INTRODUCTION

Inflammatory diseases including different types of rheumatic diseases are very common throughout the world. Although rheumatism is one of the oldest known diseases of mankind and affects a large population of the world, no substantial progress has been made in achieving a permanent cure. The search for screening and development of drugs for antiinflammatory activity is an unending problem. There is much hope of finding active antirheumatic compounds from indigenous plants as these are still used in therapeutics despite the progress made in conventional chemistry and pharmacology for producing effective drugs.

A systematic study of antiinflammatory effects of Indian medicinal plants was done by Gujral and co-workers, who screened a number of plants for their antiarthritic effect. Subsequently, various workers from different laboratories in India and abroad have screened a number of plants for their antiinflammatory activity and some have shown significant results. Recent review on "Plant Antiinflammatory Agents" indicates that a wide variety of chemical constituents possess antiarthritic activity.

1.1 PLANTS WITH ANTIINFLAMMATORY ACTIVITY

Literature survey reveals that the species of 94 genera belonging to 54 families contain antiinflammatory agents.
These plants have been reviewed here.

**Acacia farnesiana** Linn. (Leguminosae)

This tree with bright yellow flowers is found throughout India. The glycosidal fraction obtained in 0.28% yield from the ethanolic extract of its unripe pods inhibited the carrageenan and formaldehyde induced inflammation (% inhibition 38.2 and 26.2, respectively).\(^9^0\)

**Acanthopanax chiisanensis** Nakai (Araliaceae)

A Korean folk medicine, leaves and stem bark of *A. chiisanensis* used as an antirheumatic, antiinflammatory and as a tonic. Chiisanoside, a glycosilated 3,4-seco-\(^\_\)triterpene of lupane-type with significant antiinflammatory activity has been isolated from the leaves and the stem bark of the plant.\(^9^1\)

**Achyrocline satureiodes** (Lam.) DC (Compositae)

This South American aromatic shrub popularly known as 'Marcela' has been used in folk medicine for gastrointestinal disturbances and for inflammatory conditions. Quercetin, luteolin and quercetin-3-methyl ether present in the inflorescence of the plant have been found responsible for exhibiting antiinflammatory activity.\(^9^2\)

**Aconitum spp.** (Ranunculaceae)

The monoglycerides obtained from *A. chinensis* Sieb. showed antiinflammatory activity.\(^9^3\) Yunaconitine, the major alkaloid
obtained from *A. pseudogoniculatum* W.T. Wang, and its chemically transformed products pseudoaconine and tetraacetyl pseudoaconine showed antiinflammatory activity.  

*Aegle marmelos* Correa (Rutaceae)

Marmin (1), a coumarin isolated from ethanolic extract of the roots of *A. marmelos* showed antiinflammatory effect in carrageenan induced inflammation in rats (1 g/kg, p.o. inhibited 62.5% of inflammation).

(Aesculus hippocastanum) L. (Hippocastanaceae)

The seeds of *A. hippocastanum* have been used as a folk medicine in France and the tincture of this drug has been used successfully for haemorrhoid. The major component aescin, whose yield is about 13%, is a mixture, though it is obtained in crystalline form. It is a β-amyrin derivative. Aescin is used as antiinflammatory and in the treatment of vericose vein.
Anacardium occidentale Linn. (Anacardiaceae)

Epicatechin (2) isolated from the seed coat of A. occidentale appears to be as active as phenylbutazone against various test models. Commercially it is popular as cyanidanol and is a component of a number of condensed tannins. For the last 10 years this has been in use in Europe for the treatment of liver diseases.

Angelica pubescens Maxim. (Umbelliferae)

Chinese crude drug called 'Qu-feng-shi-yao' has been used in traditional Chinese medicine as a remedy for arthritis. The roots of A. pubescens popularly known as 'Duo-huo' in China and 'Dokkatsu' in Japan have been used in Chinese medicine for arthritic diseases and common cold. Osthol (3) a coumarin obtained from A. pubescens showed significant inhibitory activity
Antizoma angustifolia (Burch.) Miers ex Harv. (Menispermaceae)

During search for biologically active compounds from indigenous South African flora, a folklore medicinal plant A. angustifolia yielded a morphinandienone-type alkaloid sinoacutine in 2.8% yield. This alkaloid exhibited slight antiinflammatory activity (26% inhibition of phlogistic response at 300 mg/kg).\textsuperscript{101}

Arnebia hispidissima DC (Boraginaceae)

Roots of a number of Arnebia species like A. nobilis, A. guttata, A. benthamii, A. euchroma and A. hispidissima yielded red dye. Vitexin isolated from the later species exhibited moderate antiinflammatory activity.\textsuperscript{102}

Azadirachta indica A. Juss. (Meliaceae)

The leaf extract (400 mg/kg) inhibited carrageenan-induced rat paw oedema and is shown to be equipotent to 50 mg/kg acetylsalicylic acid and 4 mg/kg indomethacin, respectively.\textsuperscript{103}

The seed oil is said to be effective in rheumatism and skin diseases and is useful as a liniment for rheumatic affections. Nimbidin isolated from the seed oil of A. indica has shown potent antiinflammatory activity in experimental models.\textsuperscript{104}

Two water-soluble polysaccharides isolated from the bark of A. indica have also been tested for antiinflammatory effect on carrageenan model.\textsuperscript{105}
Baldwins augustifolia (Compositae)

The antiinflammatory activity of helenalin (4) isolated from B. augustifolia tested in Sprague Dawley rats at 5 mg/kg x 2
compared favourably with indomethacin at 10 mg/kg and resulted in greater than 75% reduction in inflammation.106

Boesenbergia pandurata Roxb. Schltr. (Zingiberaceae)

B. pandurata indigenous to Thailand occurs in four varieties attributed to the colour white, yellow, red and black present in the rhizome. All varieties have potential value in Thai-traditional medicine. The antiinflammatory activity of 5,7-dimethoxyflavone isolated from black rhizomes of the plant has been assessed. It was found to possess comparable effect to aspirin on the rat oedema model, and it showed no inhibition on cotton pellet-induced granuloma formation. On the rat pleurisy model, it exhibited an antiexudative effect, interfered with leukocyte migration and markedly inhibited prostaglandin biosynthesis.107

Boswellia serrata Roxb. ex Coleb. (Burseraceae)

In Ayurvedic system of medicine 'Salai guggal', the oleogum resin of B. serrata is reportedly employed for the
treatment of rheumatism and nervous diseases as an ingredient of certain ointments. Antiinflammatory and antiarthritic activities against carrageenan-induced paw oedema adjuvant arthritis in rats have been established.\textsuperscript{108-110} It was shown to be effective in controlled clinical trials in arthritis patients. It has been established that antiinflammatory and antiarthritic activities are due to the presence of boswellic acid and other related pentacyclic triterpene acids.\textsuperscript{111} In India it has been released for therapeutic use under the trade name 'Sallaki'.

