INTRODUCTION
Health is man's most precious possession. One of the earliest concern of mankind was a desire for protection against disease and suffering. Since early man had no apparent explanation for many of the diseases which afflicted him and for some of the calamities which befell, he attributed them to spirits of various kinds. To ward off these spirits divine intervention was sought. In those days medicine was intermingled with religion, superstition, magic, witchcraft and the medicine men were often witch doctors and priest physicians (1). In this phase religion dominated the practice of medicine. During the course of cultural evolution, mankind began to appreciate the curative power of natural products and separation of medicine from religion took place gradually (1). The belief that nature alone could provide the means to eradicate diseases and suffering began to take ground leading to the search for remedies in nature. Since plants, animals and minerals were easily available in the surroundings they were the first to be explored as possible remedies. This interaction seems to be the important basis for the evolvement of different types of traditional systems of medicine. Majority of the traditional systems even today depend on natural drugs especially those of plant origins (2). Well documented evidences are available (3) to show that use of plants for therapeutic purpose was common even at the earliest part of recorded history. Almost all well known early civilization had evolved well developed medical system. Ancient Egyptians, Assyrians, Chinese, Red Indian cultures of central and South America like Mayans, Inca, Aztec, Transcans and Zapotees all had well developed natural product based medical systems (1,4).

Egyptian medicine dates back to 3000 B.C. Since they were among the first few civilization to use hieroglyphic writings: extensive information is available on their medical system. One of the best known work Eber Papyrus (1500 BC) records some 800 prescriptions based on 700 drugs (4,5).

Chinese medicine is also believed to be equally old. The Pen Tsao, a well known compilation of medicinal plants is believed to be written around 2,700 B.C. (4).

Greek medicine was fairly well developed and was greatly influenced by Egyptians. The Greeks were the first to adopt scientific methods to therapeutic practice. Hippocrates (460-370 B.C.) considered as one of the greatest physician of that period, was a Greek. He advocated the usage of simple remedies after careful observation of the cause of the diseases (4,6).

After the decline of Greek civilization the centre of civilization shifted to Rome. Roman medicine was almost a continuation of Greek medicine. Romans gave importance to promotion of public health. Celsus (25BC-50AD) and Galen (131-200 AD) were considered among the greatest medical men of this period. Galen, who propounded polypharmaceutical approach to therapeutics, had written about 500 treatises on medical subjects. His
teaching were followed without questioning for the next few centuries till the period of renaissance (16th century AD) (4).

During the mediaeval period the progress in the field of medicine was limited in Europe. However, during this period phenomenal growth was seen in Arabic medicine. Arabs integrated Greko-Roman knowledge into their medical system. This Greko-Roman system came to India along with Muslim invaders and later came to be known as Unani system of medicine (4).

Ayurveda, literally means science of life, and Siddha are our country's indigenous systems of medicines (7) (8). Ayurveda is practiced throughout the country but the Siddha system of medicine is confined mainly to Tamilnadu. Ayurveda is considered among the oldest and well developed traditional systems of medicine. Citation about medicinal plants are available in Rig Veda, which is considered to be compiled before 4000 BC (8). Reference to medicinal plants are available in other Vedas also i.e. Yajur veda, Sama veda and Atharva veda. Ayurveda, according to many scholars developed from the medical knowledge contained in Atharva veda and is often considered to be an Upaveda of it. It has an elaborate conceptual base to explain the basis of aetiology of disease and method of their treatment. Besides treating diseases, it advocates an holistic approach towards maintenance of positive health through physical, mental, social, moral and spiritual welfare (7,8). The system extensively deals with the knowledge of life, indicating measures for disease-free living for full span of life (7).

Charaka Samhita and Sushruta Samhitas are the two most important ancient classics of Ayurveda. These books are considered to have been written between 1000 to 500 BC and redacted thereafter by many subsequent scholars of Ayurveda (7). The period between 8th century BC and 6th AD is considered to be the golden period of Ayurveda (7). Many Ayurvedic classics were written during this period. Bhela Samhita, Kashyapa Samhita and Harita Samhita are the other well known classic written during this period Astanga hridaya and Astanga Sangraha are two well known classic compiled by Vagbhata. These classic give conceptual description about the fundamental principles governing drug composition and action (8).

