anti-inflammatory of Petroleum ether and Chloroform extract of plant of Pergularia daemia Forsk were studied .The analgesic activity was found out by eddy’s hot plate method by using standard Diclofenac sodium . The antipyretic activity was found out by yeast induced pyrexia method by using standard Paracetamol. The anti-inflammatory activity was found out by Carragenan induced paw edema method by using standard Diclofenac sodium. Preliminary phyto chemical screening showed the presence of glycosides, alkaloids,
phytosterols, saponins, fixed oils and fats, flavonoids and coumarins are present in extracts. In carrageenan induced paw edema method the chloroform extract of *pergularia daemia* showed more significant inhibition than petroleum ether extract. The results were found to be highly significant (p<0.01) in comparison to the control. In eddys hot plate method the chloroform extract of *pergularia daemia* exhibited significant analgesic activity than petroleum extract. In antipyretic activity the chloroform and pet ether both extracts having significant activity.

Jayabharathi et al.\(^8\) reported that the ethanolic extract of the flowers of Moringa concanensis (family:Moringaceae) was tested for phytochemicals, anti-inflammatory, analgesic and antipyretic activity. Qualitative phytochemical analysis of Moringa concanensis flower extract was carried out with a view of developing leads for new therapeutic products. The results indicate that Moringa concanensis is rich in phytoconstituents and the studies also indicate that the ethanolic extract showed significant antiinflammatory, analgesic and antipyretic activity when compared with standard drug.

Fadeyi et al.\(^8\) reported that four-Substituted derivatives of salicylic and anthranilic acids: 2-hydroxy-5-azidosulfonylbenzoic acid (HASBA, 1), 2-acetyloxy-5-azidosulfonylbenzoic acid (AASBA, 2), 2-acetamido-5-azidosulfonylbenzoic acid (AMASBA, 3) and 2-acetamido-5-sulfonamidobenzoic acid (AMSABA, 4) were synthesized and evaluated for their analgesic, antipyretic, anti-inflammatory and cytotoxic activities. HASBA, AASBA and AMASBA showed higher analgesic activity than aspirin (ASA) at 100 mg/kg dose, while AMSABA showed the least analgesic property. AMASBA exhibited higher antipyretic activity than paracetamol (PCM), while HASBA, AASBA and AMSABA also showed antipyretic effects which were of equal potency to that of PCM. The order of anti-inflammatory effects of the four compounds is: AASBA > AMASBA > HASBA > AMSABA. The effects of the substituents on the biological activities of the synthesized compounds are discussed.

Clement et al.\(^8\) reported that the analgesic activities of the aqueous extract of *Carpolobia lutea* was evaluated in mice and rats using the mouse writhing, tail flick and
formalin induced pain tests. Analgesic studies were performed using three models; mouse writhing assay, formalin test and tail flick assay. The extract (1500 to 2500 mg/kg) and acetylsalicylic acid (100 mg/kg) produced a significant (P<0.05) inhibition of the second phase in the formalin pain model, while the antinociceptive effect was not produced in the first phase. The extract also showed a dose dependent inhibition of acetic acid induced abdominal writhings. The tail flick latency was not enhanced by the extract. Oral administration of the extract up to 2500 mg/kg did not produce any toxic effects in the acute toxicity studies in mice. The LD50 of the extract when administered orally was 3338.83 mg/kg. The data obtained shows that C. lutea posseses analgesic activity that is peripherally mediated.

3.4 Review of literature for Analgesic activity:

Rajesh et al91 reported that the methanolic extract of the leaves of Hedera helix L. (Araliaceae) which contains mainly saponins and carbohydrate showed significant analgesic and anti-inflammatory activities (P<0.05) in the tail flick/ hot-plate test and egg albumen-induced rat paw oedema tests that were comparable to the test drugs (morphine 20mg/kg and indomethacin 50mg/kg respectively). These findings suggest that the methanol leaf extract of Hedera helix L. possess analgesic (which might have been peripherally mediated) and anti-inflammatory activities; and may lend credence to the ethnomedical claim of the use of the plant for the management of pain and inflammatory conditions.

