Review Article

A Review on *Millingtonia Hortensis* Linn

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ABSTRACT

Millingtonia hortensis Linn. (Bignoniaceae) commonly known as Cork tree, Akash neem, Neem chameli. It is an important medicinal plant in Southern Asia ranging from India, Burma, Thailand and Southern China. Cultivated in most parts of India in gardens and avenues. It can grow up to 25 meter tall. Flowers have very rich and pleasant scent, used in the treatment of asthma, sinusitis, cholagogue, tonic and in rituals. The stem bark is used traditionally as mainly lung tonic, anti asthmatic and antimicrobial properties. Leaves and roots of cork tree used as antiasthmatic and antimicrobial activity. Fruit is very long and narrow, pointed at both ends and contains thin, flat seeds. Trees do not seed very easily in India. The plant has antifungal, antibacterial, larvicidal, antioxidant, antiproliferative, antimutagenic, antihelmintic and hepatoprotective activities. This paper gives information about the plant's medicinal aspects, pharmacognosy, phytochemistry and pharmacological activities of the plant.

Keywords: *Millingtonia hortensis*, Cork tree, Bignoniaceae, Antiasthmatic, Antimicrobial, Medicinal aspects.

INTRODUCTION

Thousands of indigenous plants have been used by man from prehistoric times on all continents for relieving and curing ailments. In spite of tremendous development in the field of allopathy medicinal plants and their derivatives still remain one of the major sources of drugs in modern and traditional systems throughout the world playing a major role in medicinal therapy. In India about 7300 plant species are used in traditional health care systems. 90% of the medicinal plants which find place in day-to-day uses, many of these, are used as herbal remedies. The expanding domestic and global demand of herbal products has put the native medicinal plant resources under significant stress.

The use of medicinal plants as a source for aid from illness can be traced back over five millennia to written documents of the early culture in China, India and the Near east, but it is, without a doubt, an art as old as mankind[1]. Many of these plants and their extracts were used in traditional medicine both as antimicrobial and antifungal agent. Medicinal plants play a key role in health care with about 80% of the world's populations relying on the use of traditional medicine which is predominantly based on plants[2, 3]. Herbal products prepared either from single or multiple botanical ingredients are usually complex and variable in nature. Undoubtedly, the plant kingdom still holds many species of plants containing substances of medicinal value that have yet to be discovered[4].

Medicinal plants are of great importance to the health of individual and communities. The medicinal value of these plants lies in some chemical active substances that produce a define physiological action on human body. The most important of these chemically active constituents of plants are alkaloids, tannin, flavonoid and phenolic compounds. Many of these indigenous medicinal plants are also used for medicinal purposes[5]. In recent years, use of antimicrobial drugs in the treatment of infectious disease has developed multiple drug resistance and with increase in production of new antibiotics, by pharmaceutical industry, resistance to these drugs has also increased[6].

The increasing failure of chemotherapeutics and antibiotic resistance exhibited by pathogenic microbial infectious agents has led to the screening of several medicinal plants for their potential antimicrobial activity. India is a varietal emporium of medicinal plants and is one of the richest countries in the world in regard to genetic resources of medicinal plants. Thus, it is anticipated that phytochemicals with adequate antimicrobial efficacy will be used for the treatment of bacterial infections[7]. Herbal extracts were showing a promising result in controlling both plant disease particularly fungal and bacterial diseases.

Millingtonia hortensis Linn. is an important medicinal plant in southern Asia ranging from India, Burma, Thailand and South China. Commonly known as Cork tree. It is also called as Akash neem, Neem chameli. *Millingtonia hortensis*, Tree Jasmine or Indian Cork tree, the sole species in the genus *Millingtonia*[8] is a tree native to South-East Asia. The name *Millingtonia* comes from Thomas Millington, an English botanist while *hortensis* means "grown in gardens". The tree is favorite garden and avenue tree[9].

