WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Phytochemical Profile and Anti-Inflammatory Potential of Tylophora Indica in Respiratory Diseases

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ABSTRACT:

Tylophora indica is a perennial climbing plant native to India, renowned for its medicinal properties in treating various health ailments, including asthma, bronchitis, and rheumatism. This plant has been traditionally used to cure respiratory problems. The leaves of Tylophora indica have been included in the Bengal pharmacopeia since 1884 and are valued for their expectorant, emetic, and diaphoretic properties. The plant is used to treat a range of health issues, including respiratory infections, bronchitis, whooping cough, diarrhea, dysentery, intermittent fever, inflammatory conditions like osteoarthritis pain, and asthma and allergies. Tylophora indica is considered an effective remedy for asthma and is becoming increasingly popular for its treatment. Due to its vast medicinal importance, Tylophora indica is exploited on a large scale, and its uncontrolled and unmonitored harvesting from the wild has led to its categorization as an endangered plant species.

Keywords: Anti-inflammatory; carrageenan; formalin; ibuprofen; *Tylophora asthmatica*, Tylophorine, Alkaloids, Endangered.

Introduction:

About 60 species of thin climbing perennial plants from all over the world belong to the Tylophora family. Tylos, which means "knot," and phoros, which means "bearing," are two ancient Greek words from which this name is derived.

Tylophora indica (Burm f.) Merill. (Family: Asclepiadaceae) commonly known as Antmul is a twining perennial This name has been derived from two ancient Greek words – 'Tylos' meaning "knot" and 'phoros' plant distributed throughout southern and eastern part of India in plains, forests, and hilly places [1]. The plant is found growing normally in Uttar Pradesh, Bengal, Assam, Orissa, Himalayas and sub-Himalayas in India [2]. It is a branching climber or shrub that grows up to 1.5 meters, leaves are obviate-oblong to elliptic-oblong, 3-10cm long and 1.5-7cm wide [3]. Roots Long fleshy with longitudinally fissured light brown, corky bark. Flowers minute, 1-1.5 cm across, in 2-3 flowered fascicles in axillary umbellate cymes. Calyx divided nearly to the base, densely hairy outside; segments lanceolate, acute. Corolla greenish yellow or greenish purple; lobes oblong, acute. Fruit a follicle, up to 7 × 1cm, ovoid lanceolate, tapering at apex forming fine micro, finally striate, glabrous, Seeds 0.6-0.8 × 0.3-0.4cm long [4]

The leaves & roots of Tylophora indica have been included in Bengal Pharmacopoeia since 1884.

Tylophora indica (Burm. f.) Merrill (family Asclepiadaceae) commonly known as 'Antmool'. Plant is traditionally used as a folk remedy in the treatment of bronchial asthma, bronchitis, rheumatism, allergies, inflammation, dysentery, whooping cough, diarrhea. The leaves and roots of the plant contain 0.2-0.46 % therapeutically important alkaloids viz. tylophorine, tylophorinine and tylophorinidine.

Tylophora Indica is an important Indian medicinal plant used to traditionally used respiratory diseases, especially for bronchial asthma. Its leaves and roots contain bioactive compounds such as alkaloids, which have immunomodulatory, anti-inflammatory, and bronchodilatory effects, which help to relieve respiratory symptoms. While clinical studies have shown some benefits, scientific evidence is not widespread, and there are concerns about safety during pregnancy and breastfeeding.

FIGURE No.1

Botanical Name: Tylofora Indica (Berm F.) Merrill.

Synonym: Tylophora asthmatica (Linn. F.).

Common Name: Antmul.

Tam. - Naye-pallai

Phytochemical Profile:

The active constituents of Tylophora indica are phenanthroindolizidine alkaloids like tylophorine, tylophorinine, tylophorinidine and septidine. Recently some rare alkaloids namely tyloindicines A, B, C, D, E, F, G, H, I, and J, desmethyltylophorine, desmethyl tylophorinine, isotylocrebrine, anhydroustylophorinine, anhydrous-dehydrotylophorinine, γfagarine, skimmianine, 14- hydroxyisotylocrebrine, 4,6- desmethylisodroxy-oMethyltylophorinindine have been reported. The non-alkaloidal compounds isolated from Tylophora indica are kaempferol, quercetin, α- and β- amyrins, tetratriacontanol, octaosanyl octacosanoate, sigmasterol, β-sitosetrol, tyloindane, cetyl-alcohol, wax, resin, coutchone, pigments, tannins, glucose, calcium salts, potassium chloride, quercetin and kaempferol.

