

## Review Article

### *Tylophora indica* : A brief review on pharmacological Aspects

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#### Abstract

Herbal medicines have been used in the ancient practice in India because the subcontinent is rich in plants and herbs with useful biological effects of medicinal importance. In this review article we are giving an update on pharmacological updates in short about indigenous plant *Tylophora indica* in Indian subcontinent with the objective to see an insight on its role in its contribution in curing various illness and diseases. *Tylophora indica* is a climbing perennial plant which grows wildly in the southern and eastern belt of India. It has been known to show various biological effects like laxative action, expectorant, ant allergic, antifungal, anticancer etc. The plant has a long reputation in curing various health ailments including asthma, bronchitis, rheumatism and other respiratory problems. It also reported as anti-inflammatory effect so used in treatment of inflammatory conditions like osteoarthritis, and bronchitis. It is used too in hay fever, bronchitis, common cold could be responsible for its biological activity.

**Keywords:** *Tylophora indica*, anticancer, anti-inflammatory, antiallergic

#### Introduction

*Tylophora indica* (Burm f.) Merrill. (Family: Asclepidaceae) generally popular as Antmul is a twining perennial plant seen in southern and eastern region of India in planes, forests and hilly areas. This is seen growing in many states in India like Bengal, Uttar Pradesh, Assam, Orissa (Wealth of India, 1969-1972). The plant is a climber or shrub with branches and is observed growing up to height of 1.5 meters, Leaves shape are ovate-oblong to elliptic-oblong with 3-10 cm length and 1.5-7 cm width (Kirtikar and Basu, 1991). Plant roots are long fleshy and fissured along the length and are with light brown, corky bark. The plant has little size flowers and are 1-1.5 cm across, in 2-3 flowers fascicles (bundle) in axillary umbellate cymes. Calyx has divisions almost to the base, looks massively hairy from outside; segments lanceolate, acute. Corolla is green to yellow or green to purple, lobes oblong and acute. Fruit a follicle, up to 7 X 1 cm, ovoid lanceolate, tapering at top forming fine mucro, finally striate, glabrous, seeds 0.6-0.8 X 0.3-0.4 cm long. The

plant is originated from India. The plant can be found at an elevation of 1260 m in the sub Himalayan tract, central, peninsular India. It is seen in Eastern, North-east and Bengal and parts of South India. *Tylophora indica* is a perennial plant with long thick roots branching climber. The plant is observed growing in planes and hilly land in India upto an altitude of 1000 meter in various states like Assam, Bengal, Orissa (Gupta, 2003).

#### Phytochemistry

The plant contain various active ingredients like tylophorine, tylophorinine, tylophorinidine and in plant body, leaves roots (Mohammad, 2008) Roots and leaves of plant also contain septidine too.

The plant body also contain alkaloids were reported desmethyltylophorine, methyltylophorinidine, isotylocrebrine, skimmianine, gamafagarine. The compounds which are non alkaloidal and isolated are quercetin, kaempferol, octacosanoate, sigmasterol, beta-sitosterol, tyloindane, cetylalcohol, wax, resin, couthone, pigments, tannins, glucose, calcium salts, potassium chloride (Gupta et al., 2010).