The plant is also popular for its ornamental value. The other species are *phellodendron amurense, phellodendron chinense, phellodendron japonicum, phellodendrum lavallei, phellodendron sachalinense, phellodendron wilsonii* are the other related species of

the Cork tree[9, 10]. A very tall and straight tree with brittle wood and liable to damaged by storms. It can grow up to 25 meter tall and it can reach 80 meter in height. Flowers have very rich and pleasant scent. In Thailand, the flower is called 'peep' and used for the treatment of asthma, sinusitis and as a cholagogue and tonic. The flowers are also used in rituals and have good antimicrobial properties. The stem has brittle wood and liable to damaged by storms, stem bark is used traditionally as mainly lung tonic, antiasthmatic and antimicrobial properties. Leaves and roots of cork tree used as antiasthmatic and antimicrobial activity. Fruit is very long and narrow, pointed at both ends and contains thin, flat seeds. Trees do not seed very easily in India. Roots can be used for the treatment of tuberculosis and as an antiasthmatic. The leaves of Cork tree are very ornamental and extracts of leaves has good antimicrobial activity. The leaves of *Millingtonia hortensis* are used as antipyretic[11] antiasthmatic, sinusitis, cholagogue and tonic in folklore medicine.

PLANT PROFILE

Classification

Kingdom : Plantae

Division : Magnoliophyta

Class : Magnoliopsida

Order : Lamiales

Family : Bignoniaceae

Genus : *Millingtonia*

Species : *hortensis*

Common names: Cork tree, Tree Jasmine, Akash neem, Neem chameli

Vernicular names

Hindi : Neem chameli

Kannada : Akash mallige, Beratu, Birate mara

Konkani : Akash nimb

Malayalam : Katesam

Marathi : Akash chameli, Buch, Kava lnimb

Oriya : Bakeni, Mach-Mach, Sitahara

Tamil : Kat-malli

Telugu : Kavuki

Synonyms: *Bignonia suberosa* Roxb., *Millingtonia hortensis* L. f

GEOGRAPHICAL DISTRIBUTION

The tree is indigenous to Burma and the Malay Archipelago, but grows wild in most parts of India as well as being extensively cultivated. It is important medicinal plant in Southern Asia ranging from India, Burma, Thailand and South China.

BIOPHYSICAL LIMITS

Habit and Habitat: Tall deciduous tree, mostly found in tropical forests low altitude slopes 500-1200mts. typically found at an altitude of 0-922mts. It can grow in various soil types and climates with a preference for moist climate[12].

ECOLOGY

It is a drought resistant tree. Cork tree widely grows in the central India. It is mostly found in the tropical forests. It requires full sunlight for its growth and can grow in various types of soils but prefers moist climate. The tree do not flowers in some places like Chennai. Propagation occurs by seeds, suckers which it produces in large numbers.

BOTANICAL DESCRIPTION

It is a tall deciduous tree grows up to height of between 18 to 25 meters and has a spread of 7 to 11 meters. It can reach height of 80 meters. It has brittle wood liable to damaged by storms. It can be grown as a small compact tree if trimmed or as a nice container specimen. It reaches maturity between 6 to 8 years of age and lives for up to 40 years. It is a versatile tree which can grow in various soil types and climates with a preference for moist climate[12]. It has corky bark and straight trunk and has few branches. It flowers at night and shed flowers early in the morning. In the cooler months, the tree blooms in the night and early in the morning; fragrant flowers falling and carpeting the ground around.

Figure 1: Leaves and flowers of *Millingtonia hortensis* Linn.

Stem bark

The tree is evergreen and has an elongated pyramidal stem. The soft, yellowish white wood is brittle and can break under strong gusts of wind[12]. It has corky bark. It is dark brown colored and characteristic odor. It has straight trunk and has few branches. The inferior cork is processed from its corky bark thatswhy it is called cork tree. Externally rough with irregular ridges and fissures[9, 10].

