Ethnopharmacology review on Endangered Medicinal plant

*Mallotus philippinensis* (Lam.) M.Arg.

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**INTRODUCTION**

India is one of the Mega biodiversity regions. Tropical forest of India serves as a hub of various plants having medicinal values. *Mallotus philippinensis* is one of them. *Mallotus philippinensis* (Lam.) Muell. Arg. is belonging to the family Euphorbiaceae. It is a perennial shrub or small tree found in tropical and subtropical regions. It is commonly called as Kamala and locally known as Shendri. Mature fruits are reddish brown in color. Flowers mature from March to April and fruits mature in July-August. Germination rate of *Mallotus* seeds is often very poor because of hard seed coat. In natural conditions seeds germinate about 5%. [1]. The tree also reproduces from root suckers but the growth is very slow. The tree is subject to attack by several rot-causing fungi, *Fomes conchatus*, *Hexagonia discopoda*, *Polyporus adustus*, *Stereum hirsutum*, *Ganodema applanatum* etc. Traditionally it is used for the treatment of Skin problems, bronchitis, antifungal tape worm eye disease, cancer, jaundice, Malaria, urinogenital infection, rheumatism etc. This plant also show antifilarial [2] anti-bacterial, anti-inflammatory, [3] anti-oxidant, pestecidal, heptoprotective activities [4]. It is important medicinal plant and because of its high use and low rate of seed germination and attack of microbes, it has been reached to endangered level. So, micro propagation is in demand for the conservation of this multi-medicinal property plant. This review is an attempt to evaluate various traditional uses, pharmacological studies as well as tissue culture studies of *Mallotus philippinensis*.

**Key words:** *Mallotus philippinensis*, anti-cancer, endangered level, tissue culture.

**ABSTRACT**

*Mallotus philippinensis* (Lam.) Mull. Arg. is widely distributed perennial shrub commonly known as ‘Kamala’. It is an important medicinal shrub of Ayurvedic system. Traditionally it is being used in the treatment of bronchitis, abdominal diseases, Jaundice, Malaria, Urinary complications, and parasitic affections etc. It also possesses various pharmacological activities like anti-oxidant, anti-tumor- anti-cancer, anti-filarial, anti-fertility, anti-HIV activity etc. But because of its’ over use and due to various microbial infections and lower seed germination problem it has been reached to endangered level. So, micro propagation is in demand for the conservation of this multi-medicinal property plant. This review is an attempt to evaluate various traditional uses, pharmacological studies as well as tissue culture studies of Mallotus philippinensis.

**Scientific Classification:**

kingdom: Plantae

division: Magnoliophyta

class: Magnoliopsida

order: Euphorbiales

family: Euphorbiaceae

genus: *Mallotus*

species: *philippinensis*
English Name: Kamala tree
Hindi: Kamala, Sindur, Rohini and Kambhal
Other vernacular names- Tamil: Kapli, Kungumam, Kurangumanjanatti. Tamil: Kapli, Kungumam.

**DISTRIBUTION**
*M. philippinensis* is found in tropical and subtropical regions of India special in Punjab, uttar-pradesh, Bengal, Assam, Mumbai. It is also found in Singapore, China, Australia, Pakistan and Andaman islands [5].

**GROWTH CONDITIONS**
Temperature- 16-28°C
Annual rainfall – 800-2000 mm
Soil- it grows mostly in every soil types, including infertile soil, limestone and rocky lands.

**PARTS USED IN MEDICINES**- Glandular hair of the fruit.

**MORPHOLOGY**
Mallotus is small sized tree upto 25 m tall. Leaves are alternate and simple, 3-nerved at base, hairy, long petiole around 1-4 cm long in size, According to Ayurveda, leaves are bitter, cooling. Flowers are small. It has unisexual flowers. Male flowers in terminal and axillary position, and solitary. Female flowers have spikes and 5-9 cm long in size. Flowers have extra floral netarines attracting ants. Fruits are globose, 3-lobed capsule densely covered with reddish brown coat. And seeds are black and 4mm in diameter [6].