#### Pharmacological activities

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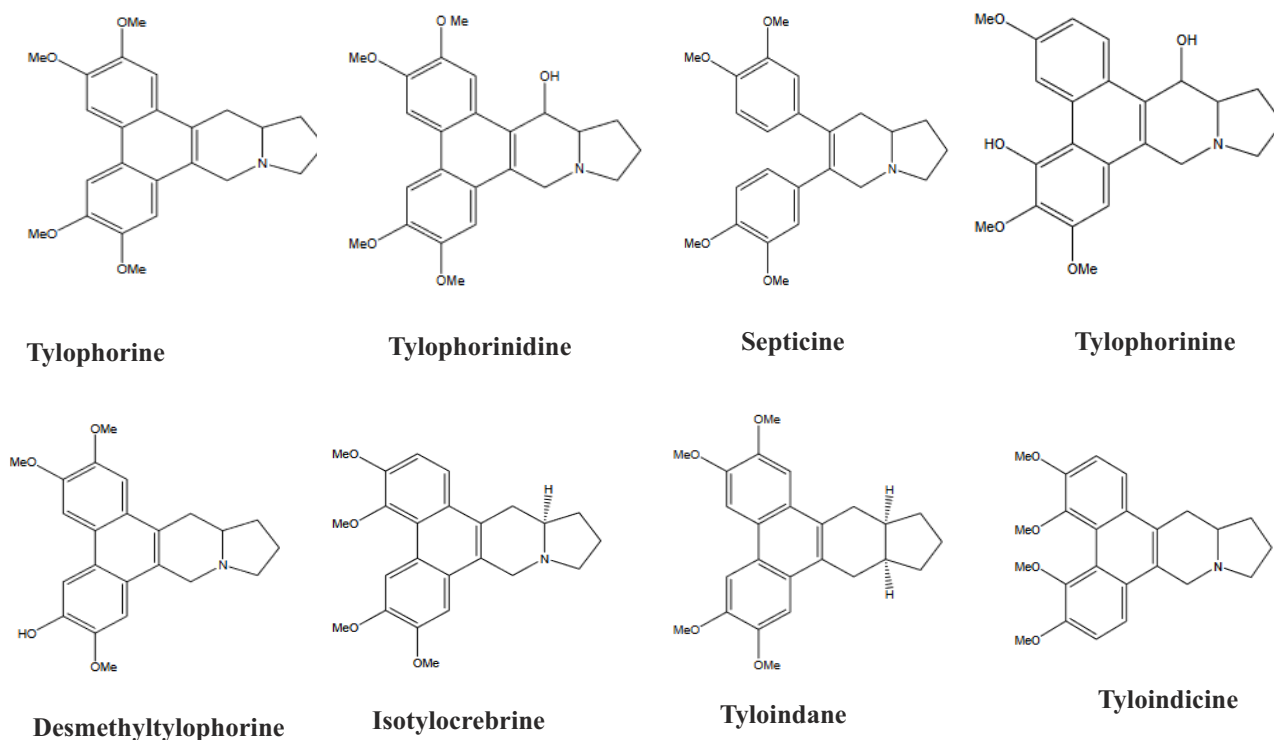
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**Figures 1.** Structures of major constituents

### Hepatoprotective activity

*Tylophora indica* was tested for hepatoprotective activity in carbon tetrachloride induced hepatotoxicity in albino rats with their methanolic extract of leaves. Various biochemical parameters like serum glutamate oxaloacetate transaminase, serum glutamate pyruvate transaminase, total protein and level of serum bilirubin were measured too. A comparison of hepatoprotective activity of methanolic extract was made with silymarin treated animals. It concluded that *Tylophora indica* leaves showed reduction in serum hepatic enzymes when compared to rats treated with carbon tetrachloride alone which were well supported by histopathological studies performed later (Gujrati et al., 2007).

### Diuretic activity

*Tylophora indica* leaves solvent extracts was tested for diuretic activity and it was found that the aqueous and alcoholic extracts of *Tylophora indica* leaves have significant diuretic activity. It was found that ethanolic extract was more effective in increasing concentration of all the electrolytes sodium and potassium ions followed by chloroform and aqueous extracts than other extracts (Meera et al., 2007).

### Antiasthmatic activity

Traditionally the plant has been utilized in therapy of asthma in ayurvedic treatments history. The powder of alkaloid of

*Tylophora indica*, about 400-500mg given once daily for asthmatic patients for six days to cure asthma (Shivpuri et al., 1968). Traditionally doses of 250mg 1-3 times daily standardized to 0.1% of plant per dose have been used. Some experts have suggested the administration of plant leaves in the amount of 200-400mg dried herb daily too. Some findings based on clinical trial have suggested the use of alcoholic extract of *Tylophora indica* daily for a week too with dose 40mg. The root or leaf powder have been given in diarrhea, dysentery, intermittent fever. It was seen in a study that when asthmatic children human peripheral leukocytes were exposed to plant alkaloid Tylophorine it led to stimulation of adenylcyclase and the same was not seen in the leukocytes with the children adults having no asthma (Shivpuri et al., 1972).

### Antiallergic activity

Studies were made to find the anti-allergic activity of tylophorine and other related alkaloids and a comparison was made of anti-allergic effect of aqueous extract of *Tylophora indica* with that of disodium cromoglycate on perfused rat lung in sensitized rats by observing the changes in the volume of the perfusate per minute. Intraperitoneal administration of extract intraperitoneally (5 mg/kg) increased the rate of flow from 7.65 to 19.55 ml/min. It was concluded that the action of *Tylophora indica* may be due to

direct bronchodilation and immune-suppressive effects (Sundana et al., 1979).