The steam distillation of an intoxicated extract of air-dry root powder gave a small amount of P-Methoxylisaldihyde and oily substance

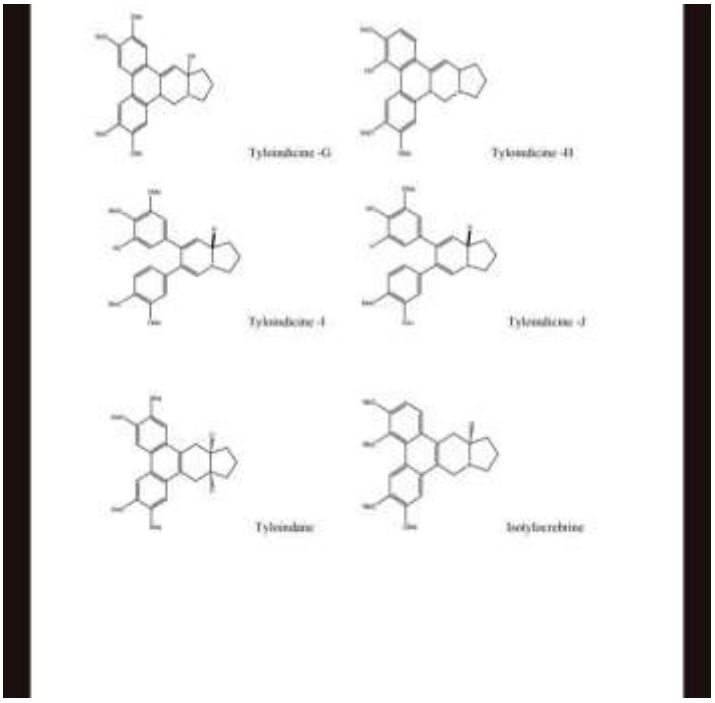

FIGURE No.2

Pharmacological effects:

1. Anti-inflammatory activity:

Tylophora indica has been used traditionally as a remedy for various anti-inflammatory activities against asthma, bronchitis, bronchial asthma, hay fever and rheumatism. The major alkaloid tylophorine is conceivable to account for the therapeutic efficacies. Anti-inflammatory activity of phenanthroindolizidine alkaloids were examined in an in vitro system mimicking acute inflammation by studying the suppression of lipopolysaccharide (LPS)/interferon (IFN) induced nitric oxide production in RAW264.7 cells. Two of the phenanthroindolizidine alkaloids, tylophorine and ficuseptine-A, exhibited potent suppression of nitric oxide production and did not show significant cytotoxicity to the LPS/IFN stimulated RAW264.7 cells

2. Anticancer activity:

Tylophorine and its analogs have gained attention for drug development and have been proposed to exert antitumor effects in a novel mode of action 16. Tylophorine analogs were found to inhibit the activity of cAMP response elements in HepG2 lung carcinoma cells treated with forskolin, TPA, and TNFα respectively. Tylophorine retarded S-phase progression along with arrest of growth at G1 phase in HepG2, HONE-1 and NUGC-3 in carcinoma cells. Another two phenanthroindolizidine alkaloids namely, pergularine and tylophorinidine, were found to inhibit the activity of dihydrofolate reductase and thymidylate synthase, highlightening the mechanism of action for anticancer activity.

3. Antihistaminic activity:

Studies were carried out to elucidate the anti-allergic activity of tylophorine and other related alkaloids. The anti-allergic effect of aqueous extract of Tylophora indica was compared with that of disodium cromoglycate on perfused rat lung in sensitized rats by observing the changes in the volume of the perfusate per minute. Administration of extract intraperitoneally (5 mg/kg) increased the rate of flow from 7.65 to 19.55 ml/min. The action of Tylophora indica may be due to direct bronchodilator property and membrane stabilizing and immuno-suppressive effects.

4. Liver-shielding activity:

Alcoholic (ALLT) and aqueous (AQLT) extracts of leaves of Tylophora indica were assessed for hepatoprotective activity in ethanol-induced hepatotoxic rats. Ethanol produced significant changes in physical, biochemical, histological and functional liver parameters but pretreatment with ALLT or AQLT extract significantly prevented all these changes induced by ethanol in the liver. This clearly indicates that both the extracts possessed hepatoprotective activity although it was much higher in the alcoholic extract as compared to aqueous extract 21. Methanolic extract of T. indica leaves was also screened for hepatoprotective activity in carbon tetrachloride induced hepatotoxic albino rats 22. Significant reduction in serum hepatic enzymes was observed when compared to rats treated with carbon tetrachloride alone.

