Chapter 2

Review of literature
2. REVIEW OF LITERATURE

Parmar et al., (1978) have reported the anti-inflammatory activity of gossypin (bioflavonoid) isolated from *Hibiscus vitifolius* and the anti-inflammatory activity of gossypin has been studied in comparison with the standard non-steroidal anti-inflammatory drug (NSAID) phenylbutazone against various experimental models of inflammation and increased vascular permeability. It produced significant inhibition of the accumulation of pouch fluid and granulation tissue formation in the carragereenan induced granuloma pouch in rats which could be attributed to the decreased formation of collagen tissue. It was found to significantly reduce the rat paw oedema and the increased vascular permeability induced by various phlogistic agents.

Solimabi et al., (1980) have reported the antispasmodic and anti-inflammatory activity of carrageenan extracted from *Hypnea musciformis*, a red algae and have shown that it antagonizes histamine-induced spasm in guinea pig ileum and possesses anti-inflammatory activity against rat hind paw oedema induced by commercial carrageenan.

Gupta et al., (1980) have reported the antiphlogistic activities of \( \beta \)-sitosterol isolated from *Verbena officinalis*.

Shipochliev et al., (1981) reported that the extracts of leaves of *Plantago lanceolata* and *Plantago major* possessed antiphlogistic activity in carrageenan- and PGE1-induced inflammations in rats.

Antarkar et al., (1983) reported the anti-inflammatory activity of the water extract of the roots of *Rubia cordifolia* in rats with carrageenan induced paw oedema.
in comparison with the standard drug phenylbutazone and found the plant showed significant anti-inflammatory activity at a dose of 10 and 20 ml/kg of the water extracts.

Gupta et al., (1986) isolated the four anti-inflammatory agents viz., Luteolin, β-Sitosterol, Lawson and Laxanthone-II from the leaves of *Lawsonia inermis* and their anti-inflammatory efficacies were established using animal models. Hydrocortisone and phenylbutazone were employed as the standard drugs for the study. β-Sitosterol exhibited greater anti-inflammatory activity than the standard drug phenylbutazone.

Ageel et al., (1986) have reported that the aqueous extract of *Capparis spinosa* significantly inhibited carrageenan-induced rat paw oedema.

Al-Said et al., (1988) have isolated the polyphenols cappaprenol 12, 13 and 14 from *Capparis spinosa* of which cappaprenol 13 inhibited carrageenan-induced rat paw oedema to 44% nearly as potently as the reference oxyphenbutazone.

The essential oil of *Artemisia caerulescens* which contains santonin, thujon, camphor, β-caryophyllene, borneol, nerol, α-terpineol inhibited carrageenan-induced rat paw oedema (0.3 ml/kg = 43.4% inhibition; 1.0ml/kg = 87.0% inhibition) comparable to lysine acetyl salicylate (75 mg/kg = 39.4% inhibition; 200mg/kg = 79.4% inhibition) (Moran et al., 1989).

Ozaki et al., (1989) examined the antiphlogistic activity of a 70% methanolic extract of *Myristica fragrans in vivo* using a carrageenan-induced rat paw oedema. The extract inhibited the oedema at 1.5 g/kg (indomethacin 10 mg/kg), and the activity was traced to myristicin which inhibited at 0.17 g/kg.
Ageel et al., (1989) reported that after oral application of 500mg/kg of ethanolic extract of *Smilax sarsaparilla* carrageenan-induced rat paw oedema was reduced by 25%.

Berkan et al., (1991) have studied the effect of *Centaureum erythraea* in the Mycobacterium adjuvant polyarthritis model and showed that there was a clear reduction of the inflammation and of weight loss in higher test concentrations from 50 to 500 mg/kg.


Chattopadhyay et al., (1993) evaluated the effect of *Azadirachta indica* leaf extract on inflammatory oedema induced by chemical mediators (5-HT, histamine, bradykinin and PGE1) to find out its possible mechanism of reported anti-inflammatory effect against carrageenan- induced rat hind paw oedema. The leaf extract showed significant anti-inflammatory effect against 5-HT and PGE1 induced inflammation but not on the inflammation induced by histamine and bradykinin. Their study suggests that *Azadirachta indica* extract’s anti-inflammatory effect may be due to antagonism of the deleterious effect of 5-HT and PGE1 on blood vessels.

Murai et al., (1995) reported that, acteoside, the main phenylethanoid from *Plantago lanceolata* inhibits arachidonic acid induced mouse ear oedema in rats.

Ammon et al., (1996) have evaluated the *in vivo* activity of the essential oil of *Matricaria recutita* and the active principle α-bisabolol reduces carrageenan-induced
paw oedema and adjuvans arthritis and is also anti-ulcerogenic. They also reported that α-bisabolol inhibits 5-LOX in vitro conditions.

Hiermann et al., (1998) have reported the antiphlogistic activity of ethanolic extract of the roots of *Peucedanum ostruthium* and the active coumarin ostruthin was evaluated in carrageenan-induced rat paw oedema test system.

The genus *Artemisia* has over 300 species, making it one of the largest genera of the northern hemisphere. Artemisia species are in use for the treatment of malaria, hepatitis, cancer, inflammation, bacterial, viral and fungal infections (Tan et al., 1998).

The anti-inflammatory activity of *Curcuma amada* rhizome was studied using acute carrageenan induced rat paw oedema and chronic granuloma pouch model and the plant showed to possess potent anti-inflammatory activity (Mujumdar et al., 2000).

The saponins verbascosaponin and verbascosaponin A, and the iridoids scrovalentinoside and scropolioside A were isolated from *Scrophularia auriculata* and tested in a number of in vivo inflammatory models. Verbascosaponin showed the strongest inhibition of carrageenan- induced rat paw oedema. TPA-induced ear oedema was inhibited by both saponins. Both the iridoids had weaker, yet significant activities. After multiple topical applications of TPA (a model for chronic inflammation) the oedema was still significantly inhibited (0.5 mg/ear) by verbascosaponin A, verbascosaponin, scrovalentinoside and scropolioside A inhibition (Giner et al., 2000).
Giner-Larza et al., (2001) have tested oleanolic- and oleanonic acid, two triterpenes from *Pistacia terebinthus* galls in a number of *in vivo* inflammation models.

Yesilada et al., (2001) showed that the diterpenoids genkwadaphin and 1, 2-dehydrodaphnetoxin and the coumarin daphnetin from *Daphne oleoides*, inhibit the proinflammatory cytokines, IL-1β, IL-1α and TNFα at test concentrations 1–30 µg/ml.

Vetrichevan et al., (2002) reported the effect of alcoholic extract of whole parts of *Achyranthes bidentata* on acute and sub-acute inflammation in Swiss male rats using carrageenin induced rat paw oedema and chronic granuloma pouch model. The extract exhibited maximum percentage of inhibition in the acute model of inflammation using carrageenan.