Lokesh et al92 reported that Pergularia daemia (Forsk.) Chiov. (Asclepiadaceae) is used in Ayurveda for the treatment of inflammation, fever, strangury, asthma, diseases of vata and kapha. It is known as Uttaravaruni and Yugaphala in Sanskrit. The present study was undertaken to evaluate the analgesic activity of the aqueous and alcohol root extracts of Pergularia daemia (Forsk.) Chiov. using eddy’s hot plate and heat conduction method. In eddy’s hot plate method the aqueous extract showed significant analgesic activity at the doses of 500 mg/kg (p<0.01) and 1000 mg/kg (p<0.001) and alcohol extract showed significant analgesic activity at the doses of 500 and 1000 mg/kg (p<0.001). In heat conduction method both extracts showed significant analgesic activity.
at the doses of 500 & 1000 mg/kg (p<0.001) as compared to control group, when analyzed statistically by Tukey Kramer Multiple Comparison Test. The result obtained show that the aqueous and alcohol root extracts of *Pergularia daemia* (Forsk.) Chiov. possesses significant analgesic activity which confirms the traditional claims of the plant mentioned in Ayurveda.

**Zulfiker et al**\(^9^3\) reported that fruits and whole herb of two medicinal plants, *Ficus racemosa* Linn. (Moraceae) and *Scoparia dulcis* L. (Scrophulariaceae) were extracted in 95% ethanol to evaluate for centrally acting analgesic potential using hot plate and peripheral pharmacological actions using acetic acid induced writhing test in mice. The crude extracts of both the plants were found to have significant (p<0.001) analgesic activity at the oral dose of 100 & 200 mg/kg b. wt., in the tested models. In hot plate test *S. dulcis* showed increased latency period than *F. racemosa* whereas in acetic acid induced writhing test *F. racemosa* showed reduced number of writhes than *S. dulcis* at two dose levels which are significant (p<0.001) compared to control. The results obtained support the use of fruits of *F. racemosa* and whole herb of *S. dulcis* in painful conditions acting both centrally and peripherally.

**Ibrahim et al**\(^9^4\) reported that the work was aimed at investigating toxicity and analgesic potentials of the ethanol leaf extract of *Vernonia amygdalina* Del. in mice. Acute toxicity was evaluated by intraperitoneal administration of the extract whereas acetic acid-induced writhing in mice method was used for the analgesic study. The extract was found to have an LD\(_{50}\) of 288.5 mg/kg body weight *i.p.* and a significant (p < 0.05) dose-dependent analgesic activity with the highest percentage inhibition (71.9%) at 100 mg extract/kg against the acetic acid-induced writhing in mice. This activity was higher than that of the standard analgesic: *ketonal* (67.5%) used at 10 mg/kg. The results obtained showed that the plant has a relative toxicity to the mice and was found to have a dose-dependant analgesic property. The plant could therefore, serve as a potential source of analgesic.

**Mohammed et al**\(^9^5\) reported that this work has been done for the investigation and study of analgesic and antipyretic activity of *Moringa oleifera* lam. seeds extract.
Analgesics and antipyretics compounds in the market still present a wide range of undesired effects leaving an open door for new and better compounds. Natural products are believed to be an important source of new chemical substance with potential therapeutic applicability. Qualitative chemical investigation for the identification of chemical constituents. Identification of the active principles by TLC and Column chromatography and further studies them for possible analgesic activity by using Hot plate method and Tail immersion method and antipyretic activity by Yeast induce hyperpyrexia method in Female albino rats. The present study indicates that Hot plate and Tail immersion model tests suggests that the ethanolic extract seems to possess an intensity of analgesic effect that is mostly mediated via a peripheral mechanism by inhibition of the PGs-mediated potential of analgesic action of bradikinin and Yeast induced Hyperpyrexia method showed that the ethanolic extract at dose (30 mg/kg) caused significant lowering of the body temperature up to 2 hr, as the mean temperature 38.28 oc was reduced to 37.30 oc. It is thus evident that Moringa oleifera Lam. is a weak analgesic and antipyretic agent as compared to Aspirin.

3.5 Review of literature for Antipyretic:

Nagaveni et al. reported that the present study is designed to investigate preliminary photochemical characteristics and anti-pyretic effect of the Indian medicinal plant Mangifera indica which belongs to the family Anacardiaceae. The genus of this plant cited in Indian system of medicine, Ayurveda for the treatment of pain and fever associated various diseases. Naturally occurring terpenoids are unique phyto constituents of the genus Mangifera indica, but there is no scientific evidence has been demonstrated against the effect of this plant extract in pyretic invivo models. The ethanolic extract of mangifera indica bark shows potential antipyretic activity at a dose of 400 mg/kg.