#### Antimicrobial activity

*Tylophora indica* was checked for antimicrobial activity for its alkaloids of phenanthroindolizidine nucleus i.e. tylophorinidine hydrochloride, tylophorinidine hydrochloride. These were isolated from the plant and checked for antifungal and antibacterial activity in vitro. Antifungal effect with minimum inhibitory concentration in the range of 2-2.5 microgram/ml against the candida species was noticed (Reddy et al., 2009). One more study where, antimicrobial and antifeedant effect was noticed later where crude and pure extracts of *Tylophora indica* displayed strong antibacterial activity at lower concentration in all tested bacterial strains except *E. coli* while all the crude and pure compounds had strong antifungal activity against *Aspergillus niger*, *Aspergillus fumigates*, *Trichoderma viridae*, the pure compounds had strong antifungal activity compared to crude extracts (Dhiman et al., 2012).

#### Mast cell stabilization activity

Geetha et al. (2009) did a study and tested the mast cell stabilizing effect of the alkaloids of the plant with disodium chromoglycolate against three different mast cell degranulators, diazoxide, carbachol and polymixin B, in vitro and the results were concluded that *Tylophora* alkaloids may have similar mechanism of action like of disodium cromoglycolate via cyclic AMP (Geetha et al., 2009).

#### Anticancer activity

It was investigated and found Tylophorine not only slow down the S-Phase advancement but also strongly capture the cell at G1 phase in HepG2 HONE1 and NUGC-3 carcinoma cells and tylophorine exposure led to down regulated cyclin A2 expression and over expressed cyclin A2 rescues the G1 arrest by Tylophorine. It was reported that the down regulated cyclin A2 have key role in arrest of G1 by tylophorine in carcinoma cells (Chia Mao et al., 2009). Later on in a study by Kanakarajan et al. (2014) checked the anti-proliferative effect of *Tylophora indica* using its alcoholic extracts of on HCT-15 colon cancer cell lines. Antioxidant activity was checked too and was confirmed by In vitro free radical scavenging assays. During the experiments dose dependent invitro studies were made which gave confirmation of an IC50 value of 40 mcg/ml with MTT and neutral red uptake assays. Increased LDH leakages seen and indicated rise in cell membrane damage treated by ethanolic extracts of plant. EtBr/Acridine orange staining methods indicated the presence of apoptotic/ necrotic cells upon treatment with extracts, so therapeutic potential of ethanol extracts of *Tylophora indica* against colon cancer found (Kanakarajan et al., 2014).

#### Antitumor Activity

*Tylophora indica* contain phenanthroindolizidine alkaloid Tylophorine anti-inflammatory and antitumor activity, and its contribution in tumor angiogenesis, the important process during the progress of tumor and metastasis, and the behind molecular mechanism is still not found. Saraswati et al. (2013) checked its anti-angiogenic effects and mechanisms in vitro and in vivo, they used tylophorine and evaluated its inhibitory effects on human umbilical vein endothelial cells (HUVEC) in vitro and Ehrlich ascites vivo. Tylophorine found to stop processes like angiogenesis induced by VEGF endothelial cells proliferation, migration, and tube formation. Direct stopping of VEGFR2 tyrosine kinase activity and its downstream signaling pathways including Akt, Erk and ROS in endothelial cells also seen. They also demonstrated using HUVECS tylophorine inhibited VEGF-stimulated inflammatory responses including IL-6, IL-8, TNF-a, IFN-y, MMP-2 and no secretion. Tylophorine inhibited neovascularization in sponge implant angiogenesis assay and also inhibited tumor angiogenesis and tumor growth in vivo. Molecular docking simulation indicated that tylophorine could form hydrogen bonds and aromatic interactions within the ATP-binding region of the VEGFR2 kinase unit. Tylophorine exerts anti-angiogenesis effects via VEGFR2 signaling pathway thus, may be a viable drug candidate in anti-angiogenesis and anti-cancer therapies (Saraswati et al., 2013). Later on a study was made where polar various tylophorine derivatives with phenanthrene nucleus were produced in the lab and evaluated for cytotoxic activity against the A549 human cancer cell line. These were quite potent with IC50 values of 0.16 to 0.27µM & effect was comparable with antitumor drugs (Wei et al., 2006; Gao et al., 2006).