**COMMON ADULTRANTS**
Glandular hair powder of *M. philippinensis* is commonly adulterated with Annato dye (*Bixa orellana* Linn.), ferric oxide, brick dust, and ferruginous sand. *Casearia tomentosa* (stem bark powder), *Carthamus tinctorius* (flower powder), *Ficus benghalensis* (fruit powder), and *Flemingia macrophylla* (hairs of fruits) are also reported to be used as adulterant or substitute of Kampillaka [7].

**PHYTO CHEMICAL CONSTITUENTS**
Major secondary metabolites present in *M. philippinensis* are phenols, diterpenoids, steroids, flavonoids, cardenolides, triterpenoids, coumarin, isocoumarins, and many more to discover. rottlerin is being tested for various activities of *M. philippinensis*.

**TRADITIONAL USES**
All parts of plant like glands and hairs from the capsules or fruits are used as heating, anthelmintic, detergent and alexiteric and are useful in treatment of bronchitis, abdominal diseases, and spleen enlargement, and if taken with milk or curd (yoghurt), it can be quite useful for expelling tapeworms [8]. It is also used in the treatment of jaundice, Malaria and urinogenital infections. The powder and a few other parts of Kamala are also used in external applications to promote the healing of ulcers and wounds. They are used to treat parasitic affections of the skin like scabies, ringworm, and herpes.

**PHARMACOLOGICAL ACTIVITIES**
1) *Ant filarial Activity-*
R. Singh et. al. Reported the effect of aqueous and alcoholic extracts of the leaves of Mallotus philippensis (Lam.) Muell. Arg. on the spontaneous movements of the whole worm and nerve-muscle (n.m.) preparation of *Setaria cervi* and on the survival of microfilariae in vitro. Both the extracts caused inhibition of motility of whole worm and the n.m. preparation of S. Cervi characterized by initial stimulation followed by depression in amplitude. Aqueous extract at higher concentration showed immediate reduction in tone. The concentration required to inhibit the movements of n.m. preparation was 1/5th for aqueous and 1/11th for alcoholic extract compared to that for the whole worm, suggesting a cuticular permeability barrier. The stimulatory response of acetylcholine was blocked by aqueous extract on whole worm movements. On the microfilariae the LC50 and LC90 were 18 and 20 ng/ml for aqueous and 12 and 15 ng/ml for alcoholic extracts respectively [9].
S. C. Thakur et al. tested the Seeds extract of *M. philippinensis* different

2) Antifertility Activity- reproductive parameters of female rats. According to the study, extract reduces serum FSH and LH levels, probably by affecting hypothalamic/pituitary axis in experimental animals. This reduced level may affect follicular development, quality of ovulated eggs, corpus luteum formation, estrus cycle, and maintenance of pregnancy in rats [10].

M. L. Gujral et al. showed that anti-fertility effect of *Mallotus* is caused by rotterin, it is a phloroglucinol derivative [11].

3) Anti-microbial activity-

Jayaraman Velanganni et al. showed the antimicrobial activity of hexane, chloroform and ethanol leaf extract of *Mallotus philippensis* against the human pathogens such as *Streptococcus pneumoniae* causing brain abscesses, pneumonia and septic arthritis, *Proteus vulgaris*, *Pseudomonas aeruginosa* causing urinary tract infections and septicaemia, *Salmonella typhi* causing typhoid fever, *Vibrio* species causing diarrheal infections and the fungus *Candida albicans*. The antimicrobial activity of the hexane, chloroform and ethanolic extract of stem showed concentration-depandant activity against all the tested bacteria with zone of inhibition ranged from 12-26mm. But only But only the ethanol extract showed antimicrobial activity against the fungi *A. flavus* and *C. albicans* with the zone of inhibition ranged from 16-22mm at various concentrations.