Md. et al reported that the main aim of this study is to evaluate antipyretic activity on Murraya koenigii spreng. leaves extracts. Murraya koenigii spreng. leaves were collected from rural area and extracted with Petroleum ether, Chloroform, Ethanol and the extract was screened for antipyretic activity by Yeast induced hyper pyrexia method. Paracetamol (150mg/kg) was used as standard drug. It was observed that
Petroleum ether and chloroform extracts did not show significant decrease in elevated temperature with respect to corresponding control. The Ethanolic extract gives significantly reduced elevated temperature. The present study indicates that *Murraya koenigii* spreng. leaves Ethanol extract possess good significant antipyretic activity as compared to control group, where as Petroleum ether extract, Chloroform extract.

Sushil et al.\(^9\) reported that the aqueous extract of *Swertia chirata* Buch Ham. Root (ASC) (Family: Gentianaceae) was evaluated for its antipyretic potential on Brewer’s yeastinduced pyrexia in albino rats and Typhoid-Paratyphoid A, B vaccine induced Hyperexia in rabbits. In both models, the extract, at dose of 200 mg kg\(^{-1}\) body wt. and 400 mg kg\(^{-1}\) body weight, produced significant (p<0.001) reduction in elevated body temperature in a dose dependent manner. The antipyretic effect of the extract was comparable to that of paracetamol (150 mg kg\(^{-1}\) body weight, p.o.), a standard antipyretic agent.

Mohammed et al.\(^9\) reported that this work has been done for the investigation and study of analgesic and antipyretic activity of *Moringa oleifera* lam. seeds extract. analgesics and antipyretics compounds in the market still present a wide range of undesired effects leaving an open door for new and better compounds. Natural products are believed to be an important source of new chemical substance with potential therapeutic applicability. Qualitative chemical investigation for the identification of chemical constituents. Identification of the active principles by TLC and Column chromatography and further studies them for possible analgesic activity by using Hot plate method and Tail immersion method and antipyretic activity by Yeast induce hyperpyrexia method in Female albino rats. The present study indicates that Hot plate and Tail immersion model tests suggests that the ethanolic extract seems to possess an intensity of analgesic effect that is mostly mediated via a peripheral mechanism by inhibition of the PGs-mediated potential of analgesic action of bradikinin and Yeast induced Hyperpyrexia method showed that the ethanolic extract at dose (30 mg/kg) caused significant lowering of the body temperature up to 2 hr, as the mean temperature
38.28 oc was reduced to 37.30 oc. It is thus evident that *Moringa oleifera* Lam. is a weak analgesic and antipyretic agent as compared to Aspirin.

**Amiya et al**\(^{100}\) reported that the objective of the present work was to study the antipyretic activity of plant *Capparis zeylanica* Linn. belonging to family Capparaceae, known as “Karambha” in Sanskrit & “Asadhua” in Oriya. Materials & Methods- The Methanolic extract was taken for the study and evaluated for antipyretic activity using Brewer’s yeast induced pyrexia in Wister strain albino rats. The methanolic extract at a dose of 100mg/kg & 200mg/kg were evaluated for antipyretic activity. Result - The extract of *C. zeylanica* plant showed a significant (P < 0.01) dose dependent antipyretic effect in yeast induced elevation of body temperature in experimental rats. Conclusion - The Methanolic extract of *Capparis. zeylanica* Linn. plant have significant antipyretic activity when compared with the standard drug. So. It can be recommended for further studies.

3.6 Review of literature for Anti-inflammatory activity:

**Tailor et al**\(^{101}\) reported that in the present Study of Ethanolic extract of Stem of *Rubia cordifolia* Linn.(Rubiaceae) was screened for anti-inflammatory activity in carrageenan induced paw oedema rats. The effect was assessed by Difference in paw oedema volume, before & after the low & high dose administration of the extract in Rats. Ethanolic extract of *Rubia cordifolia* stem (20 & 40 mg./kg./ml.) were administered orally. Anti-inflammatory effects were compared with Standard drug- Indomethacin (10mg./kg/ml.). These observations helped us to conclude that Ethanolic Extract high dose is endowed with anti-inflammatory property.