#### Nootropic Activity

Juvekar et al. (2009) conducted the studies on the possibility of nootropic activity of aqueous extract of *Tylophora indica* on cognitive functions in mice using elevated plus maze model and morris water maze model using Piracetam as standard drug for comparison. They concluded that plant roots aqueous extract appeared to be a drug for improving memory and further efforts can be made to establish the potential of plant in treatment of Alzheimer's disease, Dementia (Juvekar et al., 2009).

#### Anti-Inflammatory Activity

Anti-Inflammatory effect of *Tylophora indica* in 2006 on carrageenin induced hind paw oedema and cotton pellet granuloma in albino rats and the comparison with the

Indomethacin. They concluded that the plant possess anti-inflammatory effect in both acute and subacute inflammation (Raj et al., 2006).

#### Antioxidant activity

A study for finding the antioxidant use of plant by using its aqueous and alcoholic leaf extract of *T. indica* leaves, in vitro by doing the LPO, CAT and SOD assay procedures. It was found that that aqueous extract has superior antioxidant property than of alcoholic extract. Experimental results disclosed that the leaf extract of *T. indica* (AQTL) given rise in the activity of superoxide dismutase and decreased the level of LPO, and it was comparable to L-ascorbic acid. So it was observed that *T. indica* leaves has antioxidant potential and must be further explored for therapeutic uses (Bhatia et al., 2013).

#### Antidiabetic activity

Researchers study to find out the effect of methanolic extract of *Tylophora indica* (Asclepiadaceae) leaves on the level of blood glucose and other biochemical parameters in rats where diabetes was induced by giving alloxone (120 mg/kg. b.w., i.p). Significant decrease ( $p < 0.001$ ) in blood glucose levels was observed. Change in lipid metabolism was seen as decrease in serum total cholesterol (TC), triglyceride (TG) and low-density lipoprotein cholesterol (LDL) levels and high-density lipoprotein cholesterol (HDL) concentration increases in diabetic rat ( $p < 0.001$ ). It concluded that *Tylophora indica* have anti diabetic effects in alloxone induce diabetes and also suggested to work further to explore the

possibility to cure diabetes (Swathi et al., 2012).

#### Cardiac activity

The hydrochloric extract of plant was checked on experimentally induced myocardial infarction in rats. Pretreatment of albino rats with plant extract was 100mg-200mg/Kg dose was done with Propranolol 10mg/Kg for 30 days & later Isoprenaline was given subcutaneously in dose of 150mg/Kg for two days to induce myocardial infarction. Pretreatment of extract and propranolol gave the myocardial protection indicated by significant decrease in lactate dehydrogenase and creatinine phosphokinase activities in serum and increase in activities of these enzymes in heart tissue homogenate. It was concluded that plant extract in higher doses improves the myocardial infarction (Asdaq and Sowmya, 2009).

#### Anticonvulsant activity

An anticonvulsant effect of ethanolic extract of *Tylophora indica* with dose 100mg/kg on MES (maximal electric shock) and PTZ (Pentylene tetrazole) induced convulsions in albino rats and it was observed that inhibition of tonic hind limb extension in MES seizures, decreased in duration convulsions in PTZ induced observed (Hafis et al., 2017).

#### Antiulcer activity

The methanolic extract of *T. indica* leaves at dose (50, 100, 200 mg/kg) produced 9.66%, 16.09%, 47.53% ulcer

**Table 1.** Pharmacological activities reported for *Tylophora indica*

Activity	Part Used	References
Antiulcer	Leaves	Ghodekar et al. (2010)
Leaves	Leaves	Ganguly et al. in (2001)
Antioxidant	Leaves	Bhatia et al. (2013)
Anti-Inflammatory Activity	Plant aerial parts	Raj et al. (2006)
Nootropic activity	Roots	Juvekar et al. (2009)
Anticonvulsant	Leaves	Hafis et al. (2017)
Antidiabetic	Leaves	Swathi et al. (2012)
Cardiac activity	Leaves	Asdaq and Sowmya, (2009)
Antitumour	Leaves	Saraswati et al., (2013)
Anticancer	Whole plant	Kanakarajan et al. (2014); Chia Mao et al. (2009)
Mast cell stabilising	Leaves	Geetha et al. (2009)
Antimicrobial	Leaves	Dhiman et al. (2012)
Antiasthmatic	Leaves	Shivpuri et al. (1972)
Antiallergic	Leaves	Sundana et al. (1979)
Diuretic	Leaves	Meera et al. (2007)
Hepatoprotective	Leaves	Gujrati et al. (2007)

inhibition and 6.57%, 8.95%, 18.68% ulcer inhibition in naproxen and histamine induced ulcer respectively. At different dose methanolic extract showed antiulcer activity against naproxen and histamine induced ulcer probably by reducing level of lipid peroxide and doing H<sub>2</sub> receptor blocking (Ghodekar et al., 2010).