Letitia et al., (2002) selected thirty-five plant species from the published literature as traditionally used by the indigenous people of the boreal forest in Canada for three or more symptoms of diabetes or its complications. Antioxidant activities in methanolic extracts support the contribution of these traditional medicines in a lifestyle historically low in the incidence of diabetes. In a DPPH assay of free radical scavenging activity 89% of the methanol extracts had activity significantly greater than common modern dietary components, 14% were statistically equal to ascorbic acid and 23% had activities similar to green tea and a Trolox® positive control. The majority of the species (63 and 97%, respectively) had scavenging activities similar to ascorbic acid in the superoxide and peroxyl radical scavenging assays.
Plants often contain substantial amounts of antioxidants, including tocopherols, (vitamin E), carotenoids, ascorbic acid, flavonoids and tannins. The 1, 1 diphenyl-2-picryl-hydrazyl (DPPH) assay used for hydrogen donating capacity is commonly employed for screening plant extracts. Vitamin C (ascorbic acid) is an important dietary antioxidant. Vitamin E is a dietary antioxidant which has been investigated for its affect on diabetes. The combined antioxidant activity of the two dietary antioxidants vitamin E and vitamin C is greater than their individual actions. Tea, especially green tea, has been studied extensively for its antioxidant activity in relation to cancer and cardiovascular disease. Tea contains tannin, with most of its antioxidant activity attributed to catechins. Rather than being a single chemical, tea has the combined activity of flavonoids, most being catechins, theaflavins and flavonols that can lead to enhanced activity (Letitia et al., 2002).

Abbas et al., (2003) reported the antioxidative potential of *Ocimum sanctum* in streptozotocin induced diabetic rats. Significant alteration in both the malondialdehyde (MDA) level and antioxidant activity was observed when the above herbal hypoglycemic agent was administered to the diabetic rats.

Atta-ur-Rahman et al., (2003) isolated nine isoflavonoids from *Iris germanica* and tested their antiphlogistic activity in an *in vitro* assay based on the reduction of the tetrazolium salt WST1 in the presence of activated human neutrophiles, which can be measured spectrophotometrically. The 50% inhibition values ranged 51–487.08 µM (positive controls: IC$_{50}$ = 67.74 µM, indomethacin IC$_{50}$ = 81.36 µM).

Hajhashemi et al., (2003) have studied the effect of the water/ethanol extract, a polyphenolic fraction and the essential oil of the leaves of *Lavandula angustifolia* in formalin- and acetic acid-induced writhing tests in mice and carrageenan-induced
oedema test in rats. At 400–1600mg/kg the extract inhibited only the second phase of formalin test. The polyphenolic fraction (800 and 1600 mg/kg, p.o.) and essential oil (100 and 200 mg/kg, p.o.) suppressed both phases. In acetic acid-induced writhing test the polyphenolic fraction (400 and 800 mg/kg, p.o.) and the essential oil (100 and 200 mg/kg, p.o.) reduced the number of abdominal constrictions. Essential oil at a dose of 200 mg/kg also inhibited carrageenan-induced paw oedema.

Jiang et al., (2003) have reported the in vivo antiphlogistic effects of an aqueous extract of Smilax glabra rhizomes in adjuvant arthritis model. The production of IL-1, TNF, NO was significantly reduced at 400 or 800mg/kg.

The anti-inflammatory and analgesic activities of the aqueous extract of the aerial parts of the plant namely Spilanthes acmella (SPA) in experimental animal models was evaluated by carrageenan-induced rat paw edema. The analgesic activity was tested by acetic acid-induced writhing response in albino mice and tail flick method in albino rats. The aqueous extract of SPA in doses of 100, 200 and 400 mg/kg showed 52.6, 54.4 and 56.1% inhibition of paw edema respectively at the end of three hours and the percentage of protection from writhing was 46.9, 51.0 and 65.6 respectively. In the tail flick model, the aqueous extract of SPA in the above doses increased the pain threshold significantly after 30 min, 1, 2 and 4 hours of administration. SPA showed dose-dependent action in all the experimental models (Chakraborty et al., 2004).

Monica et al., (2004) evaluated the acute and chronic treatments with Harpagophytum procumbens on Freund’s adjuvant-induced arthritis in rats. Harpagophytum procumbens acts by way of interleukins and leukocyte migration to the painful and inflamed joint area. Chemically, its secondary tuberous roots contain
iridoid glycosides, harpagogide, procumbide, and harpagoside, as the active principle. In the present study, evaluation of the therapeutic potential as anti-inflammatory and analgesic agent in rat model of Freund’s adjuvant-induced arthritis both in the acute and chronic phases was carried out. The animals were injected with Freund’s adjuvant in sub-plantar tissue of the right posterior paw and randomly assigned in acute (25, 50, or 100 mg/kg) or chronic (100 mg/kg) treatments with Harpagophytum procumbens solution test or vehicle. Then, submitted to behavioral test and assessment of body weight and right paw’s measurements. The results show that Harpagophytum procumbens extract increased the animals ‘latency of paws’ withdrawal, indicating a protective effect against the pain induced by the thermal stimulus, both in acute and chronic treatments. In addition to reduction in the right paw edema in the experimental groups when compared to control group was also noted.

Pal et al., (2005) reported the anti-inflammatory activity of petroleum ether and methanolic extracts of leaves of Garcinia xanthochymus in rats using carrageenan-induced paw oedema. The petroleum ether extract reduced the paw oedema volume by 86.4% and methanolic extract by 80.7% respectively compared to the standard drug ibuprofen in dose dependent manner.

Lakshman et al., (2005) carried out the comparative anti-inflammatory activity of four species of Sariva, an important ayurvedic drug. In the comparative study, the roots of the four species of sariva viz., Decalipis hamiltonii, Cryptolepis buchananii, Ichnocarpus frutescens and Hemidesmus indicus were investigated for their anti-inflammatory activity in carrageenan-induced raw paw oedema. The ethanolic extracts of roots of all the four species of Sariva exhibited significant anti-inflammatory activity at a dose of 350 mg/kg when compared to the standard drug phenylbutazone.
Sarkar et al., (2005) reported the effect of leafy exudates of Aloe vera on nitric oxide production by macrophages during inflammation. The acute anti-inflammatory activity was evaluated using carrageenan and dextran as phlogistic agents while its chronic anti-inflammatory effect was studied using complete Freund’s adjuvant-induced model of arthritis. The effect of Aloe vera leaves on nitric oxide production in mouse peritoneal macrophages was measured by using Griess agent. Aloe vera leaves (25 mg/kg) significantly reduced carrageenan and dextran induced oedema in rats by 61.9% and 61.7% respectively and 10 µg/ml caused a decrease in nitric oxide production in macrophages without causing toxicity.

Lie-Fen et al., (2005) examined antioxidant activities of twenty-six medicinal herbal extracts that have been popularly used as folk medicines in Taiwan. The results of scavenging DPPH radical activity revealed that, among the 26 tested medicinal plants, Ludwigia octovalvis, Vitis thunbergii, Rubus parvifolius, Lindernia anagallis, and Zanthoxylum nitidum exhibited strong activities and their IC\textsubscript{50} values for DPPH radicals were 4.6, 24, 27, 36, 50 µg/mL, respectively. They also reported the superoxide anion scavenging activity (IC\textsubscript{50}, µg/mL), and among the twenty-six herbal extracts, the top five most significant activities were observed in plant extracts of Ludwigia octovalvis (26 µg/mL), Vitis thunbergii (58 µg/mL), Prunella vulgaris (113 µg/mL), Saurauia oldhamii (124 µg/mL), and Rubus parvifolius (151 µg/mL). The IC\textsubscript{50} values for DPPH and superoxide anion of catechin (positive control) were 2.5 and 7.2 µg/mL, respectively.