\textbf{Bougainvillea glabra} DC (Nyctaginaceae)

The leaves of \textbf{B. glabra} have been used by some tribal people in North Bengal (India). Antiinflammatory activity was observed in preliminary screening.\textsuperscript{112} The petroleum ether fraction of the methanolic extract of \textbf{B. glabra} leaves showed significant antiinflammatory activity when given intraperitoneally to rats at a dose of 100 mg/kg and the activity was attributed to the presence of a steroidal component in the leaves.\textsuperscript{113}

\textbf{Bryophyllum pinnatum} Lam. (Crassulaceae)

\(\beta\)-Sitosterol and aliphatic alcohols obtained from \textbf{B. pinnatum} leaves showed antiinflammatory activity against carrageenan-induced oedema in rats.\textsuperscript{114}

\textbf{Bumelia sartorum} Mart. (Sapotaceae)

\textbf{B. sartorum} has been mentioned in Brazilian folklore for its reputed use in the treatment of inflammatory disorders.
The ethanolic extract of the root bark of this tree elicited significant antiinflammatory activity. Basic acid (5) has been isolated from the extract and this has been shown to be responsible for antiinflammatory activity.\textsuperscript{115}

\textbf{Bupleurum} spp. (Umbelliferae)

The essential oil of \textit{B. fructicosum} L. has shown significant antiinflammatory activity in carrageenan-induced rat paw oedema model.\textsuperscript{116} The activity can be attributed in part to the two major components, $\alpha$-pinene and $\beta$-pinene. It has also been shown that thymol and carvacrol, although present in extremely low levels, potentiate the pharmacodynamic action. The anti-inflammatory activity of the essential oil of \textit{B. gibraltaricum} Lam. was found to be more in comparison to \textit{B. fructicosum}. The activity in the former is due to the presence of the major component $\Delta^3$-carene, which is considerably more potent than that of either $\alpha$- or $\beta$-pinene.

The roots of \textit{B. falcatum} L. are used in Chinese medicine for the treatment of inflammation of diaphragm and enlargement
of liver caused by hepatitis. A number of saikosaponins have been isolated from the drug, and the aglycone part was found to have oleanane—type structure with a characteristic unsaturation at C-11 and a 13β,28-oxide system. The administration of saikosaponins has no side effect such as shrinking of adrenal gland that often occurs with the administration of prednisolone. Saikogenin A obtained from B. falcatum also possessed antiinflammatory activity.

**Calophyllum inophyllum** Linn. (Guttiferae)

Calophyllolide (6) isolated from *C. inophyllum* effectively reduced the increased permeability induced by the chemical mediators involved in inflammation like histamine, serotonin and bradykinin. The ED$_{50}$ was found to be 144.1, 250 and 133.5 mg/kg, p.o., respectively against these mediators. Various xanthones isolated from *C. inophyllum* have shown antiinflammatory activity both by intraperitoneal and oral routes in rats as tested by carrageenan—induced paw oedema, cotton pellet
granuloma and granuloma pouch techniques, in normal and adrenolectomised rats.\textsuperscript{124}

*Canscora decussata* Schult. (Gentianaceae)

This is one of the popular Indian plant bitters. Magniferin, a xanthone-C-glycoside from *C. decussata* has been found to possess antiinflammatory properties.\textsuperscript{125}

*Catasetum barbatum* Lindle. (Orchidaceae)

'Tamanda cuna', a folk remedy in Paraguay to have antiinflammatory activity when applied topically, is from Orchidaceous plant *C. barbatum*. The ethanolic (70\%) extract of the aerial parts was found to have antiinflammatory activity when topically applied to rats and on histamine-induced contraction in guinea pig ileum. The chromatographic separation of the extract gave 2,7-dihydroxy-3,4-dimethoxyphenanthrene, 2,7-dihydroxy-3,4,8-trimethoxyphenanthrene, 2,7-dihydroxy-3,4-dimethoxy-9,10-dihydro-phenanthrene and 3,4'-dihydroxy-5,5'-dimethoxydihydrostilbene. All these compounds showed inhibitory effect on contraction of guinea pig ileum induced by histamine, while the topical application of 2,7-dihydroxy-3,4-dimethoxyphenanthrene showed inhibition of oedema in carrageenan-induced rat paw oedema model.\textsuperscript{126}

*Chrysanthemum indicum* Linn. (Compositae)

Chrysanthenol isolated from the flowers of *C. indicum* showed strong antiinflammatory activity in mice.\textsuperscript{127}
Cimicifuga dahurica Maxim. (Ranunculaceae)

The roots of *C. foetida* Linn. popularly known in Punjab (India) as 'Junti' have been used for the treatment of neuralgia and rheumatism. Isoferulic acid obtained from the crude extract of *C. dahurica* rhizomes reduced carrageenan-induced oedema.

Cocculus scop. (Menispermaceae)

The roots of *C. hirsutus* Linn. (syn. *C. villosus* DC) have been used for the treatment of rheumatism. Two alkaloids, trilobine and isotrilobine isolated from *C. trilobus* showed inhibitory effect against cotton pellet and adjuvant arthritis in rats.

Coix lachryma-Jobi L. (Gramineae)

The roots of *C. lachryma* var. *ma-yuen* Stapf have been used in China for a long time for the treatment of rheumatism and neuralgia. Japanese workers at Hiroshima University have developed a new rapid in vitro screening technique using rat peritoneal mast cells, which contain large amount of histamine for testing antiinflammatory activity. Two benzoxazinoid compounds (7,8) isolated from roots of *C. lachryma* showed
85.5% and 47.3% inhibitory activity of histamine release, respectively.

**Commiphora mukul** Hook. ex Stocks (Burseraceae)

'Guggulu', an oleogum resin that exudes spontaneously as a result of injury to the bark of *C. mukul* (syn. *Balsamodendron mukul* Hook. ex Stocks) a tree of arid zones of Central India, has been in use in Ayurvedic system of medicine for a variety of metabolic disorders including rheumatoid arthritis and obesity. Bioactivity directed extraction and fractionation led to the separation of ethyl acetate-soluble part carrying both the hypocholesterolemic and antiinflammatory activities. The ethyl acetate-soluble portion was separated into basic, acidic and neutral fractions. The neutral portion carried practically all hypocholesterolemic activity, while the acidic fraction displayed significant antiinflammatory activity.

**Conyza canadensis** (L.) Cronq (Asteraceae)

Antiinflammatory activity of the petroleum ether and ethanol extract of *C. canadensis* (syn. *Erigeron canadensis* L.) has been reported. The fractionation of the petroleum ether extract led to the isolation of eight sesquiterpenes (β-santalen, β-himachalen, cuparene, α-curcumene, γ-cardinene and three unidentified compounds).

**Copaifera** spp. (Leguminosae)

The oleoresin from Brazilian *Copaifera* species showed the presence of copalic acid and sesquiterpenes, β-bisabololene,
β-caryophyllene, β-cubellene, aromadendrene, β-elemene, humullene and α-copaene. The oral administration of the oleoresin inhibited the development of carrageenan-induced oedema in rats in a dose dependant manner. However, this effect was not as pronounced as that seen with 50 mg/kg of calcium phenylbutazone.

*Cordia obliqua* Willd. (Boraginaceae)

α-Amyrin and taxifolin-3,5-dirhamnoside isolated from *C. obliqua* (syn. *C. dichotoma* Forst.) seeds showed significant antiinflammatory activity (71.4% and 67.8%, respectively) by an oral dose of 1 g/kg, which were nearly equivalent to the inhibition of inflammation produced by 100 mg/kg of oxyphenylbutazone (67.8%).

*Cotinus coggyria* Scop. (Anacardiaceae)

A flavonoid preparation made of *C. coggyria* (syn. *Rhus cotinus* L.) leaves has an antiphlogistic effect.