V. P. Kumar et al. studies on antimicrobial activity of Mallotus and concluded that the crude extract of *M. philippinensis* exhibited significant antimicrobial activity [3] and properties that support folkloric use in the treatment of some diseases as broad-spectrum antimicrobial agents.

M. Gangwar et al. reported that the Glandular hair of fruits of *Mallotus* exhibits significant antibacterial activity against human pathogenic bacteria with MIC ranging 15–20mg/mL. This extract does not show any inhibition against different species of *candida*. This shows that fruit extract possesses antibacterial activity without any antifungal potential. The results of the study may justify the use of the plant against bacterial pathogens. This probably explains the use of these plants by the indigenous people against a number of infections [12].

S. F. H. Zaidi et al. showed that ethanolic extract of *Mallotus philippinensis* possess anti-*Helicobacter pylori* activity at the concentration of 15.6–31.2mg/L against eight *H. pylori* strains. Further purification of extract revealed that rottlerin exhibits potent bactericidal effect with minimal bactericidal concentration (MBC) of 3.12–6.25mg/L against different resistant strains of clarithromycin and metronidazole including Japanese and Pakistani strains.

4) Antioxidant Activity and Antiradical Activity-

M. Arfan et al. studied the different fractions of bark and fruit of *Mallotus* for its total antioxidant activity (TAA) and antiradical activity against DPPH on a Sephadex LH-20 column using ethanol and acetone-water as mobile phase. Among different extracts, bark fraction showed the strongest antiradical activity (TAA value—5.27 mmol Trolox equiv./g) and reducing power. Another extract, that is, phenolic fraction, shows TAA ranging from 0.58mmol Trolox/g (fraction I) to 6.82mmol. Trolox/g (fraction IV); this is the strongest fraction showing antiradical activity against DPPH and reducing power. TAA of other extracts ranged from 0.05 to 1.79mmol Trolox equiv./g.

5) Anti-cancerous activity-

V. Sharma tested that the glandular hair extract of *Mallotus* fruit powder against 14 human cancer cell lines among different fractions; 95% ethanolic extract showed the highest cytotoxic effect as compared to 50% ethanolic and aqueous portion. Further, the chromatographic analysis of the said fraction afforded a polyphenolic molecule rottlerin in *Mallotus* plant.

6) Anti-tuberculosis Activity-

Q. Hong et al. used organic extract of Mallotus plant which yields five compounds after bioassay-directed fractionation. The most active compound against *Mycobacterium tuberculosis* was 8-cinnamoyl-5, 7-dihydroxy-2, 2-dimethyl-6-geranylchromene for which the name mallotophilipp F is suggested. The second compound 8-cinnamoyl-2,2- dimethyl-7-hydroxy-5-methoxychromene was isolated from a natural source for the first time, while the remaining three compounds, rottlerin, isoallorottlerin, or
isorottlerin and the so-called “red compound,” 8-cinnamoyl-5,7-dihydroxy-2, 6-trimethylchromene, had been already isolated from this plant. Isolated compounds were identified by 2D-NMR and C-13 NMR [17].

7) Antiallergic Activity-
A. Daikonya et al. identified two new phloroglucinol derivatives from the M. philippinensis fruit by using chemical and spectral data, as 1-[5,7-dihydroxy-2,2-dimethyl-6-(2,4,6-trihydroxy-3-isobutyryl-5-methyl-benzyl)-2H-chromen-8-yl]-2methyl-butan-1-one and 1-[6-(3- Acetyl-2,4,6-trihydroxy-5-methylbenzyl)-5,7-dihydroxy-2,2 -dimethyl-2H-chromen-8-yl]-2-methyl-butan-1-one. and named the compounds mallotophilia A and B respectively. These compounds inhibited the production of nitric oxide (NO) and inducible NO synthase (iNOS) gene expression by a murine macrophage-like cell line (RAW 264.7), which was activated by lipopolysaccharide (LPS) and recombinant mouse interferon-g (IFN-g). Further, phloroglucinol derivatives inhibit histamine release from rat peritoneal mast cells induced by compound 48/80. This study suggests its anti-inflammatory activity.