The ancient universities, Takshashila and Nalanda, which were well known throughout the world at that time taught Ayurveda as one of the main subjects. The great physician Jiwaka was a product of Takshashila university. Students from different parts of the world came to these universities to learn Ayurveda (7). Advent of Buddhism (4th BC) had considerable influence on the mode of Ayurvedic practice. In consonance with the principle of non-violence propounded by Buddhism practice of surgery, which was quite advanced for that time, was restricted. As a consequence of this, other disciplines of Ayurveda received increased importance to compensate for the loss of knowledge of surgery. It is during this phase that the discipline of Rasashastra came into prominence. It mainly deals with usage of minerals
and metals for the preparation of medicines. The practice of Ayurveda declined after 15th century due to many social, political and historical reasons and thereafter no significant progress was made. Unfortunately some of the authentic literature on Ayurveda were destroyed during the following period. However, Ayurveda is still widely practiced in India. According to one estimate 75% of the population in our country mainly consult traditional physicians of whom Ayurvedic practitioner form the major part (9,10).

RESEARCH ON MEDICINAL PLANTS IN INDIA

Scientific investigations on medicinal plants in India began with the advent of Europeans in early 1800(11). Many books were written on medicinal plants and materia medica (12-14). The Govt. appointed a central committee to evaluate the clinical efficacy of many indigenous drugs. This central committee appointed several regional committees to help in its task (15). Many medicinal plants were evaluated during this period.

Col. R.N.Chopra, through his pioneering monumental work on medicinal plants laid firm foundation for undertaking scientific investigations on medicinal plants(16). However, the real spurt to medicinal plants research came from the report on the clinical efficacy of *Rauwolfia serpentina* in hypertension (17) and isolation of reserpine and related alkaloids (18). Research studies were initiated at various centres throughout the country. Since all these were independent efforts without any co-ordination they did not add significantly to the progress of therapeutic application of medicinal plants (16). To rectify this state of affairs, Indian Council of Medical Research (ICMR), New Delhi formulated an integrated, multidisciplinary scheme named Composite Drug Research Scheme (CDRS) to carry out coordinated research on medicinal plants in 1960. This scheme was transferred to Central Council for Research in Indian Medicine and Homoeopathy (CCRIMH), New Delhi in 1970, which was newly created at that time to initiate, aid develop and co-ordinates scientific research on different disciplines of traditional systems of medicine. At about the same period research studies were initiated at National Laboratories under Council for Scientific and Industrial Research (CSIR). Mainly at Central Drug Research Institute (CDRI), Lucknow (19) and Regional Research Laboratory, Jammu (20). Extracts of more than 3,000 plants have been screened for different biological activities at CDRI till the last report (21-33). Results of studies on medicinal plants have been reported by number of other centres also. These include departments attached to different universities and teaching Institutes and some private organisations (34,35,36,37,)

Though phenomenal successes has been achieved in controlling number of dreaded diseases, especially infectious diseases like tuberculosis, malaria etc. through the use of synthetic chemicals complete remedy or curative therapy is not available for a number of so-called refractory diseases like rheumatoid arthritis, asthma, cancer, hepatitis, AIDS, etc. Use of synthetic compounds is attendant with the risk of drug induced disturbances and side effects.
It is commonly believed, though scientific evaluation is lacking, that usage of natural products is free from such risks. Medicinal plants form a vast reservoir of source material to search for remedies for the above diseases. Research on medicinal plant may reveal a novel chemical configuration possessing remarkable therapeutic utility which could be used as a basic structure to improve on through chemical manipulation (38). It is also possible that a novel biological activity may be found in a known phytochemical moiety. This is exemplified by the report on forskolin, a labdane diterpenoid, isolated from Coleus forskohlii (39), which is reported to possess a unique ability to activate adenylate cyclase in the absence of a functional guanine nucleotide regulatory protein (40).

More than 2,00,000 species of flowering plants are estimated to exist on the earth (3). Only a small percentage of these have been examined chemically and much less for biological activity. If immediate efforts are not made to study their chemical composition and define biological activity profile, some of them may be lost for ever. This is especially true with regards to developing countries where majority of these plants are found. This is mainly due to increased pressure on land due to ever increasing population leading to destruction of plant habitat. If concerted efforts are made in this regard it would provide scientific data to the concerned authorities to decide on the priority for the conservation of gene pools of important plants (41).