*Croton lechleri* L. (Euphorbiaceae)

*C. lechleri* commonly called 'Sangre de grado', is a tree of upper Amazon valley of Peru. The bark, when slashed, produces a red viscous sap which is used by the Peruvian Indian for...
rheumatism. Taspine (9) previously reported from Leontice eversmanii Bge. (Berberidaceae) has been isolated from the sap and its hydrochloride salt was shown to elicit antiinflammatory activity in three different models. \(^{142}\)

**Cryptomeria japonica** D. Don (Taxodiaceae)

The leaves of *C. japonica* have been traditionally used as a substitute for 'Sanyo', which is derived from the leaves of Cunninghamia lanceolata (Lamb.) in Chinese medicine, for the treatment of eczema, eruption, swelling, injury etc. by topical application. The ether-soluble fraction of the methanol extract from the leaves of *C. japonica* showed antiinflammatory effect when applied topically to rats and an inhibitory effect on histamine-induced ileum contraction. The activity was attributed to the active compound cis-communic acid (10) \(^{143}\)

![cis-communic acid](image)

**Curcuma longa** Linn. (Zingiberaceae)

Rhizomes of *C. longa* (syn. *C. domestica* Velton) are the source of turmeric used as condiment and also in formulations used for sprains and bruises. The petroleum ether extract of the rhizomes showed significant antiinflammatory properties and
was found effective in delayed hypersensitivity without toxic
effects. A comparison of various extracts of turmeric
has been made. In the granuloma pouch method the water extract
was the most potent with activity similar to that of hydrocortisone whereas in cotton pellet test the petroleum ether
extract was most potent with activity comparable to indomethacin. Curcumin (11), a constituent of turmeric has been shown to be
effective antiinflammatory agent. It is as potent as an

\[
\begin{align*}
\text{H}_3\text{CO} & \quad \text{O} \\
\text{H} & \quad \text{CH} = \text{CH} - \text{C} = \text{C} - \text{CH} = \text{CH} - \text{CH} = \text{CH} - \text{C} = \text{C} - \text{CH} - \text{OH} \\
\text{OCH}_3 & \quad \text{OH}
\end{align*}
\]

(11)

phenylbutazone in the carrageenan oedema test but half as
potent in chronic tests. It possesses much lower ulcerogenic
index than phenylbutazone, but at 2 x ED\text{50} administered for
six days it, however, produced gastric ulceration in rats. The marked reduction in mucin content of gastric juice seems
to be responsible for the ulcerogenic effect. A study of the
effect of curcumin on biochemical changes produced during
subacute inflammation in rats has shown it to be more potent
than ibuprofen as a stabilizer of lysosomal membrane and as
an uncoupler of oxidative phosphorylation. Two naturally
occurring curcumin-related analogues, feruloyl-4-hydroxcinnamoyl
methane and bis(4-hydroxycinnamoyl)methane have shown
antiinflammatory activity. Water-soluble sodium curcuminate
showed better antiinflammatory activity than curcumin and
Various analogues of curcumin have been prepared. The potencies of these analogues and phenylbutazone in carrageenan oedema and cotton pellet granuloma tests were in the order: sodium curcuminate > tetrahydrocurcumin > curcumin > phenylbutazone > triethylcurcumin. Ferulic acid and diacetylcurcumin were found to be devoid of activity. Curcumin analogues were less effective in inhibiting the granulomatous tissue formation. Maximum activity was observed with triethylcurcumin whereas curcumin, sodium curcuminate and phenylbutazone were almost half as effective as triethylcurcumin. The results of short-term, double blind, cross-over clinical study showed convincing evidence of antirheumatic activity of curcumin in patients with rheumatoid arthritis. The activity of 1200 mg of curcumin/day was comparable to that of 300 mg of phenylbutazone/day.

*Cyperus rotundus* Linn. (Cyperaceae)

β-Sitosterol isolated from *C. rotundus* possessed potent antiinflammatory activity against carrageenan and cotton pellet induced oedema in rats and was comparable to hydrocortisone and phenylbutazone when administered intraperitoneally. β-Sitosterol showed a wide margin of safety since the approximate LD₅₀ was 3 g/kg, i.p. in mice and the minimum ulcerogenic dose was 600 mg/kg, i.p. in the rats.
Dalbergia volubilis Roxb. (Leguminosae)

Earlier antiarthritic activity of crude extract of D. lanceolaria has been reported. The flavonoid glycoside chrysoeriol-7-O-β-D-glucopyranosidyl (2→1)-D-apiofuranoside isolated from leaves of D. volubilis exhibited significant antiinflammatory activity.

Desmodium gangeticum DC (Leguminosae)

The roots of D. gangeticum constitute one of the ingredients of a very popular Ayurvedic tonic 'Dashmoolarishtha'. Gangetin, one of the pterocarpans, isolated from hexane extract of the roots of D. gangeticum produced significant antiinflammatory activity in exudative and proliferative phases of inflammation at 50 and 100 mg/kg, p.o. in rats.

Dianthus barbatus C.V. (Caryophyllaceae)

Two saponins barbatoside A and B obtained from aerial parts of D. barbatus were shown to have analgesic and anti-inflammatory activities. The aglycone of each saponin was identified as quillaic acid. The sugar moieties of barbatoside A consisted of rhamnose, arabinose, fucose, xylose, galactose and glucose whereas those of barbatoside B contained arabinose, fucose, xylose, mannose, galactose and glucose.

Dioscorea mexicana (Dioscoreaceae)

Cryptogenin, a steroid isolated from D. mexicana reduced the kaolin oedema in rats to half, five hours after injection.
Dryopteris pacifica Tagawa (Polypodiaceae)

Margaspidin, an active principle isolated from D. pacifica, when administered orally in a dose of 50 mg/kg exerted significant inhibition of granular tissue formation induced by cotton pellet model. Margaspidin has earlier been isolated from D. marginalis A. Gray.\textsuperscript{161}

Dysoxylum binectariferum Hook. (Meliaceae)

Dysobinin (12), a tetranortriterpene of the meliacin group showing mild antiinflammatory activity has been isolated from the fruits of D. binectariferum.\textsuperscript{162,163} The alkaloid rohitukin (13), isolated from the stem bark displayed anti-inflammatory activity in carrageenan-induced rat paw edema (ED\textsubscript{50}, 9 mg/kg, p.o.) and inhibited the reverse passive Arthus reaction in rats (50.8% inhibition at 2.5 mg/kg, p.o.).\textsuperscript{164}
Ecballium elaterium (L.) A. Rich. (Cucurbitaceae)

The fruit juice of *E. elaterium*, used as a folk medicine in Turkey for the treatment of sinusitis, has been investigated for its antiinflammatory activity. Cucurbitacin B, the active principle isolated from chloroform extract as well as water-insoluble part of the fruit juice of *E. elaterium* at 200 mg/kg, p.o. dose, showed significant antiinflammatory activity (69.6% inhibition of oedema). 165

Echinacea angustifolia DC (Compositae)

The polysaccharide fraction from *E. angustifolia* has been shown to exert a noticeable antiinflammatory activity both after systemic administration and topically. Polysaccharides may be considered as the main active principles involved in anti-inflammatory activity of *E. angustifolia*. 166

Eisenia bicyclis (Kjellman) Setchell

A complex polymer obtained from an alga *E. bicyclis* collected from the shores of Korea has shown antiinflammatory activity. This on chemical degradation has yielded glucose, phloroglucinol and trimethylamine. 167

Elytropappus rhinocerotis Less. (Compositae)

Rhinocerotinoic acid, a labdane diterpene isolated from *E. rhinocerotis* exhibited antiinflammatory activity. 168

Embelia ribes Burm. (Myrsinaceae)

Embelin obtained from *E. ribes* and its 2,5-isobutylamine salt have been reported to possess antiinflammatory activity in carrageenan-induced paw oedema and cotton pellet granuloma.
formation.

**Ephedra spp. (Gnetaceae)**

A survey of active principles of a crude Chinese drug 'Maó', prepared from the herbs of certain species of *Ephedra* used as antitussive in Oriental medicine revealed that the most active antiinflammatory agent is pseudoephedrine which elicited inhibitory actions on a number of acute inflammations. Ephedroxane, an analogue of ephedrine, has also been isolated as the minor antiinflammatory principle.

**Eriobotrya japonica** Lindl. (Rosaceae)

Topical application of the alcoholic extract of *E. japonica* has been traditionally used for the treatment of prickly heat, eczema and other skin diseases. Maslinic acid isolated from the ether-soluble fraction of ethanol extract from the leaves of *E. japonica* showed antiinflammatory activity on carrageenan-induced oedema. It also exhibited inhibitory effect on histamine-induced contraction in ileum isolated from guinea pig.