Leaves

The leaf is imparipinnate[8] and resembles that of the neem. Leaves are prone to attack by *Acherontiastyx* and *Hyblaeapuera*[13]. Leaves are large, very ornamental and

pinnately compound[14]. Long leaves bear two or three widely spaced pinnae, each with 5-7 smooth leaflets, oval, pointed and slightly round-toothed, 1-3 inches long. Sometimes the lower pinnae are again divided and bear one pair of three leaved pinnae, 1-2 pairs of leaflets and one leaflet at the end. Between January and March the leaves are shed and renewed during April and May, although the tree is never quite naked. The leaves give no odor and slightly bitter in taste.

Flowers

The tree flowers twice a year and the white flowers come as large panicles which emit a pleasant fragrance. They are bisexual and zygomorphic. The bell-shaped sepals of the flower have five small lobes. The flower has four stamens with parallel anthers unlike in most other plants of this family where the anthers are divergent. The corolla is a long tube with five lobes[8]. Flowers are white, waxy, trumpet-shaped and somewhat two lipped with five subequal lobes. The flowers are in corymbose, long tubular, white and delightfully fragrant. Because of the perfume of the flowers they are very much sought after. The waxy characteristic of the flowers ensure their freshness for a long time.

Flowering period

From April until the rains and again in October to December.

Fruit and Seed

The fruit is a smooth flat capsule and is partitioned into two. It contains broad-winged seeds[8]. The fruits are fed on by birds which aid in seed dispersal. In cultivation, the viability of seeds is low unless they are sown immediately after the fruit ripens, so the plant is generally propagated through cuttings. Fruit is a 2-valved septicidal capsule, oblongoid, acute at both ends, flat, woody; seeds discoid, compressed, winged, except the base, the wing narrow at the apex, non endospermic. Trees do not seed very easily in India.

Fruiting period: November-February[10].

COMMON USES

The tree is considered ornamental and the pleasant fragrance of the flowers renders it ideal as a garden tree. The wood is also used as timber and the bark is used as an inferior substitute for cork. The leaves are also used as a cheap substitute for tobacco in cigarettes[15].

TRADITIONAL USES

Leaves and Root

Leaves and roots of cork tree used as anti asthmatic and antimicrobial activity. Extract of the leaves of *Millingtonia hortensis* has good antimicrobial activity. The leaves of *Millingtonia hortensis* are used as antipyretic, sinusitis, cholagogue and tonic in folklore medicine.

Stem

Stem also having great medicinal value using as lung tonic and cough disease

Bark

Used as a yellow dyes.

Flowers

Flower buds are used in the treatment of asthma, sinusitis, cholagogue and tonic. The flowers are used in rituals. The flowers are added to tobacco for smoking as treatment for throat ailments.

Whole plant

Antipyretic, antitubercular, antimicrobial, larvicidal, antimutagenic, anticancer, antifungal[9, 10].

PHYTOCHEMICAL STUDIES

Roots

Lapachol, β-sitosterol and poulownin were isolated from the roots of *Milligtonia hortensis*[16].

Bark

From the heartwood and bark β-sitosterol was isolated[17, 18]. Bitter substances and tannins were also identified[19].

Leaves

From the leaves of *Millingtonia hortensis,* hispidulin was identified[20], Rutinoside[19]. A flavonoid dinatin together with β-carotene was reported[21].

Flowers

From the fresh flowers of *Millingtonia hortensis* isolation of a new glycoside (scutellarein-5-galactoside) and scutellarein was observed[22].

From the flowers of *Millingtonia hortensis* flavonoids scutellarein, hispidulin and scutellarein-5-glucuronide were isolated[20].

From the dried flowers of *Millingtonia hortensis* a flavonoid hispidulin was isolated by using TLC[23].

From the powdered flowers of *Millingtonia hortensis*, hortensin, 3, 4-dihydroxy-6, 7- dimethoxyflavone, has been isolated and characterized through its spectroscopic properties, including CSCM ID and selective INEPT experiments[24].