In majority of the developing countries, Traditional systems of medicine, which mainly depend on drugs of natural origin, especially medicinal plants, cater to the primary health care needs of the major portion of the populace. According to one estimate 80% of the world population is dependent on traditional system of medicine for health care (42). In our country 75% of the population is reported to mainly consult traditional physicians (10). Even in developed countries plant extracts or active principles obtained from medicinal plants are used in significant quantities (43). Besides this, large quantities of medicinal plants are used to prepare herbal tea (43). Recognising the important role of traditional systems of medicine in primary health care, World Health Organisation (WHO) in 30th world Health Assembly (WHA-30-49-1977) (44) adopted a resolution urging interested member countries to give due importance to the traditional systems of medicine of the respective countries in providing primary health care to their people. WHO has established several collaborating centres in different parts of the world to co-ordinate research studies on medicinal plants and traditional systems of medicine (45).

In the light of the reasons presented above, it can be stated that continued research on medicinal plants is vital for the development of new remedies for treating diseases for which no satisfactory therapy is available at present.
Current status and future outlook:

It is paradoxical that inspite of tremendous amount of efforts made in the field of medicinal plant research the success achieved in finding new remedies is disappointing. Only few plant based drugs have been introduced into therapeutics after the introduction of reserpine (9). However in the view of some investigators (46), the most productive phase of medicinal plant research may lie in the coming years. Especially, if we take into consideration the remarkable progress made in instrumental technology in phytochemical, cell and tissue culture research. In addition enormous data base has been compiled on the biological activity profile and chemical composition of number of medicinal plants. This would be of great help in planning future research studies.

Inflammatory disorders:

Rheumatic diseases are a group of inflammatory disorders that cause tremendous amount of human morbidity and mortality. Rheumatoid arthritis (RA) the prototype disease of this group, is prevalent throughout the world and is reported to afflict all races. It has a global prevalence rate of more than 1% (47). Due to its chronic and crippling nature, widespread prevalence and progressive nature it has great socio economic importance. Because of these reasons it is considered among the most important diseases afflicting mankind. Among the presently available drugs non-steroidal anti-inflammatory drugs offer only significant symptomatic relief but they donot arrest or modify the course of the disease. Steroids, though can afford significant relief, can not be used for longer duration due to manifestation of serious untoward effects(48). Gold salts, anti- malarial drugs, penicillamine and immunomodulating drugs though can check, to some extent, demineralisation and degenerative changes in the bone and cartilage are slow in onset and their continued use leads to manifestation of serious side effects. Hence, efforts are on in many laboratories through out the world to obtain disease modifying or remission inducing drugs which would be capable of arresting the degenerative changes observed in RA.

Gujral and co-workers (44,50) were the first to undertake a systematic investigation on the medicinal plants for anti-inflammatory activity. Subsequently, scientific investigators from different laboratories have undertaken evaluation of number of medicinal plants for anti-inflammatory and anti-arthritic activity (51). Out of the nearly 3,000 plants screened for different biological activity at CDRI, Lucknow, 40 have been reported to possess definite anti-inflammatory activity (52). At RRL, Jammu extracts of 343 plants have been screened for anti-inflammatory activity and some of them have been shown to possess anti-inflammatory activity. Many reviews have been written about medicinal plants possessing anti-inflammatory activity (51, 53, 54, 55, 56, 57). In spite of making such efforts to identify potential anti-inflammatory agents from plants the results have not been promising (55). Screening of test drugs for anti-inflammatory activity is a complex problem. So far, it has not been possible
to identify a structural configuration to which anti-inflammatory activity could be attributed. This is exemplified by the fact that anti-inflammatory activity has been reported from a broad spectrum of phytochemical classes like alkaloids, flavonoids, glycosides, sterols, triterpenes, xanthones, lactones, saponins, essential oils and even in some unidentified crystalline compounds.

The available experimental models of inflammation are largely empirical and generally measure only a gross and isolated aspects of a very complex and dynamic phenomenon. There is much more scope for refinement of the existing models and to evolve new methods which may simulate the human disease to a greater extent than the models available at present. Some reviewers (55) advocate intensive studies involving phytochemical, pharmacological, toxicological and chemical evaluation, on selected medicinal plants, with a view that they may be more rewarding than large scale screening.