**Maminur et al**\(^{102}\) reported that previous phytochemical analysis of methanolic extract of *Acalypha indica* L. has indicated the presence of steroid, flavonoid and terpenoid types of compounds. Since these compounds are of pharmacological interest, coupled with the use of this plant in traditional medicine, prompted us to check *A. indica* L. for possible analgesic and antiinflammatory activities. The methanolic extract of *A. indica* L. showed statistically significant (P<0.001) analgesic activity in mice in a dose-dependent manner. A sustained and significant (P<0.001) inhibition of carrageenan-
induced inflammation of rat paw was observed with 125 mg/kg and 250 mg/kg body weight. The methanolic extract of *A. indica* L. also demonstrated antiinflammatory effect in a dose-dependent manner. Maximum inhibition by the extract was observed at 250 mg/kg body weight after three hours of ingestion, which was comparable to that of the standard drug phenylbutazone at a dose of 100 mg/kg body weight. The obtained results provide a support for the use of this plant in traditional medicine.

Govindappa et al\textsuperscript{103} reported that ethanol extract of leaf, stem and flower of *Wedelia trilobata* was assessed for its antimicrobial, antioxidant and anti-inflammatory activity and phytochemical screening. Total phenolic content was assessed using Folin-Ciocalteu’s method. The antioxidant activity was determined by measuring the scavenging activity of DPPH radical and FRAP assay. The antimicrobial efficacy was determined using paper disc method against different fungi and bacteria. Sensitivity in terms of zones of inhibition and phytochemical composition of the all parts extracts were also determined. *In vitro* anti-inflammatory activity was evaluated using albumin denaturation, membrane stabilization assay and proteinase inhibitory assay. Aspirin was used as a standard drug for the study of anti-inflammatory activity. The results show that, all parts extracts effective against all the bacteria tested, whereas all the extracts were failure in inhibiting the growth of all *Alternaria* sp., *Cercospora carthami* and *Nigrospora oryzae*, but other fungi also were showed moderate inhibition against all the three extracts. Phytochemical analysis revealed the presence of tannins, flavonoids, terpenoids, phenols and saponins. Leaf and stem ethanol fractions showed highest total Phenolic content. The leaf and stem ethanol extract possessed strong scavenging activity in both DPPH and FRAP methods. In DPPH and FRAP method, the leaf and stem had showed free radical inhibition of 86, 82 and 630.72, 508.81 respectively. The leaf and stem ethanol extract also showed *in vitro* anti-inflammatory activity by inhibiting the heat induced albumin denaturation and red blood cells membrane stabilization with 87.14 and 86.76 and 78.11, 74.17 g/ml respectively. Proteinase activity was also significantly inhibited by the leaf (84.19 g/ml) and stem (81.84 g/ml). From the result, it is concluded that phytochemicals (tannins, flavonoids, terpenoids, phenols and saponins) present in the
W. trilobata extract may be responsible for the antimicrobial, antioxidant and antiinflammatory activity.

Amar et al\textsuperscript{104} reported that 2H-1,4-pyridooxazin-3(4H)-one was synthesized by condensation of 2-amino-3-hydroxy-pyridine with chloroacetylchloride by using standard procedure. Esterification with ethylchloroacetate and further condensation with hydrazine hydrate produced hydrazide of 2H-1,4-pyridooxazin-3(4H)-one. Schiff base derivatives of 2H-1,4- pyridoxazin-3(4H)-one were synthesized by the acid catalyzed condensation 2-(3-oxo-2,3-dihydro-4H-1,4- pyridoxazin-4-yl)acetohydrazide with various benzaldehyde derivatives. Schiff base derivatives were characterized by FT-IR, 1H-NMR. All compounds were screened for anti-inflammatory activity by carrageenan induced edema in mice paw against diclofenac sodium as a standard drug. The activity reflects their ability to provide protection (45.00-70.00\%). The safety of these schiff base derivatives are reflected by toxicity studies.

Biswa et al\textsuperscript{105} reported that the bark of Xeromphis spinosa extracted by a mixture of equal proportions of petroleum ether, ethyl acetate and methanol at an oral dose of 200 and 400 mg/ kg body weight exhibited significant anti-inflammatory activity when compared with control.