Hortensin, isolated from *Millingtonis hortensis* and analysed 3, 4'-dihydroxy-6, 7- dimethoxyflavone, has been found to be different from a synthetic samples. Reinterpretation of the reported data and comparisons with authentic samples show that hortensin is 5, 4'-dihydroxy-6, 7- dimethoxyflavone(Cirsimaritin)[25].

The original structure of hortensin from *Millingtonia hortensis*, and analysed as 4'- hydroxy-6, 7- dimethoxyflavonol, has been changed once to 5, 4'-dihydroxy-6, 7- dimethoxyflavone(Cirsimaritin). A further reinterpretation of the NMR data of newly isolated

'hortensin' showed that it is 5, 7-dihydroxy- 6, 4'-dimethoxyflavone(Pectolinarigenin). Several related flavonoids from the same plant were identified[26].

After repeated column chromatography, followed by HPLC of a hot methanolic extract of the dried flowers of *Millingtonia hortensis*, 21 compounds were (1-21) were isolated. Compounds 1-12 were identified as known compounds by means of their spectral data. Compounds 1-4 were phenylethanoid glycosides. Compound 1 was salidroside. This compound was supposed to be a biogenetic precursor of cyclohexylethanoids through mimic chemical reaction[27]. Compound 2 was 2-phenyl rutinoside previously isolated from *Citrus unshiu*[28]. Compound 3 was 2-(3, 4-dihydroxyphenyl)-ethyl glucoside. Compound 4 was acteoside. Compound 5 and 6 were phenylpropanoid glucosides, p-coumaryl alcohol glucoside (5) and isoeugenol glucoside (6), both of which have been obtained from *Lilium cordatum*[29]. Compounds 7-12 were cyclohexylethanoids identified as cornoside (7), racemic rengyolone (8), rengyoside B (9), rengyol (10), rengyoside A (11) and isorengyol (12)[30, 31], respectively. Cornoside (7) has been isolated from *Cornus femina* and many other species, and compounds 8-12 are constituents of *Forsythia suspense* ('rengyo' In Japanese). Except for 12, the isolation of these cyclohexylethanoids from the bignoniaceae has not been reported previously. Compound 13, $C_{14}H_{26}O_8$ showed 14 signals in its ^{13}C NMR spectrum, six of them were attributed to a β-glucosyl moiety. Enzymatic hydrolysis of 13 with β-glucosidase afforded 12 and D-glucose. Comparison of the ^{13}C NMR spectra of 13 with 12, revealed a glucosylation shift around C-8. Thus the structure of 13 was characterized as 8-O-β-D-glucopyranosyl isorengyol. Compound 14, $C_8H_{12}O_3$ showed a similar ^{13}C NMR spectrum to that of 8, but in place of the carbonyl carbon signal (δ 196.9) of 8, a carbinyl methine signal (δ 65.9) appeared and double bond signals were shifted. Since the oxidation of 14 with CrO_3 afforded 8, the basic structure of 14 was a 4-hydroxyl congener of 8. Naturally obtained 15, $C_8H_{14}O_3$, was identical with the reduction compound of 14 by means of NMR. However, the specific optical rotation of natural 15 was significantly smaller than that of 15 derived from 14; natural 15 seemed to be racemic. Compound 16 had the same molecular formula as 15 and ^{13}C NMR data indicated that it was a 2, 4-trans isomer of 15, i.e. the 4-epimer of 15. Since the specific optical rotation of 16 was small, it might be partially racemic. As in the case of 15, the structure is tentatively illustrated as one of the enantiomer. Compound 17 $C_8H_{12}O_3$, had a similar ^{13}C NMR spectrum to that of 8, except for the appearance of two methylene signals (δ 34.1 and 35.7) in place of the double bond carbon signals. From the ^{1}H NMR and ^{13}C NMR data, 17 was shown to be the saturated congener 8, as illustrated. Because of the small specific optical rotation and no cotton effect in the CD spectrum, 17 appeared to be racemic. Compound 18, $C_{14}H_{22}O_8$, was a non-separable mixture of diastereomeric glucosides judging from a very close set of dual peaks in the ^{13}C NMR. Comparison of the ^{13}C NMR of 18 with that of 7, the shown structure was suggested. Enzymatic hydrolysis of 18 with β-glucosidase afforded 17. This was analogous to the reaction of 7 to form 8 [8]. Only one of the diastereomeric forms of 18 is illustrated. Compound 19, $C_{14}H_{22}O_9$, was also a mixture of diastereomeric glucosides showing dual signals. Compound 20, $C_{15}H_{24}O_9$ was similarly characterized to be the C-6 methoxylated congener of 18. Compound 21, $C_{12}H_{22}O_3$, seemed to be a related cyclohexylethanoid compound but its 13C NMR showed an additional four signals[32].