Number of medicinal plants have been advocated in Ayurveda for the treatment of rheumatic disorders (58, 59). Vitex species, especially *Vitex negundo* Linn is one such plant. Number of investigations have reported anti-inflammatory activity with different parts of the plant (53, 60, 61, 62). However, no detailed investigation has been attempted so far, especially to elucidate the probable mechanism of anti-inflammatory effect produced by the plant. *V. altissima* is a plant related to *V. negundo* no attempts have been made to either evaluate it for anti-inflammatory activity or to define its pharmacological activity profile. The present study is an attempt to elucidate the mechanism of anti-inflammatory activity of *V. negundo* leaf and to screen *V. altissima* leaf for anti-inflammatory effect, if the anti-inflammatory activity is present then to elucidate the mechanism of action.

**VITEX LINN.**

A genus of trees or shrubs, widely distributed in the tropics and warm temperate regions of both the hemispheres. About 14 species are found in India. Several species, including a few chiefly occurring in parts of the Deccan Peninsula and North-East India, yield timbers of some commercial importance. Young shoots hairy or tomentose, leaves opposite, digitately 3-5 foliolate (some times simple as in *V. trifolia*). Flowers in sessile or pedunculate cymes forming large or small terminal and axillary or wholly axillary panicles or corymb; bracts small, longer or shorter than the calyx. Calyx campanulate, truncate or shortly 5-(rarely)-3) toothed. Corolla small, 2-lipped; tube short; limb 5-lobed, the middle lobe of the lower lip much the largest. Stamens 4, didynamous, usually exserted; anther-cells at first parallel and pendulous, afterwards divaricate, often twisting so that the lower ends are erect. Ovary 2-4 celled; ovules 4; style filiform; stigma shortly 2-fid. Fruit a globose or ovoid drupe, invested at the base by the somewhat enlarged calyx; endocarp bony, normally 4-celled and 4-seeded, but some of the cells often suppressed. Seeds obovate or oblong; albumen 0. Species 120- Tropical and temperate regions (63).
(A) Inflorescence usually a terminal thyrsus:

1) Leaflets 3 or 5, Lanceolate, entire, toothed or pinnatifid *Vitex negundo*

2) Leaves some simple some trifoliolate; leaflets elliptic or oblong - obovate, usually obtuse, the terminal leaflet sessile (rarely very shortly petioluate) aim *Vitex trifolia*.

3) Leaves long-petiolate, digitately 5-rarely 7-foliolate; leaflets slightly tomentose above and green below canescent, lanceolate-acuminate, attenuate at the base as in *Vitex agnus castus*.

4) Leaflets usually 3, the lateral sessile or nearly so, elliptic 10-20cm. long. eg. *Vitex pubescens*.

(B) Inflorescence always axillary:

1) Leaves 3, or 5-foliolate; leaflets lanceolate, almost coriaceous, only midrib hairy on underside *V. leucoxylon*

2) Leaflets 3, membranous, lanceolate. *Vitex peduncularis*

3) Leaves almost glabrous; leaflets 5. *Vitex glabrata*

The bark is antisyphilitic. The fruits are given for stomachache and colic, for headache, catarrh and watery eyes.

A number of species are used in medicine. The following species are used in the south of Europe and the levant *Vitex Agnus-castus* Linn; in China and the Philippine Islands.

*Vitex negundo* Linn; *Vitex trifolia* Linn; in Assam Annam.

*Vitex Trifolia* Linn-in the Gold Coast and Nigeria.

NIRGUNDI

**Botanical Identity**

*Vitex negundo* Linn. (Syn. *Vitex bicolor* willd). Fig. 1 a,b

<table>
<thead>
<tr>
<th>Family</th>
<th>Verbenaceae.</th>
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<tr>
<td>Taxonomic position</td>
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<tr>
<td>Division</td>
<td>Spermatophyta.</td>
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Fig. 1 a) *Vitex negundo* Linn. profile of Leaves. b) *Vitex negundo* Linn. tree
Sub-division : Angiospermae
Class : Dicotyledone
Sub class : Gamopetala
Group : Bicarpellata
Order : Lamiales
Family : Verbenaceae
Genus : Vitex
Species : Vitex negundo. Linn
Synonym : (Syn. Vitex bicolor wild)
Sanskrit Synonyms : (64,65)

Nirgundi, Sinduvarah, Svetapushpah, Sindukah, Nilapuspa, Indranika, Indrasuras, Shveta-suras, Vriksha.