Vigo et al., (2005) have reported that the extract of Plantago lanceolata in vitro conditions reduced the NO-production significantly and was comparable to dexamethason and indomethacin. The same extract had no significant effect on COX-2 or PGE\textsubscript{2}.
Panico et al., (2005) have studied the in vitro activity of a lyophilised extract of *Capparis spinosa* that inhibited PGE$_2$-production between 10 and 51% in the concentrations 10, 100 and 200 µg/ml.

Salem, (2005) has reported the immunomodulatory and therapeutic properties of *Nigella sativa* seed. Thymoquinine (TQ) is the major constituent of the seed oil of *Nigella sativa* that possess reproducible anti-oxidant effects through enhancing the oxidant scavenger system, which as a consequence lead to antitoxic effects. The oil and TQ have also possess potent anti-inflammatory effects on several inflammation-based models including experimental encephalomyelitis, colitis, peritonitis, oedama, and arthritis through suppression of the inflammatory mediators prostaglandins and leukotriens. The oil and certain active ingredients showed beneficial immunomodulatory properties, augmenting the T cell and natural killer cell-mediated immune responses.

Orhan et al., (2006) examined the in vivo antiphlogistic activity of ethyl acetate extract of *Viscum album* and some purified flavonones and chalcones from *Viscum album*. The extract inhibited carrageenan-induced rat paw oedema 24.7–37.2% at inhibition at 10 mg/kg. The chalcon had a similar activity (30.7–33.6% inhibition) and the three flavonones had a weak but significant antiphlogistic activity (15.1–21.3%; 8.0–25.2%; 13.3–31.5% inhibition at 10 mg/kg).

Shao et al., (2006) examined the COX-2 inhibiting effects of nine steroidal saponins from *Smilax* species. At $10^{-5}$M all of them showed significant inhibiting activity: between 59 and 82%.

An aqueous extract from *Smilax china*, which contained saponins, flavonoids and other water soluble constituents, inhibited albumin-induced rat paw oedema at
very high concentrations of 1000–2000 mg/kg. The extract reduced PGE$_2$-production, by inhibiting COX-2-activity with 81.25% inhibition at 100 µg/ml (indomethacin: 69.07% at 0.4 µg/ml (Shu et al., 2006).

Kath et al., (2006) reported that, hydro-alcoholic extracts of leaves of *Ocimum sanctum* showed significant antioxidant activity by decreasing the level of malondialdehyde (MDA) and by elevating the level of super oxide dismutase (SOD) in response to induction of peptic ulcers in albino rats and guinea pigs.

Dimo et al., (2006) established through their findings the anti-arthritic activity of the various solvent extracts of the leaves of *Kalanchoe crenata* using the acute and chronic models of inflammation in rats. Their findings also confirmed that the anti-arthritic activity is due to the blockage of histamine and serotonin pathways.

Priya et al., (2006) reported the antioxidant and anti-inflammatory activities of the aqueous and ethanolic extract of the flowers of *Tabernaemontana coronaria*. The antioxidant activity was confirmed by *in vitro* superoxide, hydroxyl radicals, nitric oxide scavenging and lipid peroxidation inhibiting activities and the anti-inflammatory activity by carrageenan-induced acute and formalin-induced chronic anti-inflammatory models. The extract showed remarkable anti-inflammatory in both the models, comparable to the standard reference drug diclofenac.

Prieto et al., (2006) evaluated the *in vivo* effect of β-sitosterol in a model of delayed-type hypersensitivity (DTH) contact dermatitis. The compound was also tested in intact, A23817 stimulated rat-peritoneal polymorphonuclear leukocytes and human platelets for the inhibition of eicosanoids release in 15 min incubations. The compound reduced in a significant manner the oedema induced by oxazolone.
only at 24 h, without any effect on the enzymes of the arachidonate pathway involved in the onset of the inflammatory process in the conditions above described. The results indicate that this compound can modulate a cell-mediated oedema without any short term in vitro effect on the arachidonate pathway of intact cells. The ubiquity of this compound can explain, and predict, the effect of many plant extracts in this in vivo model, and so this data could be of help in dereplication processes.

Chinnasamy et al., (2007) have evaluated the potential anti-inflammatory properties of crude methanolic extracts of Ocimum basilicum in human peripheral blood mononuclear cells (PBMC). The crude methanolic extracts of Ocimum basilicum showed a good inhibitory effect on the proliferative response of PBMC in mitogenic lymphocyte proliferation assays. They also reported the gene expression on Lipopolysaccharide (LPS) induced production of proinflammatory cytokines such as Tumor necrosis factor-α (TNF-α), Interleukin-1β (IL-1β) and IL-2. It also suppressed the induction of inducible nitric oxide synthase (iNOS) and the subsequent production of nitric oxide (NO) in LPS-stimulated RAW-264.7 macrophages in a time-dependent manner.

Speroni et al., (2007) have studied the effect of various extracts of Verbena officinalis (petroleum ether-, chloroform-, methanol extract, flavonoids enriched extract and a CO₂ extract) on carrageenan-induced rat paw oedema. The strongest inhibition was achieved with the CO₂-extract.

Ridtitid et al., (2007) in their experiments with albino rats found that the methanolic extract of leaves of Piper sarmentosum at doses of 50, 100 and 200 mg/kg possessed significant anti-inflammatory and antipyretic activities on carrageenan-
induced rat paw edema and brewer’s yeast-induced pyrexia in rats. The results revealed that the extract at test doses produced a significant anti-inflammatory activity at 3 hours with an inhibition of paw edema of 8.6% (P<0.05), 18.6% (P<0.01) and 24.7% (P<0.01), respectively, compared to the reference drug aspirin 200 mg/kg with an inhibition of 33.3% (P<0.01).

Tabanca et al., (2007) have examined the in vitro antiphlogistic activity of the essential oil of *Pimpinella saxifraga* and some of the oil constituents.

A number of anti-inflammatory in vivo test systems in mice and rats have been developed. Hereby pro-inflammatory substances like carrageenan, arachidonic acid or xylen are injected into paws or applied to ears to induce inflammatory reactions and swelling. An anti-inflammatory substance should reduce the swelling of the affected organ compared to control. This is measured with a plethysmograph, a micrometer device or by weighing punched out bits of ears. Variation of the oedema inducing agents helps model different types of chronic and acute inflammation. For practical and methodological reasons these assays mostly apply acute inflammatory models like carrageenan, arachidonic acid induced oedema, rather than chronic ones like adjuvant’s induced rat paw oedema (Cooper, 2007; Pretorius, 2008).