### Immunomodulatory effect

Ganguly et al. (2001) reviewed that plant block cellular immune responses like contact sensitivity to dinitro-fluorobenzene and delayed hypersensitivity to sheep red blood cells in vivo. So they further tried to find targets at cellular level *Tylophora* alkaloids in vitro. Con A induced proliferation of splenocytes was taken as a model system and alkaloidal mixture seen to block proliferation of splenocytes at higher concentrations, suppress IL-2 production in Con A stimulated splenocytes at the inhibitory or higher concentrations. Macrophages, T cells found vulnerable to *tylophora* alkaloids. It was concluded that *Tylophora indica* alkaloids have a conc. dependent biphasic effects on Con A induced mitogenesis. At low concentrations they augment Con A induced lympho proliferation by increasing IL-2 production. Inhibition of proliferation at high concentrations of alkaloid is because of inhibition of IL-2 production & activation of macrophages, which have a cytostatic effect (Ganguly et al., 2001).

### Conclusion

As per the literature review it is found that there is still lot of scope and plant can be exploited for further investigation to establish its unrevealed potential and uses.

**Conflict of interest:** None

### References

- Ali Mohammad. 2008. Pharmacognosy CBS publisher & distributors, Vol-1; pp 653.
- Anonyms, The Wealth of India 1978. NISCAIR, CSIR, New Delhi,,Pg-398-399.
- Arora S, Rawat AKS. 2007. Lysosomal enzyme inhibiting activity of flavones fraction from *Tylophora indica* leaves in arthritis rats. *Pharmacognosy Magazine*, 3(12); 225-231.
- Basheeruddin AS, Sowmya KS. 2010. Effect of Hydroalcoholic Extracts of *Tylophora indica* Leaves in Isoprenaline-Induced Myocardial Damage in Rat Heart, *International Journal of Pharmacy & Technology*, 9(1): 15-20.
- Bhatia A, Anand M, Singla R, Sharma A. 2003. Antioxidant activity of native and micropropagated *Tylophora indica* leaves extract: A comparative study. *Journal of Natural Product & Plant Resources*, 3(1):1-7.
- Chia-Mao Wu, Cheng-Wei Yang, Yue-Zhi Lee, Ta-Hsien Chuang, Pei-Lin Wu, Yu-Sheng Chao and Shiow-Ju Lee, 2009, Tylophorine arrests carcinoma cells at G<sub>1</sub>phase by downregulating cyclin A2expression. *Biochemical and Biophysical Research Communications*, 386(1); 140-145.
- Dhiman M, Parab RR, Manju SL, Desai DC, Mahajan GB. 2012. Antifungal activity of hydrochloride salts of tylophorinidine and tylophorinine. *Natural Product Communications*, 7(9):1171.
- Ganguly T, Badheka LP, Sainis KB. 2001 Immunomodulatory effect of *Tylophora indica* on Con A induced lymphoproliferation. *Phytomedicine*, 8(6): 431-437.
- Gao W, Lam W, Zhong S, Kaczmarek C, Baker DC, Cheng YC. 2004. Novel Mode of Action of Tylophorine Analogs as Antitumor Compounds. *Cancer Research*, 64(2); 678-88.
- Geetha VS, Vishwanathan S, Kameshwaran L. 2009. Comparison of Total Alkaloids of *Tylophora indica* and Disodium Chromoglycolate on Mast Cell Stabilisation, *Indian Journal of Pharmacology*, 13(2); 119-201.
- Ghodekar SN, Garg H, Sharma A, Chhikara S, Gawande R, Shaikh JD, Namdeo AG, Bodhankar SL, Mahadik KR. 2010. Antiulcer activity of methanolic extract of leaf of *Tylophora indica* on histamine and naproxen induced gastric lesions in rats. *Pharmacologyonline*, 1: 141-147.
- Gujrati V, Patel N, Rao VN, Nandakumar K, Gauda TS, Shalam Md, Kumar SMS. 2007. Hepatoprotective activity of alcoholic and aqueous extracts of leaves of *Tylophora indica* (Burm F.) in rats. *Indian Journal Pharmacology*, 39; 43-47.
- Gupta AK. Quality standards of Indian medicinal Plants. 2003. *Indian Council of Medical Research* 1; 221-225.
- Gupta M, Hayat M, Sayeed Ahmad M. 2010. Phytopharmacological and Plant tissue culture overview of *Tylophora indica* (burm f.) Merrill. *Journal of Pharmaceutical Science & Research*, 2(7):401-411.
- Kirtikar KR, Basu BD. 1991. *Indian Medical Plants* 2<sup>nd</sup> Ed. Periodic experts book agency, New Delhi.; 1-5.
- Kulkarni MP, Juvekar AR. 2009. Studies on nootropic activity of roots of *Tylophora indica* in mice. *Journal of Natural Remedies*, 9(1):62-67.
- Manikkoth S, Hafis KT, Melinda S, Nayak RP. 2017. Pharmacological evidence for the anticonvulsant activity of *Tylophora indica* in experimental animal models. *International Journal of Basic & Clinical Pharmacology*, 6(4):750.
- Meera R, Devi P, Muthumani PB, Eswarapriya KB. 2009. Evaluation of Diuretic activity from *Tylophora indica* leaves extracts. *Journal Pharma Science & Research*,