Regional names (Vernacular names) :

Hindi : Nisunda, Nishinda, Nirgunda, Shiwari, Shambalu, Sandbhalu, Mewari, Shiwali
Gujarati : Nirgari, Nagoda.
Bengali : Nisinda, Samalu, Nirgundi.
Bombay : Nirgundi, Katri, Lingur, Nargunda, Nishinda.
Kannada : Lakki-gida, Lakki, Lakkle.
Kol : Ehuri, Sindworo, Hobaro.
Malayalam : Nocci, Karunocci, Vennocci.
Marathi : Nirgundo, Nirgur, Nirguda, Marwan, Mawa, Marwana.
Oriya : Beyguna, Beguniya.
Punjabi : Moraun.
Santal : Sinduari.
Tamil : Nocci, Karunocci, Menocci.
Telugu : Tella-vavili, Vavili, Veyali, Vavali-padu.
Arabic : Aslag, Zukham, Sate-asabea.
Burmese : Kiyow-bhan-bin, Kiyuban-bin.
Persian : Sisban, Banj-angasht.
Sinhalese : Nikka, Sudu-nikka.
Parts used : Root and Leaves

Properties and uses :

Nirgundi is used in the indigenous system of medicine since a long time. The drug has been described in Ayurvedic texts as astringent, acrid, bitter, hot and is useful in curing colic, oedema, dyspepsia, cough, asthma and eye diseases. It helps in reducing the splenic enlargement, rheumatoid arthritis, flatulence, sciatica and disease due to the morbidity of Vata.
and Kapha. The leaf has been regarded as tonic, astringent, vermifuge, carminative, stomachic, anthelmintic and expectorant (65).

**Botanical description :** (64)

*Vitex negundo* is a small tree or a large shrub with irregular trunk, stem and branches covered with thin grey bark, the branches quadrangular and finely hoary downy.

**Leaves :** Petiolate, shorter opposite, ex-stipulate, digitately three to five foliate.

**Leaflets :** Shortly petiolulate, narrow lanceolate acute or acuminate, base acute, entire or rarely crenate, glabrous above and pale whitish green and covered with a fine white tomentum beneath.

**Inflorescence :** Erect terminal, compound pyramidal panicle.

**Flowers :** Bracteate, bracts 1.4 to 2.5 mm. long, lanceolate and caudicous, bisexual, zygomorphic, bluish purple.

**Calyx :** Small dark purple or violet to whitish or grey, 2 to 3 mm. long, gamosepalous, campanulate, shortly five lobed.

**Corolla :** Small, 8mm. to 1cm. long gamopetalous, bluish-purple irregular two lipped tomentose outside, hairy inside at the insertion of the stamens, upper lip about 2mm. long divided into the base into two obtuse lobes, lower lips large 4 to 5 mm. long with the two lateral lobes, short, oblong and obtuse and the middle lobe large.

**Stamens :** Four, didynamous epipetalous, usually exserted filaments hairy at the base, anther cells at first parallel and pendulous, later divaricate.

**Pistil :** Bicarpellary, syncarpous. Ovary superior, globular or oval, 2.4 celled ovules on axile placenta. Style filiform 7 to 9 mm. long ending in a bifid or forked stigma.

**Fruit :** A globose, ovoid or obovoid, four chambered, four seeded drupe. Black when ripe supported by enlarged calyx. Seeds non-endospermic, oblong or obovate with the thick testa.

**Distribution :** Found throughout India, fairly common in waste lands, on road side, on the banks of streams or in moist places near deciduous forests.

**Cultivation :** It is often cultivated in garden as a hedge plant.
Macroscopical Structure :

The leaves are tri-to pentafoliate. The two lateral leaflets are lanceolate, acute, entire or rarely crenate, sub-glabrous above and tomentose beneath with unisporate reticulate venation and leathery texture.