Yaro et al., (2008) have reported the anti-nociceptive (analgesic) and anti-inflammatory effects of the methanolic extract of leaves of *Cissampelos mucronata* in mice and rats. The anti-inflammatory effect was studied by employing the carrageenan-induced paw oedema and anti-nociceptive study was carried out using the acetic acid-induced abdominal constriction test in mice and tail immersion test in rat. The preliminary phytochemical investigation of the methanolic extract of leaves
of *Cissampelos mucronata* revealed the presence of carbohydrates, reducing sugars, combined sugars, flavonoids, tannins, saponins, glycoside, alkaloids and steroids.

Kulkarni *et al.*, (2008) studied and reported the antioxidant and anti-inflammatory activity of the methanolic extract of the leaves of *Vitex negundo*. The total methanol extract of the plant was standardized in terms of total polyphenols. The standardized extract in a dose of 100mg/kg caused a comparable reduction in oedema with that of diclofenac sodium (25 mg/kg) using carrageenan-induced rat paw oedema method. The extract also exhibited strong free radical scavenging activity by 1, 1-diphenyl-2-picrylhydrazyl (DPPH) method and caused a significant reduction in the formation of thiobarbutiric acid by inhibiting the lipid peroxidation.

Jitender *et al.*, (2008) reported the anti-inflammatory activity of aqueous extract of leaves of *Gymnema sylvestre* in rats using two different experimental models viz., carrageenan-induced paw oedema and cotton pellet granuloma methods. They concluded that the rats dosed at 300 mg/kg decreased the paw oedema volume by 48.5% within 4 hours of administration, while the standard drug phenylbutazone (100 mg/kg) decreased the paw oedema volume by 57.6%.

The roots of *Silybum marianum* (Blessed milk thistle) is used for chronic inflammatory liver diseases, liver cirrhoses and as a complimentary treatment in cases of toxic liver injury for dyspeptic complaints. Silymarin, a mixture of flavanolignans consisting of silybin, silydanin and silychristin inhibits a number of proinflammatory factors (e.g. TNFα) and the activation of NF-κB (for example: TNFα-induced NF-κB-activation). *In vitro* silymarin inhibits IL-1β-induction and PGE₂-production. Silymarin has an inhibiting effect, in higher doses however an enhancing effect on the expression of TNFα, IL-1β and IL-6 *in vivo*. It reduced carrageenan-induced rat paw
oedema and xylen-induced mouse ear oedema to a similar extent as indomethacin did (Michael et al., 2009).

Zimecki et al., (2009) have evaluated the immunomodulatory and anti-inflammatory activity of selected osthole derivatives from the roots of *Peucedanum ostruthium*. The compounds were tested for their activity on Tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6) production, induced by Lipopolysaccharide (LPS), in cultures of rat peritoneal cells and human peripheral blood mononuclear cells. The isolated compounds inhibited Tumor necrosis factor-α (rat cells) and also stimulated the production of both the cytokines. They also exhibited strong inhibition on Tumor necrosis factor-α production in human blood cells (73, 78 and 80% inhibition at 10 µg/ml, respectively) and stimulated the interleukin-6 production (2- to 3-fold stimulation). In addition, they also reported that the osthole derivatives suppressed the carrageenan-induced inflammation in mice (56.5% and 68.3% inhibition, respectively). In summary, the compounds predominantly displayed suppressive and anti-inflammatory activities in the investigated models.

William et al., (2009) investigated the anti-inflammatory effect of methanolic extract of *Bambusa vulgaris* (MEBV) leaves on rats and mice. The anti-inflammatory effect was investigated employing acute inflammatory models: formaldehyde-induced paw oedema, acetic acid-induced vascular permeability, sub acute anti-inflammatory model- cotton pellet granuloma, estimation of plasma MDA, and carrageenan-induced peritonitis. MEBV (100, 200 and 400mg/kg, p.o) exhibited a dose-dependent and significant inhibition (p< 0.01) in all the experimental models. The results obtained suggest marked anti-inflammatory activity of the MEBV and support the traditional use of this plant in some painful and inflammatory conditions. The preliminary
phytochemical screening revealed the presence of flavonoids, carbohydrates, glycosides, proteins and alkaloids.

The possible anti-inflammatory activity of a 90% ethanolic extract of *Dalbergia sissoo* bark was studied in a model of inflammation using a right hind paw oedema method in Wistar rats. One percent carrageenan in 0.5% sodium carboxymethyl cellulose (CMC) was administered through the sub-plantar region of the right hind paw of the animals. After oral administration of ethanolic extract at different doses (300, 500 and 1000 mg/kg), inhibition of right hind paw oedema was observed at 30, 60, and 120 min time intervals. The anti-inflammatory effects of the extract were compared with a standard dose of indomethacin (10 mg/kg). In acute toxicity studies, the extract was found to be safe up to 3000 mg/kg, p.o. in the rats. The ethanolic extract of *Dalbergia sissoo* bark at 1000 mg/kg showed the most potent anti-inflammatory activity compared to the other groups (300 and 500 mg/kg) throughout the observation period. The preliminary Phytochemical investigation of bark extract confirmed the presence of carbohydrates, proteins, amino acids, tannins and flavonoids (Mohammad *et al.*, 2009).

A significant percentage inhibition in the paw oedema by carrageenan was reported in the studies conducted on the anti-inflammatory effect of aqueous extract of leaves of *Holoptelea integrifolia* in rats in dose dependent manner. Indomethacin was used as the standard anti-inflammatory drug (Shrinivas *et al.*, 2009).

Idris *et al.*, (2009) evaluated the hepatoprotective and anti-inflammatory activities of the seeds of *Plantago major* in rats. The carrageenan hind paw oedema model was employed for inflammatory studies and the hepatoprotective activity was observed when the extract was able to significantly reduce the serum alanine
aminotransferase (ALT) and aspartate aminotransferase (AST) levels when compared to the CCl₄ group.

Bachhav et al., (2009) reported the in vivo analgesic and anti-inflammatory activity of methanolic extract of the roots of *Argyreia speciosa* using acetic acid-writhing and carrageenan induced hind paw oedema. The methanolic extract of the roots significantly decreased the acetic acid-writhing and inhibition of carrageenan induced hind paw oedema in rats.

Ching et al., (2009) studied the anti-inflammatory activity of aqueous extract of stem bark of *Stereospermum kunthianum* in rats. The anti-inflammatory activity was confirmed using carrageenan-induced paw oedema, leukocytes migration, granuloma air pouch tests in rats. They concluded that the extract dosed at 400 mg/kg showed maximum activity and was higher than that of indomethacin (10 mg/kg) and the extract also significantly reduced the number of recruited leucocytes and inhibited the peritoneal exudates formation.

Saraswathy et al., (2009) conducted experiments in rats and demonstrated the analgesic and anti-inflammatory activity of *Amukkarac curanam*, a polyherbal siddha formulation. The experimental methods used were tail immersion and acetic acid writhing method for anti-analgesic activity and cotton pellet-induced granuloma formation for anti-inflammatory activity. Pentazocine (10 mg/kg, intraperitoneally) and aspirin (150 mg/kg, orally) were clinically used standard analgesics and for anti-inflammatory activity (Indomethacin, 10 mg/kg, orally) was used.