From the flower buds of *Millingtonia hortensis*, an unusual glucosidal alkaloid was isolated in diasteromeric form. Its structure has been established by chemical and spectroscopic methods[33].

A total synthesis of millingtonine A, a diglycosylated alkaloid, has been accomplished. Millingtonine A possesses a unique racemic tricyclic core structure not known from any other natural or synthetic source until now. The synthesis features a key bond-forming radical Ueno–Stork cyclization to form the heterocyclic core[34].

Fruits: Acetyl oleanolic acid[20].

MUTAGENICITY AND ANTIMUTAGENICITY ACTIVITY

The mutagenicity and antimutagenicity of hispidulin and hortensin, the flavonoids from *M. hortensis* L. (Bignoniaceae), were performed using the liquid pre incubation method of the *Salmonella/micro some* test. At the highest dose tested, 100 µg/plate, both compounds showed no mutagenicity and no cytotoxicity toward *S. typhimurium* strains TA98 and TA100 either in the presence or absence of S9 mix. However, these substances were antimutagens toward 2-aminoanthracene, aflatoxin B1 (in TA98), and dimethylnitrosamine (in TA100); but neither substance inhibited the direct mutagenic activity of (2-furyl)-3-(5-nitro-2-furyl) acrylamide nor that of sodium azide in strains TA98 and TA100, respectively[35].

ANTIMICROBIAL ACTIVITIES

Antibacterial Activity

The polar extracts of the leaves of *M. hortensiss* showed good antimicrobial activity. Twenty different bacterial strains and two yeast cultures were used .The aqueous alcohol extract showed good activity against all microbes tested particularly against *Escherichia coli* and *Salmonella typhimurium.* Both Gram-negative bacteria with MIC values of 6.25 µg/ml. The activity is compared with known antibiotics such as gentamycin and nystatin[36].

The essential oil of flowers extracted by using vapor distillation with 0.5-2% yield, tested against various species of bacteria like 4 gram-positive bacteria *(S.aureus* ATCC25923, *S. epidermidis* ATCC12228, *B. subtilis* ATCC6633 *and L. Plantarum* ATCC14917) and 2 of gram negative bacteria *(E.coli* ATCC25922 *and P.vulgaris* ATCC13315). In this study, *M. hortensis* Linn. essential oil of flower showed broad spectrum antimicrobial activity at low Concentration[37].

This study focused on the evaluation of antimicrobial activity of *Millingtonia hortensis* L. by using methanol, ethanol and aqueous extracts of leaves and flowers of *Millingtonia hortensis* L. against primary and opportunistic pathogens. The study was conducted using agar disc diffusion method. The primary pathogens used are *Klebsiella pneumoniae, Salmonella typhi, Salmonella paratyphi A, Vibrio cholerae, Shigella dysentrae and Bacillus subtilis*, and the opportunistic pathogens are *Escherichia coli*, *Stayphylococcus aureus, Enterococcus faecalis*, *Pseudomonas aeruginosa* and *Proteus mirabilis*. The methanol and ethanol extracts of leaves showed maximum activity against all organisms except *Salmonella typhi*, *Pseudomonas aeruginosa* and *Proteus mirabilis* where as flower extract showed less activity against *Proteus mirabilis*. The aqueous extract of leaves showed inhibitory activity against microorganism compared to aqueous extract of leaves showed inhibitory activity against microorganism compared to aqueous flower extract. The minium inhibitory concentration (MIC) ranged between 25 mg/ml and 50 mg/ml depending on microorganisms and various extracts[38].