T.K. chan et. al. Tested rottlerin in animal models of IgE-dependent anaphylaxis and the anti-allergic mechanisms of action in mast cells. Anti-allergic action of rottlerin has been tested in passive cutaneous anaphylaxis and passive systemic anaphylaxis mouse models and in anaphylactic contraction of bronchial rings isolated from sensitized guinea pigs. This experiment proves anti-allergic effect of rottlerin by blocking IgE-induced mast cell degranulation. This report suggests the use of rottlerin in mast cell-mediated allergic disorders including urticaria and allergic asthma.

8) Anti-Leukaemic Activity-
In order to investigate anti-leukemic effect of M. philippinensis, M. khan et al. tested the root extract of M. philippinensis on human promyelocytic leukemia HL-60 cell proliferation, cell cycle regulators, and apoptosis. Hexane fraction showed promising toxicity against p53-deficient HL-60 cells (IC50 1.5mg dry roots equivalent/mL medium) after 72 h and inhibition of cell proliferation was preceded by the up regulation of the proto oncopgenes Cdc25A and cyclin D1 within 24 hours suggesting its antileukemic effect in HL-60 cells. After isolation and identification by GC-MS, polyphenols were the main compounds of the hexane extract that inhibited proliferation and induced apoptosis.

9) Anti-HIV Activity-
H. Nakane et al. identified four phloroglucinol derivatives, named mallotophenone (5-methylene-bis-2,6-dihydroxy-3-methyl-4-methoxyacetophenone), mallotochromene (8- acetyl-5,7-dihydroxy-6-(3-acetyl-2,4-dihydroxy-5-methyl-6-methoxybenzyl)-2,2-dimethylchromene), mallotojaponin (3-(3,3(dimethylallyl) S-(3(acetyl-2,4-dihydroxy-5-methyl-6-methoxybenzyl)-phloracetophenone), andmallotolerin (3-methyl-2-hydroxybut-3-enyl)-5-(3-acetyl-2,4-dihydroxy-5-methyl-6-methoxybenzyl)-phloracetophenone), and tested them for their ability to inhibit the activity of human immunodeficiency virus- (HIV-) reverse transcriptase. The mode of inhibition of mallotojaponin was found to be competitive with respect to the template primer, (rA)n (dT)12–18, and noncompetitive with respect to the triphosphate substrate, dTTP. The K_i value of mallotojaponin for HIV-reverse transcriptase was determined to be 6.1 M.

10) Anti-tumor Activity-
R. Tanaka et. al isolated four known friedelane-type triterpenoids, friedelin, 3-hydroxy-D:A-friedoolean-3-en-2- one, 2 beta-hydroxy-D:A-friedooleanan-3-one, and 3 alpha-hydroxy- D:A-friedooleanan-2-one, and two known lupanetype triterpenoids, lupeol and betulin, from the stem bark of M. philippinensis and were tested for their inhibitory effects on Epstein-Barr virus early antigen (EBV-EA) activation induced by 12-O-tetradecanoylphorbol 13-acetate (TPA). The inhibitory effect of compounds 2 (IC50 = 292 mol ratio/32 pmol/TPA) and 4 (IC50 = 288) was stronger than those of the other compounds tested and the positive control, curcumin (IC50 = 343). Compound 3 alpha- hydroxy-D:A-friedooleanan-2-one strongly inhibited mouse skin tumor promotion in an in vivo two-stage carcinogenesis model.

MICRO PROPAGATION
In-vitro micro propagation has become a trustworthy tool for mass multiplication of plants under sterile conditions. Pure cell lines can also be obtained by using this technique. Micro propagation has
superiority over conventional method of propagation because of high multiplication rate and disease free plants. But, field performance of these tissue cultured plants depends on the selection of the initial material, media composition, growth regulators, cultivar and environmental factors. Some well developed in vitro techniques are currently available to help growers to meet the demand of the spices and pharmaceutical industry.