Ethanolic extract of the fruits of *Mitragyna parvifolia* were evaluated for anti-inflammatory, analgesic and antimicrobial activities. The extract at the dose of 500 mg/Kg showed very high % inhibition in oedema volume comparable to standard
drug Diclofenac sodium (50 mg/kg, i.p.). The plant extract did not exhibit any anti-bacterial potential against *Staphylococcus aureus, Bacillus subtilis, Escherichia coli* and *Pseudomonas aeruginosa* (Ankit et al., 2009).

Divya et al., (2009) reported the anti-inflammatory, analgesic and anti-lipid peroxidative properties of the ethanolic extract of leaves of *Wattakaka volubilis* in rats. The extract showed potent anti-inflammatory activity in carrageenan-induced rat paw oedema and acetic acid-induced writhing in mice when compared to the standard drug indomethacin in dose dependent manner. The extract also exhibited significant inhibition of FeCl$_2$ ascorbic acid stimulated mice liver lipid peroxidation.

Vimal et al., (2009) investigated twelve medicinal plants of northeast India for the presence of biologically active compounds and also carried out phytochemical screening and anti-oxidant activity of all the twelve medicinal plants. The antioxidant activity was estimated by using 2, 2- diphenyl-picryl-hydrazyl (DPPH) free radical assay. *Oroxylum indicum, Ipomoea aquatica* and *Moringa oleifera* exhibited strong antioxidant activity as compared to other plants. *Oroxylum indicum* showed the highest antioxidant activity. The present study indicated that these plants are of therapeutic potential due to their high free-radical scavenging activity.

JiSuk et al., (2009) reported the anti-inflammatory, anti-nociceptive, and anti-psychiatric effects of 80% ethanolic extracts of rhizomes of *Alpinia officinarum* on complete Freund's adjuvant (CFA)-induced arthritis in rats. The ethanolic extract showed acute anti-inflammatory activity by reducing the oedema volume in carrageenan-stimulated arthritis and inhibited NO generation in LPS-induced RAW 264.7 cells. In addition, this extract showed chronic anti-rheumatic and analgesic
activities by suppressing the swelling volume, by recovering the paw withdrawal latency, and by inhibiting the flexion scores in CFA-induced arthritis.

Tripathy et al., (2009) evaluated the anti-arthritic potential of alcoholic and aqueous extracts of the whole plant of *Hybanthus enneaspermus* on Freund’s adjuvant induced arthritis. Both the extracts significantly (p <0.001) decreased the paw thickness at the end of 30 days treatment. The result supports the folklore use of this plant against the inflammatory conditions like arthritis.

*Seseli libanotis* contains essential oil with trans-caryophyllene, spathulenol, (−)-caryophyllene oxide, euasarone and deltacadinene, and the coumarins samidin, isosamidin, cis-and trans-khellactone. In Traditional Chinese Medicine (TCM), *Seseli mairei* is used for inflammatory ailments like rheumatism and colds. Selelin a coumarin from *Seseli indicum* is reported to possess antiphlogistic activity in a TPA induced mouse ear oedema assay. In a carrageenan induced paw oedema assay, *Seseli libanotis* is moderately active (Michael et al., 2009).

Yaro et al., (2010) conducted animal experiments and evaluated the n-butanol soluble fraction of the methanolic extract of leaves of *Cissus cornifolia* for analgesic and anti-inflammatory potentials using acetic acid induced writhing and hot plate tests in mice and carrageenan-induced paw oedema in rats. The fraction significantly (P<0.005) inhibited acetic acid-induced writhing in mice at the doses tested (150, 300 and 600 mg/kg). In the carrageenan-induced paw oedema model, the fraction decreased hind paw oedema volume by 73.9% at the highest dose (600 mg/kg) tested compared to 60.9% inhibition obtained with the reference drug, ketoprofen (20 mg/kg) at the third hour after carrageenan administration.
Sini et al., (2010) evaluated the antioxidant and radical scavenging activity of methanolic extracts of selected medicinal plants, traditionally used by the tribes of Attapady (Palakkad, India) regions as folk medicines against DPPH free radical. *Cassia occidentalis, Clitoria ternatea, Trianthema decandra, Capparis zeylanica, Anisomeles malabarica* and *Plumbago zeylanica* exhibited strong antioxidant activity as compared to other plants. *Trianthema decandra* showed the highest antioxidant activity.

Chitra et al., (2010) evaluated and reported the anti-arthritic and antioxidant activity of alcoholic extract of the flowers of *Delonix regia* in adult female Wistar rats. Two doses of 200mg/kg and 400mg/kg of alcoholic extract of *Delonix regia* were administered intraperitoneally to the Freund’s incomplete adjuvant induced arthritis in rats for 28 days. During the experimental period, paw edema volume (primary lesion) was observed. Liver homogenate was utilized for the assessment of oxidative stress. Both the doses of alcoholic extract of *Delonix regia* significantly reduced the paw edema volume as compared to diseased control animals. Treatment with *Delonix regia* also showed significant increase in antioxidant enzyme levels like Catalase (CAT), Glutathione peroxidase (GPx), Glutathione –S- Transferase (GST), reduced glutathione (GSH), Vit – C with decreased protein level and the values were almost analogous to that of normal values.

Sandeep et al., (2011) evaluated the anti-inflammatory properties of Septilin in lipopolysaccharide activated monocytes and macrophages. It was observed from the present study that by employing tumor necrosis factor α (TNF-α) bioassay and reverse transcription-polymerase chain reaction (RT-PCR), Septilin inhibited TNF-α production in LPS (1 µg/mL) stimulated RAW 264.7 cells (p < 0.05). 80% inhibition
of TNF-α was observed even at 2.5% Septilin. Septilin at all the concentrations tested could also significantly block the LPS mediated nitric oxide (NO) production (p < 0.01) and expression of inducible NO synthase (iNOS) gene. LPS mediated interleukin 6 (IL-6) and IL-8 production was also blocked by Septilin at the concentrations tested. They also reported the inhibition of cyclooxygenase 2 (COX-2) activity and suppression of COX-2 and phosphodiesterase 4 B (PDE4B) mRNA expression in a concentration dependent manner. Taken together, these findings from the present in vitro study suggest the anti-inflammatory and immunomodulatory properties of Septilin.

Sandeep et al., (2011) reported that, Bresol–a poly-herbal formulation inhibits phosphodiesterase 4 gene expression and modulates the levels of select mediators of inflammation in human monocytic cells. The present study elucidated the mechanism(s) of action of bresol at the cellular and molecular levels, using human monocyte leukemia cells. The effects of bresol on phosphodiesterase 4B gene expression were analyzed using human monocytic U937 leukemia cells. The ability of bresol to stimulate cAMP formation in these cells, as well as its effects on mediators of inflammation like tumor necrosis factor-α (TNFα), nitric oxide (NO), and cyclooxygenase-2 (COX-2) in lipopolysaccharide (LPS)-stimulated U937 cells were also studied. The results indicated that bresol exhibited potential anti-inflammatory properties by inhibiting LPS-induced PDE4B gene expression in the cells. Bresol also dose dependently activated cAMP formation, and inhibited TNFα, NO, as well as COX-2 formation in the LPS-stimulated cells. Based upon the results, they concluded that the reported anti-inflammatory activity of bresol might be attributed to its abilities to inhibit PDE4B and thus elevate cAMP levels in human monocytes. The anti-
inflammatory effects of bresol might also be a result of the capacity of bresol to modulate the formation of TNFα, NO, and COX-2 in monocytes.