The antibacterial activity of crude petroleum ether, benzene, chloroform, methanol and aqueous extracts of *Millingtonia hortensis* stem bark were tested against *Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus* and *Bacillus subtilis*. The in vitro antibacterial activity was performed by agar disc diffusion method. The zone of inhibition was compared with the standard drug i.e. ampicillin. Petrolium ether extract was effective against *P. aeruginosa*, *B. subtilis* and *S. aureus*; benzene, chloroform, methanol and aqueous extracts were effective against the entire four test microorganism used respectively when compared to standard drug ampicillin. The minimum inhibitory concentration (MIC) for *S. aureus* was 50, 100, 50, 50 and 50µg/ml; MIC for *B. subtilis* was 25, 100, 50, 50 and 25 µg/ml; MIC for *E.coli* was 200, 100, 50, 50 and 25 µg/ml and MIC for *P. aeruginosa* was 10, 50, 50, 50 and 50 µg/ml for petrolium ether, benzene, chloroform, methanol and aqueous extracts respectively suggesting the antibacterial activity of *Millingtonia hortensis*[39].

Antifungal Activity

Antifungal activities of different extracts of *M. hortensis* were investigated against various fungal pathogens. Methanol extract was found to have stronger activity than fluconazole against yeast like fungi: 4 fold against *Candida krusei* with 4µg/ml minimal inhibitory concentration and 2 fold (MIC-2 µg/ml) against *Saccharomyces cerevisiae*, though it showed the same activity as fluconazole against *Candida glabrata.* Aqueous extract also exhibited 4 fold stronger activity against *Candida krusei* (MIC-4 µg/ml) and 4 fold (MIC; 2 µg/ml) against *Saccharomyces cerevisiae.* Chloroform and ethyl acetate extract showed lower activities against all fungal pathogens except for *Candida krusei*, compared with the standard. Against the filamentous fungus, *Trichosporon cutaneum,* all extracts showed less activity than the standard[40].

Antifungal activity of aqueous extracts of leaves of *Millingtonia hortensis* Linn. when tested against eight fungal species of maize at 10, 20, 30, 40 and 50 % concentration showed maximum activity against *A. flavus* at 50% concentration followed by *F. oxysporum* (90.2%), *F. solani* (89.5%), *F. moniliforme* (87.7%), *A. candidus* (78.9%), *A. niger* (78.0%), *A. flavipes* (73.2%) and *F. graminearum* (52.1%) at 50% concentration tested. Moderate activity was also observed in 20, 30 and 40% concentration and least activity was observed in 10% concentration tested. Compared to synthetic fungicide bavistin and thiram, both the fungicide recprded 100% inhibition[41].