**Euphorbia palustris** L. (Euphorbiaceae)

Blood vessel permeability at the site of inflammation produced by formalin and chicken egg albumin was significantly reduced by *E. palustris* flavonoids.

**Garcinia mangostana** Linn. (Guttiferae)

Rind of the fruit of *G. mangostana* is used in the treatment of diarrhoea and dysentery in folk remedies. Magnostin from the
rind of the fruit inhibited primary and secondary responses of adjuvant induced arthritis in rats.\textsuperscript{175,176}

\textbf{Glycyrrhiza spp. (Leguminosae)}

The roots and rhizomes of \textit{G. glabra} Linn. and \textit{G. uralensis} Fisch. ex DC and their varieties, commonly called licorice are used both in Western and Oriental medicine as an expectorant, antitussive and as sweetening adjuvant. In Chinese system of medicine licorice is used to treat throat inflammation while in Europe its extracts are also used in the form of troche for similar purposes. The main chemical constituent of licorice is glycyrrhizin, a triterpene saponin with low haemolytic index. It potentiates the antiarthritic action of hydrocortisone in rats.\textsuperscript{177} Its antiinflammatory action has been found in cosmetics.\textsuperscript{178} Topical antiinflammatory formulations have also been reported to contain glycyrrhizinates.\textsuperscript{179} The aglycone of glycyrrhizin, glycyrrhetic acid (glycyrrhetinic acid)\textsuperscript{(14)} showed antiinflammatory activity in 1/8th potency of cortisol by the cotton pellet method. The activity is potentiated to 1/5th when the sodium salt of hemisuccinate of glycyrrhetic acid (carbenoxolone) is used.\textsuperscript{180} Amagaya \textit{et al.}\textsuperscript{181} have reported that the \textit{18\alpha}-isomer of glycyrrhetic acid is more active as an antiinflammatory agent than the \textit{18\beta}-isomer using carrageenan oedema in mice. The activity of the former is similar to that of glucocorticoids. It is considered that glycyrrhizin or glycyrrhetic acid does not produce direct hormonal activities but might react indirectly to enhance the activity of both mineral and glucocorticoids in inhibiting
the metabolic inactivation of these hormones in liver. The changes in the enzymatic activity produced by hydrocortisone and glycyrrhetic acid have been correlated with their antiarthritic effects. Various modified forms of glycyrrhetinic acid, such as sodium, potassium and ammonium salts, have been synthesized\textsuperscript{182,183} and their antiinflammatory activity showing direct participation of adrenal glands but not the pituitary
has been demonstrated.\(^{184}\) Other studies with glycyrrhiza compounds have substantiated the antiarthritic and antiinflammatory actions.\(^{185,186}\) Reduced form of glycyrrhetinic acid also showed marked antiallergic and antiulcer activities without undesirable aldosterone-like properties.\(^{187}\) Moreover carbenoxolone also possesses antiulcer activity.\(^{188}\) The flavonoids liquiritigenin, liquiritin, quercetin and rutin isolated from G. glabra and G. uralensis have also shown antiinflammatory activity.\(^{189}\)

**Haematoxylon campechianum** Linn. (Leguminosae)

A naturally occurring phenolic dye hematoxylin isolated from *H. campechianum* wood exhibited significant antiinflammatory activity in the carrageenan-induced oedema test and another similar compound brazilin isolated from Caesalpinia sappan Linn. was found to be more potent than hematoxylin.\(^{190}\)

**Hedychium spicatum** Ham. (Zingiberaceae)

A flavonoid hedychenone isolated from hexane-soluble extract of *H. spicatum* showed significant activity with less ulcerogenic index than phenylbutazone.\(^{191}\)

**Heimia salicifolia** Link. and Otto. (Lythraceae)

Two alkaloids, cryogenine (20) and nesodine (21), isolated from *H. salicifolia* were shown to be 2.48 and 2.24 times as
potent as aspirin in inhibiting the prostaglandin synthetase prepared from bovine seminal vesicles. Cryogenine has been shown to exert significant antiinflammatory activity in different systems. 192-199

**Hibiscus vitifolius** Linn. (Malvaceae)

Gossypin isolated from *H. vitifolius* significantly reduced initial as well as the late phase of carrageenan-induced rat paw oedema and protein extravasation in rats, while phenylbutazone failed to reduce the initial increase of vascular permeability in response to carrageenan. Gossypin seems to reduce vascular permeability like other flavonoids by decreasing the susceptibility to various permeability factors in general. 200, 201

**Limonia crenulata** Roxb. (Rutaceae)

8-Hydroxy-6-methoxy-2-methylanthraquinone-3-O-β-D-glucopyranoside isolated from *L. crenulata* (whole plant) showed significant inhibition (65.9%) of carrageenan-induced paw oedema in rats in a dose (1 g/kg), which is equivalent to that produced by 100 mg/kg of oxyphenylbutazone (72.7%). 202

**Madhuca longifolia** (L.) Macb. (Sapotaceae)

Antiinflammatory and antiulcerogenic activities were found in Mi-saponin, the mixture of Mi-saponin A, B and C, obtained from seed kernels of *M. longifolia*. 203 The potency of antiinflammatory activity was found to be 1/4 of phenylbutazone. Mi-saponin A, B and C are bisdesmosides of an olean-12-ene type sapogenol of protobassic acid (15). 204
Maesa chisia D. Don (Myrsinaceae)

The glycosidal fraction isolated from the leaves of M. chisia var. angustifolia Hook. exhibited carrageenan rat paw oedema inhibition whereas it did not produce any effect on histamine and serotonin-induced oedema. The fraction also inhibited cotton pellet granuloma, controlled formaldehyde-induced arthritis and reduced development of Freund's adjuvant arthritis. The antiinflammatory activity resembles with known non-steroidal antiinflammatory drugs.205

Magnolia salicifolia Maxim. (Magnoliaceae)

'Shin-i' is a traditional Chinese herbal drug representing flowering buds of M. salicifolia used for the treatment of nasal diseases. Neolignans, magnoshinin and magnosalin obtained from the dried buds of M. salicifolia significantly inhibited granuloma tissue formation. The inhibitory effect of magnoshinin was particularly strong, being nearly half of hydrocortisone acetate when administered orally. The neolignans selectively inhibited granuloma tissue formation but did not affect the exudation of pouch fluid. Of all the major components isolated from M. salicifolia, magnoshinin was found to be the essential component responsible for antiinflammatory activity.206

Melilotus officinalis Lam. (Leguminosae)

In an extensive series of controlled tests on experimental arthritis in rats, it was demonstrated that the coumarins from M. officinalis exert a dose dependant antiinflammatory and antioedema activities.207
Menispermum dauricum DC (Menispermaceae)

In traditional Chinese medicine, dauricine, an alkaloid isolated from *M. dauricum* roots has been used for treating rheumatism.\(^\text{208}\)

*Mentha piperita* Linn. (Labiatae)

Polyphenols obtained from *M. piperita* have shown anti-inflammatory activity.\(^\text{209}\)

Mesua ferrea Linn. (Guttiferae)

Phenolic constituents of the seed oil of *M. ferrea* have been shown to have powerful antiasthmatic effect.\(^\text{210}\) Xanthones isolated from *M. ferrea* have been found to produce significant antiinflammatory activity in normal as well as in adrenolactomised rats by both intraperitoneal and oral routes.\(^\text{124}\)

*Myristica fragrans* Houtt. (Myristicaceae)

Mace, the aril of the fruit has been used in folk medicine for the treatment of rheumatism. Bioactivity directed extraction and fractionation has established that antiinflammatory activity in carrageenan-induced oedema in rats and vascular permeability in mice is due to the major principle myristicin.\(^\text{211}\)

Ochrocarpus longifolius L. (Guttiferae)

Flowering buds of *O. longifolius* (syn. *Mammea longifolia* Planch) popularly known as 'Nagkesar' used in traditional Indian medicine for the haemorrhoids yield a dye. An anti-inflammatory principle, vitexin has been isolated from these flowers.\(^\text{102}\)
**Panax japonica** C.A. Meyer (Araliaceae)

The rhizomes of *P. japonica* have been used since long in Japan as a substitute for *P. ginseng* roots of Chinese medicine, especially as antitussives and expectorants. A saponin glucoside chikusetsusaponin V (22) isolated from the rhizomes of the plant has shown significant antiinflammatory activity.