- 1(3):112-116.
- Mujeeb M, Aeri V, Bagri P, Khan S. 2009. Hepatoprotective activity of the methanolic extract of *Tylophora indica* (Burm. f.) Merril. leaves. *International Journal of Green Pharmacy* 3(2):125.
- Nayampali SS, Seth UK. 1979. Evaluation of Anti-Allergic Activity of *Tylophora indica* using rat Lung perfusion. *Indian Journal of Pharmacology*, 11(3); 229-232.
- Pratheesh KV. 2014. Study on the Anti-Cancer Activity of *Tylophora indica* Leaf Extracts on Human Colorectal Cancer Cells, *International Journal Pharmacognosy & Phytochemical Research*, 6(2):355-361.
- Raj David C, M. Mohamed Shabi, Brahatheeswaran D, Mahesh N. 2006. Anti-Inflammatory Activity Of *Tylophora indica* in Albino Rats. *Journal Of Pharmacology and Toxicology* 1(5):490-492.
- Reddy BK, Balaji M, Reddy PU, Sailaja G, Vaidyanath K, Narsimha G. 2009. Antifeedant and antimicrobial activity of *Tylophora indica*. *African Journal of Biochemistry Research*, 3(12); 393-397.
- Saraswati S, Kanaujia PK, Kumar S, Kumar R, Alhaider AA. 2013. Tylophorine, a phenanthraindolizidine alkaloid isolated from *Tylophora indica* exerts antiangiogenic and antitumor activity by targeting vascular endothelial growth factor receptor 2-mediated angiogenesis *Molecular Cancer*, 12:82.
- Shivpuri DN, Menon MP, Prakash D. 1968. Preliminary studies in 6932 *Tylophora indica* in the treatment of asthma and allergic rhinitis. *Journal of Association of Physicians of India*, 16(1): 9-15.
- Shivpuri DN, Singhal SC, Prakash D. 1972. Treatment of asthma with an alcoholic extract of *Tylophora indica*: a crossover, doubleblind study. *Annals of Allergy, Asthma & Immunology*, 30:407-412.
- Swathi P, Kumar E, Kumar KJ, Vijay T. 2012. Evaluation of antihyperglycemic and anti hyperlipidemic activity of ethanolic extract of *Tylophora indica* in alloxan induced diabetic rats. *International Journal of Current Pharmaceutical Research*, 4(1); 25-31.
- Wei L1, Bossi A, Kendall R, Bastow KF, Morris-Natschke SL, Shi Q, Lee KH. 2006. Antitumor agents 251: Synthesis, cytotoxic evaluation, and structure-activity relationship studies of phenanthrene-based tylophorine derivatives (PBTs) as a new class of antitumor agents", *Bioorganic and Medicinal chemistry letters*, 14(19); 6560-6569.