Anticonvulsant Activity

The functional characterization of hispidulin (4′, 5, 7-trihydroxy-6-methoxyflavone), a potent benzodiazepine (BZD) receptor ligand, was initiated to determine its potential as a modulator of central nervous system activity. After chemical synthesis, hispidulin was investigated at recombinant GABAA/BZD receptors expressed by *Xenopus laevis* oocytes. Concentrations of 50 nM and higher stimulated the GABA-induced chloride currents at tested receptor subtypes (α1–3, 5,6β2γ2S) indicating positive allosteric properties. Maximal stimulation at α1β2γ2S was observed with 10 µM hispidulin. In contrast to diazepam, hispidulin modulated the α6β2γ2S-GABAA receptor subtype. When fed to seizure-prone Mongolian Gerbils (*Merionesun guiculatus)* in a model of epilepsy, hispidulin (10 mg Kg bw/day) and diazepam (2mg Kg bw/day) markedly reduced the number of animals suffering from seizures after 7 days of treatment (30 and 25% of animals in the respective treatment groups, vs 80 % in the vehicle group). Permeability across the blood–brain barrier for the chemically synthesized, 14cs-labelled hispidulin was confirmed by a rat in situ perfusion model. With an uptake rate (Kin) of 1.14 ml min-1 g-1, measurements approached the values obtained with highly penetrating compounds such as diazepam. Experiments with Caco-2 cells predict that orally administered hispidulin enters circulation in its intact form. At a concentration of 30 µM, the flavone crossed the monolayer without degradation as verified by the absence of glucuronidated metabolites[42].

Larvicidal Activity

*M. hortensis*a plant commonly known as 'Akas neem' leaf extract (Acetone extract) has been screened against three species of mosquito vectors like *Culexquin quefasciatus, Aedes aegypti and Anopheles Stephensi.* Although some medicinal properties of this plant are known but so far there is no report of its biological activity against insects. The present communication is the first report which reveals the mosquito larvicidal property of *M. hortensis*[43].

PHARMACOLOGICAL ACTIVITIES

Induction of Apoptosis on RKO Colon Cancer Cell Line

The effects of aqueous and ethanol extracts of *M. hortensis* on the induction of apoptosis in an RKO human colon cancer cell line was evaluated. Viability of RKO cells was assessed by MTT reduction assay. The aqueous extract, but not the ethanol extract of *M. hortensis* inhibited cell growth and proliferation in a dose- and time-dependent manner. Apoptotic cells were determined by flow of cytometry and DNA fragmentation assay. Apoptic cell numbers increased in a dose-dependent manner after treatment with aqueous extract. DNA ladders were clearly observed in RKO cells treated with 200,300 and 400 µg/ml of the aqueous extract of *M. hortensis* suggesting that it inhibited cell proliferation in an RKO colon cancer cell line via the apoptosis pathway[44].

An aqueous crude extract of this plant has been shown the apoptosis induction on RKO colon cancer cells. However, its mechanism remains unknown. Further, the partially purified crude extract using Sephadex LH-20 and three aqueous fractions were collected. Each fraction was investigated for cytotoxicity using MTT assay. Fraction 1 showed antiproliferative effect on RKO cells with dose-dependent manner, while fraction 2 and 3 had no effect. Induction of apoptosis was determined using flow cytometry and DNA fragmentation method[45].

Antiasthmatic Activity

The methanol extract exhibited bronchodilating effect on isolated rat trachea, this extract was further fractionated into petroleum ether, chloroform, n-butanol and aqueous fractions. Pharmacological studies indicated that the chloroform fraction elicited the most prominent effect. Further separation of the chloroform fraction by short column chromatography enabled hispidulin, the bronchodilating agent, to be isolated. Detection by TLC indicated that hispidulin is one of the compounds present in the smoke of the dried flowers. It is therefore likely that the antiasthmatic activity of the dried flowers of *M. hortensis* Linn. is due to hispidulin. Hispidulin is more potent than aminophylline on a molar basis. It was interesting to observe that the aqueous extract of these flowers exhibits a bronchoconstricting action which gradually diminishes upon storage[46].

Antihelmintic Activity

The present study was undertaken to evaluate anthelmintic activity of different extracts (petroleum ether, benzene, chloroform, methanol and aqueous extracts) of stem bark of *Millingtonia hortensis* (Bignoniaceae) against adult earthworm *Pheretima posthuma*. Piperazine citrate was used as standard reference drug. Among all the extract tested, methanol showed dose dependent anthelmintic and better activity in comparison with reference standard. Chloroform and benzene extracts at 20 mg/ml concentration also showed similar activity in comparison with piperazine citrate at dose of 60 mg/ml. Aqueous extract was not at all active. Preliminary phytochemical screening revealed the presence of steroids, flavonoids and tannins in different extracts[47].