![Chemical structure of chikusetsusaponin V](image)

\[ R^1 = \text{glucose} \rightarrow 2 \rightarrow \text{glucuronic acid.} \quad R^2 = \text{glucose} \]

**Pedilanthus tithymaloides** Poit (Euphorbiaceae)

Literature reports are available on oral antiinflammatory activity of proteolytic enzymes. Pedilanthen, a new protease, was isolated from the latex of *P. tithymaloides* and was subjected to antiinflammatory screening in carrageenan model. Pedilanthen at 125 mg/kg onwards is more potent than phenylbutazone (100 mg/kg) after 1 h of carrageenan administration. At second hour of carrageenan injection, pedilanthen (500 mg/kg) was found to be slightly potent than phenylbutazone.
(100 mg/kg). It exhibits its maximum activity at 2nd hour of its oral administration.215

Peltophorum pterocarpum Backer (Caesalpiniaceae)

P. pterocarpum is popularly known as 'Copper pod'. It is an ingredient of gargles, tooth powders and lotions used for eye troubles, muscular pains and sores.216 Bergenin (23) isolated from the pods of P. pterocarpum was found to be equipotent to phenylbutazone in rats against carrageenan—induced oedema.217

Physalis minima Linn. (Solanaceae)

The crude extract of leaves rich in quercetin-3-O-galactoside exhibited antiinflammatory activity comparable to phenylbutazone in carrageenan—induced rat paw oedema model.218

Phytolacca americana L. (Phytolaccaceae)

The roots of P. americana reputed in Korean medicine to alleviate rheumatism, are rich in saponins having potent antiinflammatory activity.219 One of the major saponins, phytolaccoside B is a glucoside of jaligonic acid-30-methyl ether (16) exhibiting antirheumatic and antiinflammatory actions.220 Strong
anti-inflammatory saponins were obtained from callus mass derived from stems and roots of *P. americana*.221

**Picrorhiza kurroa** Royal ex-Benth. (Scrophulariaceae)

*P. kurroa* rhizomes popularly known as 'Kutki' is a reputed Ayurvedic remedy with confirmed therapeutic potential in immune disorders.222,223 A consistent but somewhat delayed anti-inflammatory activity of alcoholic extract in several models of immune and non-immune inflammation has been reported.224 The study indicated involvement of adrenergic mechanism in the anti-inflammatory effect along with an interference with release or lytic activity of the lysosomal enzymes and there appeared no likelihood of any direct or indirect glucocorticoid effect. Further studies indicated a nonneural augmentation of β-adrenerg receptor function or consequent cellular events mediate anti-inflammatory effect of *P. kurroa*.225 Relative importance of various cells involved in inflammation and in anti-inflammatory actions of *P. kurroa* has been investigated in albino rats.226

**Plagiorhegma dubium** Maxim. (Berberidaceae)

*P. dubium* [syn. *Jeffersonia dubia* (Maxim.)] is an under shrub and is distributed from Northern China to Eastern Siberia. An alkaloid jatrohhizine and a lignane glucoside dehydrodi coniferyl alcohol-4β-D-glucoside and its isomer dehydrodiconiferyl alcohol-Y-β-D-glucoside isolated from methanolic extract of cultured *P. dubium* cells have shown anti-inflammatory activity.227

**Platycodon grandiflorum** A. DC (Campanulaceae)

The saponins of a Chinese drug 'Jieseng' (Japanese name
'Kikyo'), representing the roots of *P. grandiflorum* have been studied in detail. Platycodin D, a saponin with oleanane-type sapogenin, isolated as the main constituent from the roots exhibited significant antiinflammatory activity.

**Polygonum hydropiper** Linn. (Polygonaceae)

Polygonolide (24), an isocoumarin which inhibits the reversed passive Arthus reaction (RPAR) in rats via oral administration has been isolated from the roots of *P. hydropiper*. Although the inhibitory effects on RPAR are moderate in comparison to hydrocortisone, polygonolide seems to have the potential of becoming prototype for developing a new antiinflammatory agent.

**Potentilla erecta** Uspenski, ex Ledeb. (Rosaceae)

Polyphenols obtained from rhizomes of *P. erecta* have shown antiinflammatory activity.

**Psoralea corylifolia** Linn. (Leguminosae)

It is a popular traditional remedy for leucoderma and is rich in furanocoumarins like xanthotoxin and bergapten which have photosensitizing property and used in suntan lotion. A phenolic compound bavachinin (25) isolated from the plant has
shown significant antiinflammatory activity.\textsuperscript{232}

![Pyrola rotundifolia](image)

\textbf{Pyrola rotundifolia L. (Pyrolaceae)}

\textit{P. rotundifolia} (whole herb) has been used in traditional Chinese medicine mainly for arthritic diseases. Ursolic acid and chimaphilin isolated as the active principles from the methanol extract of \textit{P. rotundifolia} have shown 24\% and 33\% inhibition of oedema, at a dose of 500 mg/kg, respectively in carrageenan—induced rat paw oedema model.\textsuperscript{233}

\textbf{Randia dumetorum Lam. (Rubiaceae)}

Oleanolic acid-3-glucoside isolated from the seeds of \textit{R. dumetorum} (25-500 mg/kg, p.o.) showed significant antiarthritic activity in the exudative and proliferative phases of inflammation in rats.\textsuperscript{234}

\textbf{Rhamnus} spp. (Rhamnaceae)

Xanthorhamnin isolated from the seeds of \textit{R. infectoria} has been patented as an antiinflammatory agent and recommended for the treatment of rheumatoid arthritis and for use in
ophthalmology, particularly for topical treatment of collyria. Kaempferol, isolated from Indian shrub \textit{R. procumbens} Linn. in the dose of 200 mg/kg, i.p., exhibited anti-inflammatory activity against carrageenan and serotonin but not against histamine-induced oedema in rats. It also inhibited the pouch fluid and granulation tissue formation induced by croton oil.\textsuperscript{235}

\textit{Rhus undulata} Jacq (Anacardiaceae)

In the course of search for biologically active compounds from South African flora, the roots of \textit{R. undulata} var. \textit{undulata} yielded apigenin dimethyl ether which exhibited significant anti-inflammatory activity.\textsuperscript{236}

\textit{Schizogyne} spp. (Compositae)

10-Acetoxy-8-hydroxy-9-isobutyroxy-6-methoxythymol isolated from \textit{S. sericea} L. fil. DC and \textit{S. glaborma} DC showed anti-inflammatory activity on carrageenan-induced oedema in rats at 50 mg/kg, i.p. dose.\textsuperscript{237}

\textit{Scutellaria baicalensis} Georgi (Labiatae)