Microscopical Structure : The petiole shows single layered epidermis covered externally with large number of hairs. Below the epidermis is a zone of collenchyma, which is well developed in the basal region and gradually becomes less in the middle and apical region and is followed by 6-8 layers of parenchyma. The pericyclic fibres are absent in the basal region, but they develop more as discontinuous band, capping the phloem of the dorsal side vascular bundle. The stele is represented by a well developed horse-shoe shaped vascular bundle on dorsal side and 3-4 small vascular bundles on the ventral side with few phloem fibers and very poorly developed xylem. In addition to these, 2-3 vascular bundles are seen opposite to the arms of large vascular bundle of dorsal side having normal arrangement of xylem and phloem.

Petiolule is circular or elliptical on outline with a ventral depression and two small bulging arms. It has almost a similar structure to petiole excepting that it has lesser number of hairs surrounding the epidermis and has a group of fibers at the opening between the arms of horse-shoe shape. Stele below the collenchyma on the ventral side.

Midrib is concavo-convex in outline. The epidermis on both the side is followed by 3-6 layers of collenchyma on the dorsal side and 8-10 layers on the ventral side. The stelar structure of midrib similar to the base of petiolule excepting that there are no additional bundle opposite to the arms of the dorsal side.

Lamina of the leaflets show a single layered hypodermis below the upper epidermis, which is followed by 4-6 cells deep palisade interrupted by transcurrent veins. The single layered hypodermis is also interrupted at places by palisade which occupies whole mesophyll.

The quantitative values of the leaflets are vein-islet number 23.99 and vein termination no 6.26.

Uses : Leaves are supposed to be very efficacious in dispelling inflammatory swellings of the joint from acute rheumatism and of the testes from suppressed gonorrhoeal epididymitis and orchitis. Fresh leaves are placed in an earthen pot, heated over fire and applied to the afflicted part as hot as can be tolerated without pain. Some times bruised leaves are applied as poultice to the affected part. Dried leaves are smoked to obtain relief from catarrh and headache. Leaf juice is used to remove foetid discharge and worms from ulcers. An oil prepared with the juice is applied to sinuses and serofulous sores. A compound oil prepared using leaf juice
of V. negundo and eleven other substances in different proportion is reported to act as a specific remedy for syphilis and other venereal diseases (66). A leaf decoction with long pepper is administered in catarrhal fever with heaviness of head and dulness of hearing (66). Leaves are administered with garlic rice and gul as a remedy for rheumatism. In konkan region leaf juice with Eclipta alba and Ocimum sanctum is extracted and bruised Ajwan seeds are steeped in it and administered to rheumatic patients. Tincture of root bark in 1 to 2 dr doses is recommended for irritable bladder and in rheumatism. Root powder is used in piles and as a demulcent in dysentery. Root is also used in dyspepsia, colic, rheumatism, worms, boils and leprosy. Flower are used as remedy in diarrhoea, cholera, fever and diseases of the liver. Powder of flowers with stalk are used to control bleeding in the stomach and bowel. Steam bath with the vapours prepared from this plant is used for treating febrile, catarrhal states and rheumatic affections. (66). An ointment prepared from leaf juice is used as a hair tonic. It is also reported to possess tranquilising effect. (63). The leaves are also reported to possess insecticidal properties and are placed over stored grains to prevent insect infestation.

In China and Malaysia the fruits are used in the treatment of headache, catarrh and watery eyes (65).

In Srilanka, the leaves, bark and roots are used for toothache, rheumatism, eye disease besides it is also used as a tonic, carminative and vermifuge (65).

The sap collected from the cut end of the extremities is used as an expectorant by mundas of Chota Nagpur area. They warm the sap and mix with clarified butter in which powdered garlic bulbs has been fried and is given to the patient to drink (65).

The bruised roots, bark, leaves are applied to the wounds. Fresh leaf juice is poured in to the nostril in stupor and coma and is also given internally (65).

Similar treatment is also given in tarantula bite.