Anti-phlorgistic activity

Hispidulin, a bioactive flavonoid isolated from the flowers of *Millingtonia hortensis* Linn. F., was tested for anti-phlorgistic effect by observing the inhibitory activity in 5-lipoxygenase pathway. The test was performed by incubating the hispidulin with 1-^{14}C-arachidonic acid and porcine leukocyte suspension containing 5-lipoxygenase. After the incubation, the 1-^{14}C-arachidonic acid and its metabolite were separated and quantified by RP-HPLC. Hispidulin showed inhibition of 65% at 64 µM[48].

Antioxidant activity

The antioxidant activity of aqueous extract of *Millingtonia hortensis* Linn. Stem bark studied by various methods. Both the extract and standard drug quercetin were evaluated for its antioxidant potential at 10, 20, 30, 40 and 50 µg/ml. In addition the amount of total phenol (241 mg/gm) and total flavonoid (172 mg/gm) were determined. The extract showed its antioxidant potential: DPPH radical scavenging activity (IC50 29.05 µg/ml), FRAP radical scavenging activity, DCF/AAPH assay (TRAP) (IC50 41.10 µg/ml), ABTS scavenging activity (IC50 24.0 µg/ml), superoxide anion scavenging activity assay (IC50 26.0 µg/ml) and Nitric oxide assay (IC50 31.0 µg/ml). The present study depicts that *Millingtonia hortensis* Linn. bark has a potential natural antioxidant that can be used as a supplementary drug for various ailments[49].

Antioxidant and hepatoprotective activity

The hepatoprotective and antioxidant potential of ethanolic extract of *Millingtonia hortensis* on carbon tetrachloride(CCl_4) induced hepatotoxicity were investigated, phytochemical studies were carried out to determine the total phenol and flavonoid contents. 30 adult wistar rats were allocated into 5 groups. Control group received vehicle, group-2 received CCl_4 alone (1ml/kg body weight, intraperitonially), group 3-5 received the ethanolic extract in 2 dose level (200 and 400 mg/kg) and curcumin (100mg/kg) as a standard for 8 days orally, followed by CCl_4 as a single dose on the 8th day. 48 hours later, blood was withdrawn, serum was subjected to biochemical assessments and liver homogenate was examined for lipid peroxides, glutathione, superoxide dismutase, catalase and total protein levels. Furthermore, hepatic tissues were subjected to histopathological studies. CCl_4 treatment produced a profound increase in the level of malondialdehyde, hepatic marker enzymes and bilirubin content compared with the control ($p<0.05$). Pretreatment with the flower extract of *Millingtonia hortensis* significantly enhanced the level of endogenous antioxidants and reduced the levels of hepatic marker enzymes in relation to the CCl_4 treated group ($p<0.05$). Ballooning degeneration and fatty changes in hepatocytes

was prevented by pre-treatment with the flower extract[50].

CONCLUSION

The current report shows that *Millingtonia hortensi* Linn. is a favourite garden tree commonly known as Cork tree. It is a perennial herb. The plant has high medicinal values and is used for indigenous treatment of numerous diseases including asthma, rheumatism, tuberculosis, cancer, antipyretic, sinusitis and as an cholagogue and tonic. This review find the description of the herb, phytochemistry, mutagenicity and antimutagenicity, antimicrobial activities like antibacterial, antifungal, anticonvulsant, and larvicidal activity, different types of pharmacologically actions like antioxidant, induction of apoptosis on RKO colon cancer cell line, antihelmintic, antiproliferative, antiasthmatic and hepatoprotective activity. This review will definitely help for the researchers as well as practioners, dealing with this plant, to know its proper usage. Therefore, considering its versatile medicinal uses, there is an ample scope for future research on *Millingtonia hortensis* Linn. and hence further pharmacological investigations are warranted.

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