This annual herb mostly found growing in fertile moist areas is a popular remedy for sore throat and boils in Chinese traditional medicine. Three flavonoids, baicalin (26), baicalein (27) and wogonin (28) isolated from \textit{S. baicalensis} showed inhibitory effect on increased vascular permeability induced by acetic acid at high doses compared with effective dose of indomethacin. Baicalin and baicalein inhibited the increase of carrageenan oedema only when given one hour after injection but wogonin did not inhibit the oedema at any time tested.
All the three flavonoids also suppressed the secondary lesion

\[
\begin{align*}
(26) & \quad R^1 = H, \quad R^2 = OCOH, \quad R^3 = OH \\
(27) & \quad R^1 = H, \quad R^2 = R^3 = OH \\
(28) & \quad R^1 = OCH_3, \quad R^2 = OH, \quad R^3 = H.
\end{align*}
\]

in developing adjuvant arthritis in rats.\(^{238}\)

**Sechium edule** Sw. (Cucurbitaceae)

\(\beta\)-sitosterol-\(\beta\)-D-glucopyranoside and stigmasterol-\(\beta\)-D-\(\beta\)-glucopyranoside isolated from the fruit of *S. edule* exhibited antiinflammatory activity.\(^{239,240}\)

**Serratia piscatorum**

The polysaccharide produced by *S. piscatorum* exhibited antiinflammatory activity\(^{241-243}\) which was completely lost when the polysaccharide was hydrolyzed by acid or alkali into smaller molecules or when hydroxyl groups were partially acetylated. The presence of hydroxyl groups in the molecular polysaccharide moiety may be playing an important role in the manifestation of antiinflammatory activity.
Sideritis spp. (Lamiaceae)

The ethanolic extract of various Sideritis spp. used in folklore medicine in Turkey showed significant antiinflammatory activity in carrageenan-induced hind paw oedema in mice. Hypolaetin-8-β-D-glucoside isolated from S. mugronensis Borja and sideritoflavone (5,3',4'- trihydroxy-6,7,8-trimethoxyflavone) obtained from the several Sideritis species exhibited anti-inflammatory activity. Hypolaetin-8-β-D-glucoside was weak but selective inhibitor of lipoxygenase whereas the aglycone hypolaetin was more potent and selective lipoxygenase inhibitor. The antiinflammatory and antiarthritic activities of borjatriol (7S, 14R, 15-trihydroxy-8α-13-epoxylabdane) obtained from the same plant have been demonstrated. Caffeic acid, chlorogenic acid and neochlorogenic acid from S. catillaris have also shown antiinflammatory activity.

Siegesbeckia pubescens (Asteraceae)

The sesquiterpene (29) isolated from S. pubescens at 100 mg/kg, p.o. inhibited inflammation by 44.9% in the carrageenan oedema test using male Winstar rats.
**Symplocos spicata** Roxb. (Symplocaceae)

α-Spinasterol obtained from the stem bark of *S. spicata* showed significant activity against acute inflammation induced by carrageenan in rats and was more potent than phenylbutazone but less potent than betamethasone.\(^{251}\)

**Solanum lycopersicum** Linn. (Solanaceae)

Tomatine, a steroidal alkaloid glucoside isolated from extracts of crown gall infected *S. lycopersicum* (*syn. Lycopersicum esculentum* Mill.) (tomato) or obtained commercially, when administered to intact rats intramuscularly in a dose range 1-10 mg/kg or orally in doses of 15-30 mg/kg caused significant dose dependent inhibition of carrageenan—induced paw oedema. Tomatidine, the aglycone of tomatine was not effective at the dose levels of 10-20 mg/kg.\(^{252}\)

**Solenostemma oleifolium** (Asclepiadaceae)

A steroidal compound isolated from the unsaponifiable fraction of the stem of an Egyptian plant *S. oleifolium* (Arghal) significantly reduced oedema produced by carrageenan; the effect was dose dependant and greater than that of phenylbutazone.\(^{253}\)

**Stephania** spp. (Menispermaceae)

Cycleanine, an alkaloid isolated from *S. glabra* Miers reduced the inflammatory oedema in rats with formalin-induced arthritis and inhibited the formation of granulation tissue. Cycleanine possesses adrenolytic properties.\(^ {254}\) An alkaloid tetrandrine obtained from the roots of *S. tetrandra* S. Moore also showed antiinflammatory properties.\(^ {255}\)
Terminalia ivorensis (Combretaceae)

Different parts of *T. ivorensis* are used in African ethnomedicine for treatment of various diseases including arthritic conditions.  

Screening of various extracts of the stem bark of *T. ivorensis* in carrageenan—induced rat paw oedema and in adjuvant-induced polyarthritic rat studies indicated that antiinflammatory activity was attributed to the presence of oleanane derivatives, terminolic acid (17),

\[
\text{(30)}
\]

β-glycyrrhetinic acid (14), lonchoterpene (18) and other components like quercetin and ellagic acid (30).

Thalictrum sessile Hayata (Ranunculaceae)

Thalicssiline (31), the first ajaconine type C\(_{20}\) diterpene

\[
\text{(31)}
\]

alkaloid having an oxygen function at C\(_{6}\) isolated from *T. sessile*
showed 42% reduction of carrageenan-induced inflammation in Sprague Dawley rats at 20 mg/kg. Tripterygium wilfordii Hook. (Celastraceae)

Triptotriterpenic acid (19) isolated from T. wilfordii showed antiinflammatory activity in laboratory animals. Triophora indica (Burm. f.) Mirr. (Asclepiadaceae)

Tylophorine, an alkaloid from T. indica apart from anaphylactic and immunocytoadherence action, significantly inhibited the primary and secondary responses of adjuvant-induced arthritis. Tylophorine at 25 mg/kg dose produced significant antiinflammatory effect as tested by rat hind paw oedema, granuloma pouch and cotton pellet implantation methods.

Usnea diffracta Vain (Usneaceae)

The active principles, (+)-usnic acid and diffractaic acid isolated from U. diffracta exhibited antiinflammatory activity. (+)-Usnic acid when administered orally to intact rats in a dose of 50 mg/kg, significantly inhibited the granulation tissue formation induced by subcutaneous implantation of cotton pellets.

Veratrum spp. (Liliaceae)

A preparation derived from the alkaloids obtained from V. lobelianum at the dose of 0.25 and 0.025 mg/kg when given subcutaneously has an antiinflammatory activity. The activity is due to the stimulation of adrenal activity by Veratrum.
alkaloids. Some Veratrum alkaloids namely jervine (and jervine derivatives) and protoveratrine exhibited antiinflammatory activity when administered subcutaneously. They decreased both exudative and proliferative phases consequent to subcutaneous implantation of wool pellets.

Withania somnifera Dunal (Solanaceae)

Long term effect of *W. somnifera* on adjuvant arthritic rats has been studied. The body weight loss observed during arthritic conditions was corrected on treatment with *W. somnifera* for fifteen days. The swelling of the paw during the secondary lesions was also markedly reduced. The radiographic observations revealed that *W. somnifera* prevented bony degenerative changes occurring during arthritic conditions.

1.2 REVIEW OF THE WORK DONE BY OTHER WORKERS ON:

1.2.1 *VITEX* SPECIES

*Vitex* Linn. (Verbenaceae) is a genus of trees or shrubs, widely distributed in tropics and warm temperate regions of both the hemispheres. Out of its fourteen species found in India, a number of them are used in traditional medicine. It may therefore be pertinent to review the work already done on the different species of the genus *Vitex*.

*Vitex aegnus-castus* Linn. is found from the Mediterranean region through South-West Asian countries upto Baluchistan in Pakistan. It is occasionally cultivated in Indian gardens.
Alcoholic and ethereal extracts of leaves inhibited growth of *Micrococcus pyogenes* var. *albus*. Iridoid glycosides, aucubin, agnuside and eurostoside (32) have been isolated from the leaves. The isolation of flavonoids, casticin, luteolin-7-glucoside and α-D-glucoside of tetrahydroxymonomethoxyflavone from the leaves has been reported. Homo-orientin has been isolated from the stem and leaves of the plant. In the fruits, the presence of agnuside, 3, 6, 7, 4-tetramethyl ether of 6-hydroxykaemferol, 3, 6, 7-trimethyl ether of 6-hydroxykaempherol and 3, 6, 7-trimethyl ether of quercetagetin has been reported.