Alcoholic extract of *Kaempferia galanga* was tested for analgesic and anti-inflammatory activities in animal models. Three doses, 300 mg/kg, 600 mg/kg and 1200 mg/kg of the plant extract prepared as a suspension in 2 ml of 2% gum acacia were used. Acute and sub acute inflammatory activities were studied in rats by carrageenan induced paw edema and cotton pellet induced granuloma models respectively. In both models, the standard drug used was aspirin 100 mg/kg. Two doses 600 mg/kg and 1200 mg/kg of plant extract exhibited significant (P<0.001) anti-inflammatory activity in carrageenan model and cotton pellet granuloma model in comparison to control. Analgesic activity was studied in rats using hot plate and tail-flick models. Codeine 5 mg/kg and vehicle served as standard and control respectively. The two doses of plant extract exhibited significant analgesic activity in tail flick model (P<0.001) and hot plate model (P<0.001) in comparison to control (Amberkar *et al*., 2011).

Sathisha *et al*., (2011) evaluated and reported the antioxidant potential of some herbal plant extracts produced for commercial purpose using various *in vitro* assays. Among the extracts from *Curcuma longa*, *Caffea arabica*, *Tribulus terrestris*, *Bacopa monnieri* and *Trigonella foenum*, the extracts of *Curcuma longa* and *Caffea arabica* showed greater antioxidant activity measured as scavenging of DPPH, superoxide radicals, reducing power and inhibition of microsomal lipid peroxidation.

Balakrishnan *et al*., (2011) reported the antimicrobial and antioxidant activities of the stem bark of *Psidium guajava*. Free radical scavenging assays such as DPPH and nitric oxide were used for the evaluation of the antioxidant potential of
the stem bark of *Psidium guajava*, which effectively scavenged free radicals in a dose dependent manner. The antioxidant activity was compared to standard antioxidant ascorbic acid.

Smain *et al.*, (2012) reported the potential anti-inflammatory activity of *Myrtus communis, Smilax aspera, Lavandula stoechas* and *Calamintha nepeta* along with their apoptotic effects on the pro-inflammatory cells and the correlation of these effects with the plants potential anti-oxidant activity. *Myrtus communis* extract exhibited the highest inhibitory activity in the paw oedema induced by carrageenan (60% at 3 h), whereas *Calamintha nepeta, Lavandula stoechas*, and *Smilax aspera* produced inhibitions of 49%, 38%, and 47%, respectively. None of them had an effect on the TPA-induced ear oedema. Moreover, all the extracts except *Smilax aspera* showed different degrees of anti-oxidant activity.

Dhirender *et al.*, (2012) evaluated the analgesic and anti-inflammatory activity of ethanolic bark extracts of *Pinus roxburghii* Sarg. The extract at the doses of 100 mg/kg, 300 mg/kg and 500 mg/kg body weight were subjected to evaluation for analgesic and anti-inflammatory activities in experimental animal models. Analgesic activity was evaluated by acetic acid-induced writhing and tail immersion tests in Swiss albino mice; acute and chronic anti-inflammatory activity was evaluated by carrageenan-induced paw oedema and cotton pellet granuloma in Wistar albino rats. Diclofenac sodium and indomethacin were employed as reference drugs for analgesic and anti-inflammatory studies, respectively. The bark extract of *Pinus roxburghii* Sarg. demonstrated significant analgesic and anti-inflammatory activities in the tested models.
2.1 *Anisomeles malabarica* R.Br.

Jeyachandran *et al.*, (2007) reported the anti-cancer effect of ethanolic leaf extract of *Anisomeles malabarica*. The anti-cancer activity was evaluated on Diethylnitrosoamine (DEN) in mice and concluded from the results obtained that the ethanolic leaf extract of *Anisomeles malabarica* possesses significant anti-cancer properties.

Lavanya *et al.*, (2010) reported the *in vitro* antioxidant activity of methanolic extracts of leaves of *Anisomeles malabarica* by DPPH method. They also measured the reducing power, total antioxidant activity and also the total phenolic content of the extracts.

Lavanya *et al.*, (2010) investigated the *in-vitro* anti-Inflammatory, anti-platelet and anti-arthritic activities of the methanolic extracts of the leaves of *Anisomeles malabarica*. Previous phytochemical analysis of methanolic extract of *Anisomeles malabarica* has indicated the presence of steroid, flavonoid and terpenoid types of compounds. The possible anti-inflammatory activity of *Anisomeles malabarica* was evaluated by HRBC (Human Red Blood Cell) membrane stabilization method and anti-arthritic activity by the inhibition of protein denaturation method The methanolic extracts of the plant exhibited notable anti-inflammatory activity and remarkable anti-arthritic, anti-platelet action. The maximum membrane stabilization of *Anisomeles malabarica* was found to be 98.34% at a dose of 1000mcg/0.5ml and that of protein denaturation was found to be 97.47% at a dose of 250mcg/ml. Hence, the methanolic extracts of *Anisomeles malabarica* demonstrated the anti-inflammatory, anti-platelet and anti-arthritic activities. Therefore, the study supports the isolation and the use of
active constituents from *Anisomeles malabarica* in treating inflammations and rheumatism.

Ishpinder *et al.*, (2010) reported the anticonvulsant potential of *Anisomeles malabarica* leaves against experimentally induced convulsions in rats using three different extracts viz., chloroform, ethyl acetate and methanol against pentylenetetrazole (PTZ) and maximal electroshock-induced convulsions (MES). High doses of chloroform and ethyl acetate (400 mg/kg, p.o.) extracts significantly decreased the extent of PTZ and MES-induced convulsions.

Boobalan *et al.*, (2010) evaluated the *in vitro* antioxidant and antimicrobial potential of methanolic extracts of leaves of *Anisomeles malabarica*. Antioxidant activity was measured using the free radical scavenging assays such as hydroxyl, superoxide anion radicals, DPPH and 2,2-azinobis-(3-ethyl-enothiazoline-6-sulfonic acid) (ABTS).

Pappusrinivasan *et al.*, (2010) reported the effects of anti-inflammatory and anti-pyretic activity of *Anisomeles malabarica*. The present study was carried out to investigate the anti-inflammatory and anti-pyretic properties of petroleum ether, alcoholic and aqueous extracts of leaves of *Anisomeles malabarica* using experimental animal models. The anti-inflammatory activity of the various extracts was studied based on their effects on carrageenan-induced paw oedema and cotton pellet granuloma in rats, while anti-pyretic activity was evaluated using the brewer’s yeast-induced pyrexia in rats. The extracts were screened for alkaloids, steroids, proteins, flavonoids, saponins, mucilage, carbohydrates, tannins, fats and oils. The extracts in dose levels of 50,100 and 200 mg/kg orally were used in both anti-inflammatory and anti-pyretic studies. The ethanol and aqueous extracts of leaves of
Anisomeles malabarica produced significant (P<0.05) anti-inflammatory activities in a dose-dependent manner to that of standard drug indomethacin, while petroleum ether extract exhibited minimum inhibitory effect in carageenan-induced hind paw oedema and cotton pellet granuloma in rats. The results obtained indicate that the crude leaf extracts of Anisomeles malabarica possess potent anti-inflammatory and anti-pyretic activity by supporting the folkloric usage of the plant to treat various inflammatory conditions.