Chemistry:

Number of investigations have been reported on the chemical composition of the plant. Freshly collected leaves yield a pale greenish yellow oil (0.04-0.07%) on steam distillation. The main constituents of the oil are aldehydes, ketones, phenolic derivatives and cineol. (67). The leaves also contain two alkaloids-nishindine (C_{15}H_{21}O_{1}N; m.p. 226°C) and hydrocotylene (C_{22}H_{33}O_{8}N) (63) (68,69), glucononitol (C_{9}H_{20}O_{9}m.p. 196-198°C), p-hydroxybenzoic acid, 5-hydroxyisophthalic acid (70), 3,6-dihydroxybenzoic acid, an amorphous glucoside. (C_{20}H_{26}O_{11}m.p. 93-95°C) (71), 5-hydroxy, 3,6,7,34-pentamethoxy flavone. (C_{20}H_{20}O_{8}m.p.-163) (72), Vitamin C and Carotene (73).
Isolation of 4'-4'-dimethoxy-trans stilbene and flavonoids from leaves and twigs has been reported by Banerji and coworkers (74). Iridoid glycosides 2'-P-and 6-P-hydroxybenzyl mussaenosidic acid have been isolated from ethanol extract of the leaf (75,76).

From the bark B-sitosterol, vanillin, P-aminobenzoic acid, lukoiln have been reported by Rao and coworkers (77,78). Two new leucoanthocyanidines have been isolated from stem bark by Subramaniam and Misra (79). The structure of which have been established as methyl ethers of leuco delphinidin and leucocyanidin-7-O-rhamnoglucoside through spectral data and degradation studies isolation of a new flavone glycoside from bark has also been reported (80). TLC studies carried out on the bark by Nayar and Co-workers have revealed the presence of five alkaloids, one glycoside and three terpenoid principle. (81). Root is reported to contain n-hentriacontane, B-sitosterol and stigmasterol (82).

Seed oil is reported to contain n-triacontane, n-hentriacontane, n-pentatriacontane, n-nonaacosane, B-sitosterol, P-aminobenzoic acid and 5-oxyisopthalic acid (83,84). An unsaponifiable matter obtained from the seed oil has been reported to contain a diterpene 5-B-hydro 8,11,13-abietaetrien-6-a-ol(1), a triterpene lanostan 8, 25-dies-3-B-ol and a flavonoid artemetin (2) (85,77).

Presence of Furanocremophilane (86), - flavanoners (87) and flavonoids (88) has also been reported.

**Pharmacology**

Ethanol extract of the seeds has been reported to have shown encouraging results on copper induced ovulation in rabbits. At an oral dose of 200mgkg⁻¹ for two days, the extract produced inhibition of ovulation in 60% of the animals (89). Significant anti-inflammatory effect has been reported in leaf(61,90,91), root (62) seed extracts (92) and in a diterpene (5-B-hydro,8,11,13- abietaetrien-6-a-01(1) and flavonoid, artemetin (85) obtained from the seed oil. The extracts of the leaves have been reported to possess antibacterial activity against Micrococcus pyogenes var aureus and Escherichia coli (93). Anti-tumour activity has been reported in the leaf extracts against Ehrlich ascites tumour cells (94). clinical trial of a powder from the rhizome of Alectra parasitica which grows on the root of V.negundo was found to be effective in the treatment of leprosy with no toxic effect (95).

Joshi and Nagar (96) have shown antibacterial effect in the saline extracts of the leaves. Analgesic activity has been reported by Shrivastava & Sisodia (97). According to Ravishankar and coworkers (61) Chloroform toluene (TLE) extracts of leaves possess central analgesic activity while TLE,CHE, petroleum ether (PE) and n-butanol(BE), extracts inhibited acetic acid induced writhing in mice. PE & BE were found to afford protection to mice against electroconvulsion. Significant anti-inflammatory activity was observed in all the above mentioned
extracts and cold aqueous infusion of the leaf against carrageenin induced hind paw edema in rats. The same authors, in another study (62) have reported presence of significant anti-tremor effect against oxotremorine induced tremor in mice in n-butanol (BE) and petroleum ether (PE) extracts of root powder. PE also protected mice against pentylenetetrazol induced convulsions. Chloroform (CHE) extract produced significant anti-inflammatory activity. Analgesic activity was found to be present in BE, CAI and ethanol (ETE) extracts.

Diuretic activity has also been reported (98). Preparation of Nirgundi are reported to be efficacious in the treatment of sciatica (99,100) and rheumatism (101). Anti-microbial activity has been reported in the essential oil obtained from the plant (102). Oestrogenic and pregnancy interceptory effects in mice have been reported with flavonoids isolated from the seeds (103). The flavonoids were found to produce anti-fertility effect in dogs also (104). According to a recent publications the plant was found to possess antifilarial effect against Setaria cervi (105).