*Vitex cannabifolia* Sieb. et Zucc. is a shrub found wild in China and cultivated in Japan. The fruits are used as an antiinflammatory under the name of 'Bokeishi'. The isolation of vitexilactone (33), agnuside, artemetin and p-hydroxybenzoic acid from the leaves has been reported. Earlier a sterol component isolated from the root-bark of the plant was found.
to be a mixture of \( \beta \)-sitosterol, stigmasterol and campesterol

\begin{align*}
\text{by gas chromatography.}^{278}
\end{align*}

The wood of *Vitex lucens* is reported to contain flavonoids; vitexin, isovitexin, orientin, iso-orientin and compounds of vitexin and orientin.\(^{279-281}\) In addition three apigenin derivatives (vicenins) and five luteolin derivatives (lucenins) having C-glycosyl substituents at C-6 and C-8 have been reported.\(^{281,282}\)

Isolation of 20-hydroxyecdysone (crustecdysone) (34),

\begin{align*}
\text{(34) } R^1 &= \text{OH}, R^2 = \text{CH}_3, R^3 = R^4 = R^5 = \text{H}
\end{align*}
(35) \( R^1 = \text{OH}, R^2 = \text{CH}_2\text{OH}, R^3 = R^4 = R^5 = \text{H} \)

(36) \( R^1 = \text{OH}, R^2 = \text{CH}_3, R^3 = R^4 = H, R^5 = \beta\text{-OH} \)

(37) \( R^1 = R^3 = \text{OH}, R^2 = \text{CH}_3, R^4 = R^5 = H \)

(38) \( R^1 = \text{OAc}, R^2 = \text{CH}_3, R^3 = R^4 = R^5 = H \)

(39) \( R^1 = \text{OH}, R^2 = \text{CH}_3, R^3 = R^5 = H, R^4 = \text{OH} \)

inkosterone (35), polypodin B (36), pterosterone (37), viti-
costerone E (38) from the leaves of *Vitex megapotamica* (Sprang) Maldenke has been reported.\(^{283,284}\)

*Vitex peduncularis* Wall. is a moderate-sized tree found in lower eastern Himalayas, Assam and neighbouring states of West Bengal, and parts of Bihar, Orissa and Andhra Pradesh, extending up to the river Godavari, ascending to an altitude of 900 meters.\(^{269}\) An infusion of different parts of the plant is reported to be useful in malarial and black water fevers.\(^{269}\)

The bark is said to be useful as an external application to relieve pain in the chest.\(^{269}\) The isolation of 5,4'-dihydroxy-3,7,3'-trimethoxyflavone (pachypodol), 5,4'-dihydroxy-3,6-
dimethoxyflavone (peduncularisin), vitexin, ursolic acid and 2\(^\alpha\)-hydroxyursolic acid from the leaves has been reported.\(^{285}\) Vitexin has been earlier isolated from the bark of the plant.\(^{286,287}\)

*Vitex rotundifolia* L. fil is a small wild shrub widely distributed on the sea coast in Asia.\(^{288}\) It has long been used as a medicinal plant in Japan.\(^{289}\) The aqueous extract of the fruits has been reported to reduce blood pressure in rabbits.\(^{290}\)
The diterpenes; rotundifuran (40), prerotundifuran (41),

vitexilactone (33), previtexilactone (42) together with flavones vitexicarpin (casticin), luteolin, arte.metin, and p-hydroxybenzoic acid and vanillic acid have been isolated from the fruits. 291-295

From the creeping stem of the plant taraxerol (43), lupeol and a sesquiterpene, viteralone (44) have been reported. 289 The occurrence of rotundifuran (40), agnuside, eurostoside (32) and 4-(3', 4'-dihydroxyphenyl)butane-2-one-4'-O-β-D-glucoside is
known from the leaves. The seeds contain artemetin and casticin.

\[ \text{(43)} \]

\[ \text{(44)} \]

and casticin.\(^{297}\)

**Vitex trifolia** Linn. is a stout and aromatic shrub distributed from the foot hills of the Himalayas southwards and in Andamans. The leaves are considered useful for external application to relieve rheumatic pains and sprain.\(^{269}\) An extract of the leaves showed inhibitory action against *Mycobacterium tuberculosis*.\(^{269}\) The extract also exhibited the anticancer activity.\(^{269}\) The fruit is reported to be used in amenorrhoea.\(^{269}\) The leaves have been reported to contain artemetin,\(^{298}\) casticin,\(^{298}\) 7-desmethylartemetin,\(^{298}\) 5-methylartemetin,\(^{298}\) luteolin,\(^{298}\) agnuside,\(^{299}\) luteolin-7-\(\beta\)-D-glucuronide,\(^{300}\) luteolin-3'-\(\beta\)-D-glucuronide\(^{300}\) and *iso*-orientin;\(^{300}\) friedelin,\(^{301}\) \(\beta\)-sitosterol\(^{301}\) and its glucoside\(^{301}\) and an aliphatic hydrocarbon.\(^{301}\) An alkaloid vitricine has been isolated from the fruits.\(^{302}\) The fatty acid composition of the seed oil has been studied.\(^{303}\)
The unsaponifiable matter contained small quantity of paraffin, \( \gamma \)-tocopherol and \( \beta \)-sitosterol.\textsuperscript{303}

Isolation of 20-hydroxyecdysone (34) and 11\( \alpha \),20-dihydroxy \( \varepsilon \)-ecdysone (turkesterone) (39) from the bark of *Vitex glabrata* R.Br. has been reported.\textsuperscript{304} The former compound has also been isolated from *V. mediensis* Oliver\textsuperscript{305} and *V. thyrsiflora* \textsuperscript{306}.

From the leaves and stem of *V. rehmannii* Gürke. and *V. seretii* De Wild., agnuside and ecdysterone have been isolated.\textsuperscript{307} The isolation of agnuside and aucubin from the leaves and stem of *V. pseudonequndo* (Hausskn.) Hand.-Mazz. has been reported.\textsuperscript{307} Ecdysones could not be detected.\textsuperscript{307} Isolation of \( \alpha \)-octacosanol, stigmasterol, \( \beta \)-sitosterol, ursolic acid and its acetate has been reported from *V. pubescens* Heyne.\textsuperscript{308}

**VITEX NEGUNDO LINN.**

*Vitex negundo* Linn. is an aromatic shrub and often occurs gregariously along the banks of rivers, in moist situations, open waste lands and near the deciduous forests. Almost all parts of the plant are used in Indian medicine. A decoction of the leaves was found to prevent development of swellings of joints in experimental arthritis in adult albino rats caused by formaldehyde injection.\textsuperscript{309} The leaves possess discutient properties and are reported to be applied to rheumatic swellings of joints and in sprains.\textsuperscript{269} An extract of the leaves showed anticancer activity against *Ehrlich ascites* tumour cells.\textsuperscript{269} The roots are reported to possess tonic, febrifugal, expectorant and diuretic properties and are used in dyspepsia, rheumatism
and also for boils. The powdered root is prescribed as an anthelmintic and as a demulcent in dysentery. It is also given for piles. The leaves, stem bark and roots of *Vitex negundo* have been studied. There are only a few reports regarding the chemical investigation of the seeds. The flowers have not been investigated.

The leaves of *V. negundo* have been reported to contain iridoid glycosides; agnuside, aucubin, 2',-p-hydroxybenzoyl-

![Chemical structure](image)

(45) \( R = \) ![Chemical structure](image), \( R^1 = H \)

(46) \( R^1 = \) ![Chemical structure](image), \( R = H \)

mussaenosidic acid (45), and 6'-p-hydroxybenzoymussaenosidic
acid (46), nishindaside (47), and negundoside (48); and flavonoids: artemetin, 3,5-dihydroxy-6,7,3',4'-tetra-
methoxyflavone, casticin, luteolin-7-glucoside.