Shubashini and Dulcy (2011) reported the isolation and characterization of two flavones glucosides from the acetone extract of the stem of Anisomeles malabarica R.Br.. The compounds have been characterized as apegenin-7-O-β-D (4", 6"-O-p-Coumaroyl) glucoside and apegenin-7-O-β-D (2", 6"-O-p-Coumaroyl) glucoside.

Kavitha et al., 2012 carried out the phytochemical analysis of the diethyl ether and ethanolic extracts of leaves of Anisomeles malabarica (L) R.Br. that showed the presence of alkaloids, flavanoids, tannins, saponins and glycosides.

2.2 Clerodendrum serratum L.

2.2.1 Phytochemistry

The major groups of chemical constituents present in the Clerodendrum genus are carbohydrates, phenolics, flavonoids, terpenoids and steroids.

Carbohydrates

Generally, D-mannitol has been found in the roots of the plant (Neeta et al., 2007).
**Flavonoids**

Flavonoids are further sub-grouped into catechins, leucoanthocyanidins, flavanones, flavanonols, flavones, anthocyanidins, flavanols, chalcones, aurones and isoflavones. These isolated flavonoids like hispidulin and cleroflavone possess potent anti-oxidant, anti-microbial, anti-asthmatic, anti-tumor and CNS-binding activities. Other flavonoids isolated from plants are apigenin, 7-hydroxy flavanone, scutellarein and pectolinarigenin (Neeta *et al.*, 2007; Harbone, 1984; Mann *et al.*, 1984).

**Phenolics**

The phenolic compounds in the genus *Clerodendrum* are found in both free as well as bound to sugar moieties. Some of the phenolic compounds isolated were serratagenic acid, acteoside, indolizino and verbascoside which possess biological activities such as antioxidant, anti-microbial, anti-proliferative, anti-hypertensive and anti-cancer activities (Neeta N. *et al.*, 2007; Harbone J.B., 1984; Mann J. *et al.*, 1984).

**Terpenes**

Terpenoids are generally found to be bound to sugar moieties by a glycoside linkage. Usually they are present as glycosides in their β-D-glucosidic form. Some of the terpenes isolated from the plant are betulin, oleanolic acid, clerodermic acid, betulinic acid, friedelin and monomelittoside had weak CNS activity, strong molluscicidal and fungitoxic activities (Neeta *et al.*, 2007; Harbone, 1984; Mann *et al.*, 1984).
Steroids

Steroids are terpenes based on the cyclopentane perhydroxy phenanthrene ring. Chiefly, $\gamma$-sitosterol, $\beta$-sitosterol, cholestanol, clerosterol, campesterol and 24-ethyl cholesterol were reported to be isolated from the plant (Neeta et al., 2007; Banerjee et al., 1969).

2.2.2 Ethno medicinal/traditional uses

The roots of the plant have been claimed to be used in dyspepsia, seeds in dropsy and leaves as a febrifuge and in cephalagia and ophthalmia (The useful plants of India, 1992).

Aqueous extracts of leaves of *Clerodendrum serratum* possess bronchodilator property (Kirtikar et al., 1991; Steane et al., 1999).

Roots and leaf extracts of *Clerodendrum serratum* has been used for the treatment of rheumatism, asthma and other inflammatory diseases (Hazekamp et al., 2001).

Previous studies suggest that apigenin-7-glucoside has anti-inflammatory, antimicrobial, hepatoprotective and anti-diarrheal properties. The compound also possesses significant protection against Alzheimer’s disease in mice (Babenko et al., 2008; Havsteen, 1983; Patil et al., 2003; Fuchs et al., 1993).

2.2.3 Pharmacological activities

Antioxidant activity

In DPPH radical scavenging assay, *Clerodendrum serratum* roots at various concentrations (50, 100, 150, 200, 250 $\mu$g/ml) and ascorbic acid (50, 100, 150, 200,
250 µg/ml) exhibited significant inhibitory activity with IC_{50} values of 175 and 137 respectively. In reducing power assay, a linear increase in reducing power was observed over the concentration range 20-120 µg/ml sample, equivalent to 20 -120 µg/ml ascorbic acid taken as standard. The inhibition of 73.32 ± 0.002%, and 64.49 ± 0.242% was observed for ascorbic acid and ethanolic extract of roots respectively at maximum concentrations (Bhujbal et al., 2009).

**Anticancer activity**

Aqueous extract and methanolic extract of roots of *Clerodendrum serratum* were screened for *in vivo* anti-cancer activity using Dalton’s Lymphoma Ascites (DLA) cell model at the dose 100 mg/kg and 200 mg/kg body weight. The parameters analyzed were, mean survival time, percentage increase in life span, body weight analysis, hematological parameters and biochemical parameters. The study revealed that methanolic extract exhibits significant anti-cancer activity as compared to aqueous extract. It is used in treatment of fevers, rheumatism and dyspepsia (Zalke et al., 2010).

**Anti-inflammatory activity**

Roots and leaf extracts of *Clerodendrum indicum*, *Clerodendrum phlomidis*, *Clerodendrum serratum*, *Clerodendrum trichotomum*, *Clerodendrum chinense* and *Clerodendrum petasites* have been used for the treatment of rheumatism, asthma and other inflammatory diseases (Neeta et al., 2007).

The ethanolic extract of roots of *Clerodendrum serratum* showed significant anti-inflammatory activity in carrageenan-induced oedema in rats, and also in the cotton pellet model in experimental mice, rats and rabbits at concentrations of 50, 100 and 200 mg/kg (Narayanan et al., 1999).
Stella et al., (2010) reported the anti-inflammatory activity of \( \beta \)-Sitosterol in human aortic endothelial cells. \( \beta \)-Sitosterol, normally present in vegetable-containing diets, comprises an important component of cholesterol controlling functional foods. It has been associated with cardiovascular protection, exerting its effect mainly through increasing the antioxidant defense system and effectively lowering the serum cholesterol levels in humans. This study extends existing data regarding the cardioprotective effect of \( \beta \)-sitosterol and provides new insights into understanding the molecular mechanism underlying the beneficial effect of \( \beta \)-sitosterol on endothelial function.

Sudipta et al., (2010) reported the anti-inflammatory activity of the methanolic extract of leaves of *Clerodendron infortunatum* Linn. (MECI) against carrageenan, histamine and dextran induced rat paw edema. The methanol extract (250 and 500 mg/kg body weight) exhibited significant activity (p< 0.01) against all phlogistic agent used in dose dependant manner. All these effects were compared with reference drug phynylbutazone.