Micropropagation through leaf of Mallotus-
Abbes achieved in-vitro propagation of Mallotus philippenses by leaf & obtained a continuously growing callus on MS+2-4D+ kn. This callus when sub-cultured on MS+BAP+CH (CASIN HYROLYSATE) gave rise to four type of morphologically distinct cell lines. Among these four lines, only the green compact cell line was responsive for organogenesis differentiation. Shoot regeneration occurred in this callus when sub cultured on MS+BAP+NAA.

Micro propagation through Endosperm culture-
Jaya Sharma et. al. developed an efficient protocol for in-vitro seed (endosperm) germination and seedling growth of a woody medicinal plant M. philippensis. Seeds cultured on MS media supplemented with or without any growth hormone. Seeds of different age groups like 20, 40, 60, 80 and 100 days were taken. Best seed germination (94%) is observed in MS medium (half concentration) while maximum seedling growth were observed in the MS media without any growth hormone. The seedlings developed were further used for the multiplication of shoots from different parts, for the regeneration of plants of Mallotus philipienesis.

Sehgal and Abbas, induced triploid plants from the endosperm cultures of Mallotus philippensis.

<table>
<thead>
<tr>
<th>Character</th>
<th>Kharif 2009</th>
<th>Rabi 2009</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>8 parents and 28 F₁ s</td>
<td>8 parents and 28 F₁ s</td>
</tr>
<tr>
<td>Oil content (%)</td>
<td>Protein content (%)</td>
<td>Oil content (%)</td>
</tr>
<tr>
<td>Replications (d.f. = 2)</td>
<td>0.1285</td>
<td>0.2782</td>
</tr>
<tr>
<td>Treatments (d.f. = 35)</td>
<td>0.9304**</td>
<td>0.1891*</td>
</tr>
<tr>
<td>Error (d.f. = 70)</td>
<td>0.3995</td>
<td>0.1145</td>
</tr>
</tbody>
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* Significant at 5 % level   * * Significant at 1 % level

The protein content, among the parental genotype, K-1375 (25.73%) recorded the lowest and JL-220 the highest protein content (26.30%) with the general mean of 26.16%. Six parents had higher protein content than parental mean. Protein content ranged from 26.07% to 26.67% among the F₁ s with a general mean of 26.41%, which was surpassed by thirteen F₁ s. The F₁, JL-220 x TCGS-647 had the highest protein content (26.67%) and it was lowest (26.07%) in TPT-4 x TIR-25. protein content ranged from 26.03% to 26.73% with a overall mean of 26.45% in F₂ generation. Seventeen F₂ populations mean exceeded the mean protein content (26.45%). JL-220 x TCGS-647 recorded the highest protein content (26.73%). F₂ population viz., ICGV-91114 X TCGS-584 registered the lowest harvest index (26.03%).

Insecticides have potential to affect the various developmental stages of entomopathogenic fungi. In the present study all tested insecticides displayed varying degree of potential to inhibit growth and conidial germination. Fungal germination is an important factor of pesticides compatibility evaluation with entomopathogenic fungi considering the pest management, because the beginning of epizootics is conditioned by the capacity of conidia to germinate on the host.

CONCLUSION

Now a day, medicinal plants are in demand for the formation of pharmaceutical drugs because they do not cause any sever side effect of body. Mallotus philippensis is a remarkable medicinal plant and clinical
trials are under investigation for the detection of its promising effect on various disorders. Literature search has shown that this plant has immense medicinal and economic uses throughout the world. But now it is rarely available and has been reported as an endangered species. So, different methods of its conservation should be adapted so as to prevent its extinct. In future it is also necessary to work on the detection of its mechanism of action. So, it could be use in the formation of pharmaceutical drugs.

REFERENCES
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