Review of literature for Anti Oxidant activity:

Pourmorad et al\textsuperscript{106} reported that in present study, we carried out a systematic record of the relative antioxidant activity in selected Iranian medicinal plant species' extracts. The total phenol varied from 24.1 ± 1 to 289.5 ± 5 mg g -1 in the extracts. Flavonoid contents were between 25.15 ± 0.8 and 78.3 ± 4.5 mg g-1. 1,1-diphenyl-2-picryl hydrazyl (DPPH) radical scavenging effect of the extracts was determined spectrophotometrically. The highest radical scavenging effect was observed in Mellilotus officinalis with IC50 = 0.018 mg ml –1. The potency of radical scavenging effect of M. officinalis extract was about 4 times greater than synthetic antioxidant butylated hydroxy toluene (BHT). The greater amount of phenolic compounds leads to more potent radical scavenging effect as shown by M. officinalis extract.
Panda et al\textsuperscript{107} reported that free radicals are implicated for more than 80 diseases including Diabetes mellitus, arthritis, cancer, ageing, etc. In treatment of these diseases, antioxidant therapy has gained an utmost importance & research is now directed towards finding naturally occurring antioxidant of plant origin. In a step in this direction we have evaluated antioxidant potency of the ethanol extract on the aerial parts of \textit{Cocculus hirsutus} Diels. The extract was investigated for its free radical scavenging action towards 1, 1-Diphenyl–2-picryl hydrazyl, nitric oxide, superoxide and hydroxyl radicals and found that the ethanol extract shows promising free radical scavenging activity in dose dependent manner. This antioxidant potency may be related to the presence of antioxidant vitamins and phenolic compounds present in the extract. These results clearly indicate that \textit{Cocculus hirsutus} Diels is effective against free radical mediated diseases.

Sunita et al\textsuperscript{108} reported that the methanolic (Fr-Me) and ethyl acetate fraction (Fr-Et) obtained from the aerial parts of \textit{Cressa cretica} L. (Convolvulaceae) exhibited inhibitory effect against acute and chronic models of inflammation, namely, carrageenan-induced paw edema, cotton pellet granuloma, carrageenan air pouch inflammation, vascular permeability, freuds complete adjuvant induced arthritis models. The fractions also inhibited arachidonic acid and other mediator (histamine, serotonin, prostaglandin E2)-induced paw edema in rats in a dose dependent manner. Moreover, Fr-Me and Fr-Et significantly increased plasma superoxide dismutase, catalase, glutathione and glutathione peroxidase activities. On the contrary, the malonaldehyde (as a measure of lipid peroxidation) level was significantly decreased when compared with the control group. Also, it was found that Fr-Et reduced the inflammation and revealed the antioxidant activity more significantly than Fr-Me. Thus study established the anti-inflammatory activity and scavenges the free radicals, which are important mediators that provoke or sustain inflammatory processes.

Priyanka et al\textsuperscript{109} reported that the antioxidant activity of two plants - Hadjod i.e. \textit{Cissus quadrangularis} (CQ) and Hingot i.e. \textit{Balanites aegyptiaca} (BA) was determined by the thiocyanate method. The antioxidant activity of both the plants
increased with increasing amount of extract (200μg-1000μg) added to the linoleic emulsion. The ethanolic extract of CQ was more effective than the other. Like antioxidant activity, the reducing power was also dependent upon the concentration. The ethanolic extract of BA shows more reducing power than the other. The result obtained in the present study indicates that the both the plants are potential source of natural antioxidants. In addition, we could suggest that although the reducing power of a substance may be an indicator of its potential antioxidant activity, there is not necessarily a linear correlation between these two activities.

Beniwal et al\textsuperscript{110} reported that antioxidant activity of the aqueous hot extract of heliceters isora linn (Family- Sterculiacea) fruits was investigation in various in vitro modals. The total polyphenols content of the extract was found 7.04% of ACHI. When compared to galic acid and total flavonoids content was 2.4 mg/g of AEHI, when compared to rutin. Hydrogen peroxide radical were inhibited at IC\textsubscript{50} – 165 μg/ml, while ascorbic acid inhibited at 187.33 μg/ml. AEHI inhibited the nitric oxide radical at IC\textsubscript{50} – 820 μg/ml, when it was compared with rutin as standard antioxidant with IC\textsubscript{50} – 68.52 μg/ml, superoxide radical inhibition was compared with quercertin and IC\textsubscript{50} value was found more than 1000 μg/ml.