**Wound healing activity**

Ethanolic extracts of roots and leaves of *Clerodendrum serratum* were evaluated for the wound healing potency in Albino rats. The results confirmed the wound healing potency of root extract as compared to leaf extract (Vidyai et al., 2005).

**Hepatoprotective activity**

Vidya et al., (2007) evaluated the ethanolic extracts of the roots of *Clerodendrum serratum* and ursolic acid isolated from the roots for the
hepatoprotective activity against carbon tetrachloride induced toxicity in rats. They studied various parameters like estimation of liver function serum markers such as serum total bilirubin, total protein, alanine transaminase, aspartate transaminase and alkaline phosphatase activities. The ursolic acid showed more significant hepatoprotective activity than crude extracts. The results when compared with the standard drug silymarin, revealed that the hepatoprotective activity of ursolic acid was similar to the standard drug.

The roots of *Clerodendrum serratum* have been claimed to be used in dyspepsia, seeds in dropsy and leaves as a febrifuge and in cephalagia and ophthalmia (Anonymous 1992).

Bhujbal *et al.*, (2010) reported for the first time the isolation of Apigenin-7-glucoside, \( \text{C}_{21}\text{H}_{20}\text{O}_{10} \) \((7-(\beta-D-glucopyranosyloxy)-5-hydroxy-2-(4-hydroxyphenyl)-4H-1-benzopyran-4-one)\), from the roots of *Clerodendrum serratum*. Structural elucidation of the compound was confirmed by \(^1\text{H}\) NMR and FAB-Mass spectroscopic studies.

Jayaraj *et al.*, 2011, evaluated the anticancer activity of methanolic leaf extract of *Clerodendrum serratum* on liver and kidney of 7, 12-dimethylbenz[a] anthracene (DMBA) induced skin carcinogenesis in mice. The study showed that the plant has potent anticarcinogenic efficacy against skin carcinogenesis.

### 2.3 Atalantia monophylla DC.

Himakar *et al.*, (2010) reported the comparative *in vitro* study on antifungal and antioxidant activities of whole plant of *Nervilia aragoana* and *Atalantia monophylla* and found that *Nervilia aragoana* had a better antifungal and antioxidant
activity than *Atalantia monophylla*. In fact *Atalantia monophylla* exhibited very poor antifungal and antioxidant activity.

Joshi *et al.*, (2011) evaluated the pharmacognostic and phytochemical properties of ethanolic extracts of roots of *Atalantia monophylla*.

Satheesh and Kishor (2012) evaluated the *in-vitro* antioxidant activity of methanolic extract of *Atalantia monophylla* linn bark was for the DPPH, nitric oxide and hydrogen peroxide radical scavenging activity. The *in-vitro* antioxidant activity the methanolic extract of *Atalantia monophylla* bark produced good antioxidant activity and was comparable with that of standard ascorbic acid.
TABLE 2: Some important medicinal plants used for the treatment of various inflammatory conditions

<table>
<thead>
<tr>
<th>Serial No.</th>
<th>Name of the Plant</th>
<th>Part/Constituents Used</th>
<th>Uses/Activity</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Adhatoda vasica</td>
<td>Leaf powder (poultice)</td>
<td>In rheumatic joints as counter irritant, on inflammatory swellings, on fresh wounds, urticaria and in neuralgia</td>
<td>Anonymous, 1985</td>
</tr>
<tr>
<td>2</td>
<td>Andrographis paniculata</td>
<td>Andrographolide</td>
<td>Anti-inflammatory</td>
<td>Madav et al., 1996</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Andrographolide from leaves</td>
<td>Analgesic, antipyretic and antiulcerogenic</td>
<td>Madav et al., 1995</td>
</tr>
<tr>
<td>3</td>
<td>Commiphora mukul</td>
<td>Steroids (E- and guggulsterone and Z-guggulsterols)</td>
<td>Anti-inflammatory</td>
<td>Iwu et al., 1993</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Crude gum</td>
<td>In the treatment of rheumatoid arthritis, obesity, as internal antiseptic and anti-inflammatory</td>
<td>Atal et al., 1982</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Aqueous extract (resins)</td>
<td>Anti-inflammatory</td>
<td>Duwieijua et al., 1993</td>
</tr>
<tr>
<td>4</td>
<td>Centella asiatica</td>
<td>Madecassoside and madecassic acid</td>
<td>Anti-inflammatory</td>
<td>Anonymous, 1992</td>
</tr>
<tr>
<td>5</td>
<td>Tribulus terrestris</td>
<td>Whole plant</td>
<td>Used in Bright’s disease with dropsy and also in gonorrheal rheumatism with cystis</td>
<td>Kritikar et al., 1993</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Multiherbal root formulation</td>
<td>Used as a pyretic and anti-inflammatory agent and also to treat clinical conditions like pain, backache, gout, sciatica, pyrexia, inflammation and oedema</td>
<td>Gupta et al., 1984</td>
</tr>
<tr>
<td>6</td>
<td>Asparagus racemosus</td>
<td>Methanolic extracts of roots</td>
<td>Anti-inflammatory</td>
<td>Mandal et al., 1998</td>
</tr>
<tr>
<td>7</td>
<td>Momordica charantia</td>
<td>Fruit</td>
<td>Useful in gout, rheumatism and subacute cases of spleen and liver</td>
<td>Nadkarni et al., 1976</td>
</tr>
<tr>
<td>8</td>
<td>Glycyrrhiza glabra</td>
<td>Glycyrrhetic acid</td>
<td>Anti-inflammatory</td>
<td>Rastogi et al., 1993</td>
</tr>
<tr>
<td></td>
<td></td>
<td>18-α and 18-β glycyrrhetic acid</td>
<td>Anti-inflammatory</td>
<td>Amagaya et al., 1984</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gliderinin</td>
<td>Anti-inflammatory, analgesic, antipyretic and anti-allergic</td>
<td>Rastogi et al., 1995</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Alcoholic extract of roots</td>
<td>Anti-inflammatory</td>
<td>Kakkar et al., 1998</td>
</tr>
</tbody>
</table>
2.3 Relevance of the current study

The literature survey reveals about the importance of medicinal plants and their derivatives in elevating the health of mankind. The discovery of pharmaceutically important active principles from medicinal plants continues to be a boon to the wellness of the society at large, as the derivatives from these plants has no adverse side or ill effects on the health of humans. The research work pertaining to anti-inflammatory activity from medicinal plants is limited to the study or evaluation of preliminary phytochemical investigations, or studying the anti-oxidative properties or evaluating the efficacy using animal models. But seldom, the work progresses to isolation, purification and structural elucidation of the active principles or compounds of pharmaceutical relevance. Also a very scanty literature is available on the in vitro anti-inflammatory and immunomodulatory activities using cell line assays. The literature available does not pertain to the chosen medicinal plants under current study. So in this context the present investigation was undertaken with the following objectives.

2.4 OBJECTIVES

1. To extract the bio-active constituents from the selected medicinal plants against Rheumatism.

2. To separate and isolate the constituents of interest.

3. To identify the bio-active principle.

4. To study the effects of the selected isolates in-vivo/in-vitro.