The isolation of 4,4'-dimethoxy-trans-stilbene and five flavonoids, 5,6,7,8,3',4',5'-heptamethoxyflavone, 5-hydroxy-6,7,8,3',4'-pentamethoxyflavone, gardenin A (5-hydroxy-6,7,3',4',
5'-hexamethoxyflavone), gardenin B (5-hydroxy-6,7,8,4'-tetramethoxyflavone), corymbosin (5-hydroxy-7,3',4',5'-tetramethoxy-
flavone) from the leaves and twigs has been reported. Besides this gluco-nonitol, p-hydroxybenzoic acid, 5-hydroxy-
isophthalic acid, 3,4-dihydroxybenzoic acid, hentriacon-
tane, 3'-sitosterol, an alkaloid nishindine having a quinoline structure have been isolated from the leaves. The essential oil obtained from the leaves was found to contain α-pinene, p-cymene, 1,8-cineol, bornyl acetate, salinine,
α-phellandrene, β-elemene, β-caryophyllene, caryophyllene oxide, camphene and citral. The decoction of leaves has shown antiarthritic activity against formaldehyde-induced rat paw.
oedema model. Flavonoid glucosides; 6-C-glucosyl-5-O-\( \alpha \)-rhamnopyranosyltrimethoxywogonin (49), acerosin-5-O-glucosyl-

\[
\text{HO} \quad \text{CH}_20A \quad \text{HO} \quad \text{OH} \\
\text{OCH}_3 \quad \text{OCH}_3 \quad \text{OCH}_3 \\
\text{HO} \quad \text{HO} \quad \text{OH} \\
\text{CH}_3 \quad \text{CH}_3 \quad \text{OH} \\
\text{H} 
\]

(49)

sidemonoacetate (50), 3,6,7,3',4'-pentamethoxyflavone-5-O-glucopyranosyl-rhamnoside (51), Vitexin caffeate (52), 4'-O-methylmyricetin-3-O-[4''-O-\( \beta \)-D-galactosyl]-\( \beta \)-D-galacto-

\[
\text{HO} \quad \text{OCH}_3 \\
\text{CH}_30Ac \quad \text{HO} \\
\text{HO} \quad \text{HO} \\
\text{OH} \quad \text{CH}_3 \\
\text{H}_3C0 
\]

(50)

pyranoside (53), leucoanthocyanidins; (54) and (55) have been isolated from stem bark. The isolation of \( \beta \)-sitosterol, vanillic acid, \( \beta \)-hydroxybenzoic acid,
ferulic acid\(^{326}\) and syringic acid\(^{326}\) has also been reported.

The isolation of furanoeremophilane (56)\(^ {327}\), acetyl-

The isolation of furanoeremophilane (56)\(^ {327}\), acetyl-

oleanolic acid,\(^{327}\) n-hentriacontane,\(^ {328}\) a mixture of \(\beta\)-sitosterol
and stigmasterol\textsuperscript{327,328} has also been reported from the roots.

The fatty acid composition of the seed oil has been studied.\textsuperscript{329,330} The seeds have been found to contain a mixture of n-tritriacontane, n-hentriacontane, n-pentatriacontane, n-nonacosane, \(\beta\)-sitosterol, \(\rho\)-hydroxybenzoic acid and 5-hydroxy-isophthalic acid.\textsuperscript{331} 5,7,3'-Trihydroxy-6,8,4'-trimethoxyflavone isolated from seeds has shown estrogenic properties in mice.\textsuperscript{332}

1.2.2 VANDA SPECIES

A polymorphic genus of beautiful, epiphytic orchids distributed from India and China to Australia, belongs to family Orchidaceae. About 12 species are recorded from India and several exotics are planted in gardens.\textsuperscript{333} There are only a few reports on the chemical constituents of \textit{V. roxburghii}, \textit{V. hindsii}, \textit{V. halvola}, \textit{V. luzonica}, \textit{V. parishii} and \textit{V. christata}.

\textit{V. roxburghii} R. Br. (syn. \textit{V. tessellata} Lodd. ex Loud.) is an epiphytic orchid, 30 to 60 cm high, found from Uttar Pradesh to West Bengal extending southwards to Kerala.\textsuperscript{333} The plant is used in indigenous system of medicine for its beneficial action in piles, rheumatism, sciatica and various other inflammatory and nervous disorders.\textsuperscript{334,335} Preliminary studies have revealed the presence of a non-toxic glycoside (which stimulates all organs), tannins, resin, saponin, long chain fatty components, \(\beta\)-sitosteryl and \(\gamma\)-sitosterol.\textsuperscript{336,337} Prasad \textit{et al}.\textsuperscript{338} observed that total steroidal fraction obtained from \textit{V. roxburghii} possessed significant antiinflammatory activity against acute inflammation induced by carrageenan, serotonin and formaldehyde. This fraction
on chromatographic resolution yielded heptacosane, octacosanol and stigmasterol. The aliphatic alkane and alcohol fractions were found to be active against both acute (carrageenan and formaldehyde-induced oedemas) and subacute (croton oil granuloma pouch and cotton pellet granuloma techniques) inflammations at a dose of 10mg/100g, i.p. The results compared favourably with those obtained with betamethasone (50 mg/100 g, i.p.) though the effective dose of latter was much lower.

Laburnine acetate (57) has been isolated from V. hindsii

\[
\begin{align*}
\text{(57)} & \quad R = \text{CH}_2\text{OAc} \\
\text{(58)} & \quad R = \text{CH}_2\text{OH}
\end{align*}
\]

\[
\text{[Chemical Structure Image]}
\]

\[
\text{(59)}
\]

Lindl. and V. helvolae Bl. and V. christata whereas
laburnine (58) has been obtained from *V. helvola*. An extract of *V. luzonica* Loher contained either laburnine or its enantiomer.\(^{340}\). Two glycosides tris[4-(β-D-glucopyranosyloxy)benzyl]citrate namely parishin (59) and 4-(β-D-glucopyranosyloxy)benzyl alcohol have been isolated from *V. parishii* Rchb.f.\(^{342}\) The later compound may, however, be an artefact of parishin.

1.2.3 **ACAMPE SPECIES**

This is a very small genus of epiphytic orchids (family Orchidaceae) usually with very long and stout stem. There are about a dozen species, mostly found in India, Malaya, China and Africa.\(^{343}\) *A. papillosa* Lindl. (syn. Saccolabium papillosum Lindl.) called 'Rasna' is found in Bengal and the lower Himalayan mountains. Roots of the plant are bitter-tonic and used in rheumatism.\(^{344}\) No chemical or biological work has been done on *Acampe* species.

1.3 **RESEARCH ENVISAGED**

The survey of the work done on *Vitex negundo* reveals that the flowers have not been investigated at all and there exists a few reports on the seeds though the roots, stem and leaves have been thoroughly studied. Only a very preliminary chemical study has been done on *Vanda roxburghii* whereas absolutely no work has been reported on *Acampe papillosa*. It was considered worthwhile to carry out the detailed systematic investigation of the seeds and flowers of *V. negundo*, roots of *V. roxburghii* and *A. papillosa* for the isolation of bioactive
constituents and explore their potential as effective anti-inflammatory agents. The work of systematic investigation on the seeds and flowers of *V. nequndo*, roots of *V. roxburghii* and *A. papillosa* has been undertaken at Panjab University, Department of Pharmaceutical Sciences, since late 1985.

The present thesis embodies the work done on the seeds and flowers of *V. nequndo*, roots of *V. roxburghii* and *A. papillosa*. 