5. Microbicidal activity:

Antimicrobial activity of ethyl acetate and methanolic leaf extracts of T. indica were investigated by well-diffusion method against bacterial pathogens (such as Pseudomonas aeruginosa, Klebsiella pneumoniae, Escherichia coli, Staphylococcus aureus and Salmonella typhi) mainly associated with HIV. Highest inhibitory activity when compared with all treatments was shown by the methanolic leaf extract of Tylophora indica. Similarly in another study, aqueous and alcoholic extracts of in vitro raised plants of Tylophora indica were evaluated for antimicrobial activity against Staphylococcus aureus, Streptococcus agalactiae, Enterococcus faecalis, Staphylococcus epidermidis, Streptococcus pyogenes and Bacillus species. The study clearly showed that alcoholic extract of in vitro raised plants showed significantly higher levels of antibacterial activity against Staphylococcus aureus, Staphylococcus epidermidis and Bacillus species but aqueous leaf extract showed antimicrobial activity only against S. epidermidis.

6. Fluid-eliminating activity:

Aqueous and alcoholic leaf extracts of T. indica were studied for diuretic activity in rats. Different parameters like body weight before and after test period, total urine volume, urine concentration of Na^+ , K and Cl^- were examined per rat and it was concluded that both alcoholic and aqueous extracts possessed good diuretic activity. Urine volume, cation and anion excretion, Na^+ /K^+ ratio increased thereby supporting the ethno pharmacological use of leaf extracts as a potential diuretic 25 .

7. Immunomodulatory activity:

Immunomodulatory activity of Tylophora alkaloids were studied in in vivo systems. Crude extract of the leaves of Tylophora indica inhibited delayed hypersensitivity reaction to sheep red blood cells in rats when the alkaloid mixture was administered before and after immunization with these cells. The alkaloid mixture also inhibited contact sensitivity to dinitrofluorobenzene in mice when given prior to or after contact sensitization 26 .

Indigenous pharmacological relevance:

The ethnic medicinal relevance of Tylophora Indica lies in its traditional use in Indian medicine, especially for respiratory and inflammatory conditions such as asthma and allergies. Scientific studies have validated many of these uses, showing that the plant has powerful opponents, inflammatory, immunomodulatory and anticancer activities, which are responsible for their active components such as tiloforin and other phenantroindolizidine alkaloids.

Inflammation-modulating mechanism:

Tylofora Indica mainly increases its anti-inflammatory action through alkaloid tiloforin, which interfere with mast cell activity, suppresses cellular immune responses by disrupting lymphocyte functions and prevents MRNA translation of pro-inflammatory factors, and prevents microglia cell activity to reduce microglia cell activity Controls Changes in the action of the plant also include

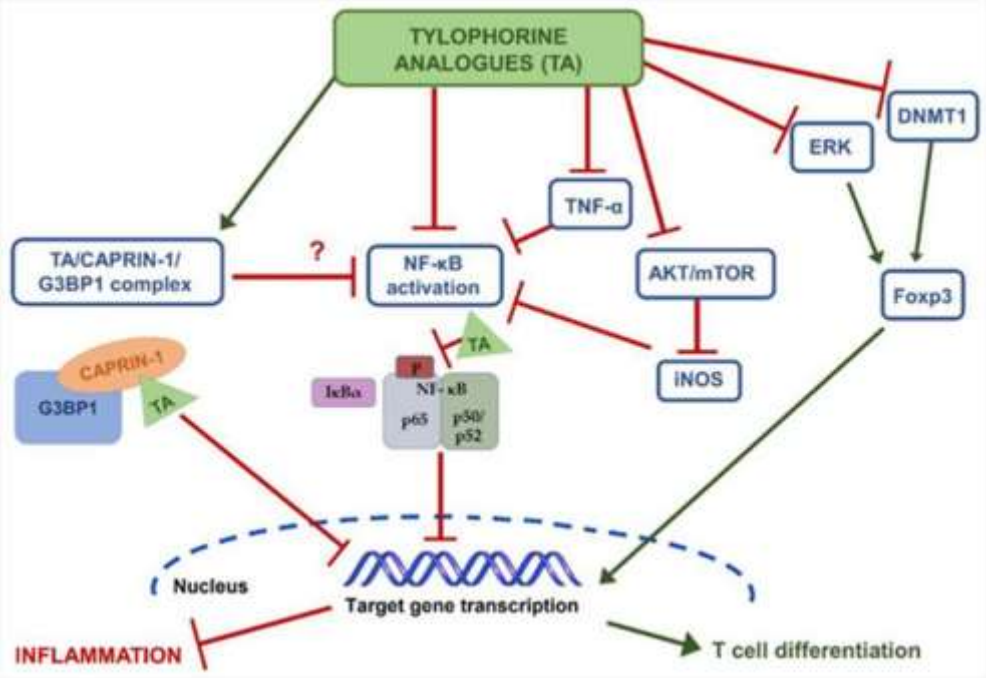

FIGURE NO.3

Interference of Mast cell:

Test tube experiments have demonstrated that tylophorine interferes with mast cells, which are essential elements in the inflammatory process.