**VITEX ALTISSIMA**

**Botanical origin:**

*Vitex altissima* Linn.

**Family** : Verbenaceae.

**Taxonomic position** :

- **Division** : Spermatophyta
- **Sub-division** : Angiospermae
- **Class** : Dicotyledone
- **Sub-class** : Gamopetalae
- **Group** : Bicarpellatae
- **Order** : Lamiales
- **Family** : Verbenaceae
- **Genus** : Vitex
- **Species** : *Vitex altissima* Linn. Fig. 2 a,b

**Regional names:**

- **Marathi** : Balage, banalgay
- **Telugu** : Nemiliadogu
- **Tamil** : Maila, mayilai
- **Kannada** : Myrole, bulgi,balgay
- **Malayalam** : Mayila
- **Assam** : Ahoi, ashoi, jhana
- **Cachar** : Selong-phang
Fig. 2 a) *Vitex altissima* Linn. leaves b) *Vitex altissima* Linn. tree
Botanical description:

A moderate to large sized tree, sometimes with dense crown, fairly straight and cylindrical bole and somewhat drooping branches. Mainly found in Assam, Meghalaya and the Deccan Peninsula. Bark grey, scaly, fibrous; leaves-3-rarely 5-foliolate; leaflets sessile, lanceolate, terminal leaflets largest; flowers numerous, small, white tinged with blue in shortly paniculate or nearly sessile cymes, arranged in large, lax, terminal panicles, drupes, irregularly globose, purple, often white dotted C-6-12 mm in diameter with persistent, flattened calyx.

It is common both in the evergreen and deciduous forests of the Western ghats as well as in open dry forests of certain parts of Deccan plateau. In Kanara, at times, it is known to attain great size. (36 m high with a girth of 5.5m.) However generally it is much smaller with a bole of 5-6 in length and 2 m girth.

The wood is quite attractive, light olive-grey to olive brown in colour with broad and dark streaks, turning darker with age. Heart wood is not distinct. The yellowish green tinge of the wood is due to a water soluble flavone. The wood is very hard, tough, strong and heavy (Sp.gr. 0.8-0.9 : av.wt. 929 kg/c.u.m.). It is very durable both on ground and under water. It is used mostly for making beams, columns, doors, windows and floor-boards. In some parts of South India the wood is considered most appropriate for building temples. The heart wood, leaves and bark contain a flavonoid vitexin (63).

Chemical constituents:
No report is available on the chemical constituents of Vitex altissima.

Pharmacological activity:
No report are available on Vitex altissima.

The study was undertaken as per the following plan of work.

PLAN OF WORK:

Preparation of methanol extract of V. altissima and V. negundo leaves through serial extraction with a soxhlet apparatus.

Part I: Acute toxicity studies in mice and rats and estimation of LD50 dose.

Studying the effect of extract on different aspects of inflammatory phenomenon like vascular permeability, cell emigration and connective tissue formation.

Assessing the extracts for membrane stabilizing, superoxide scavenging and prostaglandin synthesis inhibition effects.

Studying the effect of extracts on Freund's adjuvant induced arthritis and immunological oedema.

Assessing the role of adrenal gland and counter-irritant effect in the anti-inflammatory activity of the extracts.

Drug interaction studies: Effect of extracts on certain biochemical parameter supposed to be altered during inflammation.

**Part II:** Evaluation of ME of *V. altissima* and *V. negundo* for anti-ulcer effect or ulcerogenic potential in rats.

Evaluation for anti-ulcer effect by noting the effect of extracts on ulcer formation in pylorus ligated (18h) rats. Ulcerogenic potential assessment by observing the effect of co-administration of extracts with phenylbutazone on ulcer formation in 8h pylorus ligated rats.

**Part III:** General pharmacological screening of ME of *V. altissima* leaf. Since no details are available on the pharmacological activity profile of the leaf of *V. altissima*, ME of *V. altissima* leaf was subjected to general pharmacological screening by studying its effect in a battery of tests supposed to have predictive value for different type pharmacological effects.