Immune system modulation

• Cellular Immunity Inhibition:

Tylophora alkaloids suppress cellular immune responses, such as delayed hypersensitivity and contact sensitivity, in animal models. •Both pre clinical and clinical research have shown that Tylophora Indica has strong anti -inflammatory properties. In vitro and vivo tests showed that it can reduce the model of inflammatory indicators and inflammation, especially the active ingredient tiloforin. Although several studies have begun to examine its use, additional clinical verification of its efficacy and safety requires clinical verification, even though evidence suggest medical benefits for inflammatory diseases such as asthma, autoimmune diseases and neuroinphlamation.

Pre-Value Studies (in in vitro and vivo)

• In vitro studies: These laboratory-based research projects, which often employ cell cultures, have displayed that T. Indica extracts and its isolated compounds, such as tiloforin, can interfere with the functioning of cells, such as mast cells and microglial cells, which are important for inflammation. • In Vivo Research: T. Indica's anti -inflammatory properties are displayed in animal models, including:

• Panj Edima Model: Research on Albino mice has shown that T. In models such as indica extracts, especially methanolic extracts, formalin-induced and cargenon-induced claws, can reduce edema in models.

• Models of Neuroinflammation:

T. indica extracts have demonstrated anti-neuroinflammatory potential by inhibiting microglial cell migration, which is crucial in neurodegenerative diseases.

• Inhibition of Angiogenesis:

Tylophorine has been shown to suppress tumor growth and angiogenesis (blood vessel formation) in mice by targeting signaling pathways.

Safety and Toxicology profile:

Tylophora indica shows potential for treating respiratory inflammation but carries gastrointestinal side effects like nausea and vomiting, especially with chewing the leaves. Safety data are limited to short-term use, and comprehensive studies are lacking, so Tylophora should not be used by children,

pregnant or nursing women, or individuals with severe kidney or liver disease. The most common adverse effects are gastrointestinal, and taking leaves as capsules instead of chewing can reduce these effects.

Formification and Distribution System:

Tylofora Indica Yogas typically include extracting plant content using solvents such as ethanol or petroleum ether, followed by extracts. For respiratory conditions, this extract can be included in various delivery systems, such as capsules, a leaf powder mixed with glucose, or hydrolyic extracts, mainly with active compounds, mainly alkaloid toolophorin, targets the inflammatory passage to provide an anti -inflammatory effect.

Future Aspects:

The future possibilities of Tylophora Indica for the treatment of respiratory diseases are promising, supported by its traditional use to asthma and anti -inflammatory properties, especially its phenthroindolizidine alkaloids. Further research and clinical trials are essential to develop effective, well-tolerated pharmaceuticals, which take advantage of their ability to address anti-allergies and anti-ant-inmatic effects to address respiratory conditions.

Conclusion:

Tylophora indica is a medicinal plant that has long been used in Ayurvedic and folk medicine. Its main bioactive constituents, particularly alkaloids like tylophorine, tylophorinine, and septicine, have been shown to: Inhibit the production of pro-inflammatory cytokines (e.g., TNF-α, IL-1β, IL-6) Suppress the activation of NF-κB, a crucial transcription factor involved in inflammation; Reduce histamine release and mast cell degranulation, which limits allergic reactions; Display bronchodilatory effects, which improve airflow in obstructive respiratory conditions. Preclinical research (in vitro and in vivo models) has validated the plant's capacity to control immune cell activity, lessen eosinophil infiltration, and minimize airway inflammation. Its effectiveness in lessening the frequency and intensity of asthma attacks and enhancing respiratory function is supported by certain preliminary clinical trials and ethnopharmacological evidence. Nevertheless, several human trials have found gastrointestinal adverse effects (such as nausea and vomiting), toxicity at high doses, and issues with dose standardization. For safe clinical usage, standardized extracts and regulated dosage schedules are therefore required.

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