

PHCOG REV.: Plant Review

Toddalia asiatica (Linn.) Lam. - A Comprehensive Review

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ABSTRACT

Toddalia asiatica (Lopez root): Rutaceae, a woody liana, is used traditionally in the treatment of malaria, sprains, cough, fever, neuralgia, epilepsy, dyspepsia and other disease conditions. Extracts of the plant have been reported to have anticancer, anti-HIV, antimicrobial, antifeedant activities. A wide range of chemical constituents such as benzophenanthridine alkaloids, coumarins, cyclohexylamides and terpenoids have been isolated especially from the root bark of the plant. This review gives insight into the detailed profile of the traditional uses, chemical constituents, biological and pharmacological actions of the plant.

Key words: *Toddalia asiatica*, Chemistry, Biological and Pharmacological activities.

INTRODUCTION

Early humans recognized their dependence on nature to be healthy and fight against illnesses. Based on instinct, taste and experience, primitive men and women treated illnesses by using plants, animal parts and minerals. Physical evidence of use of herbal remedies dates back to 6000 years. Medicinal herbs are moving from fringe to main stream use with a greater number of people seeking remedies and health approaches free from side effects caused by synthetic chemicals. A recent review on national pharmacopoeias from several countries revealed that 120 distinct chemical substances from different plants that have utility as life saving drugs. This had been achieved through chemical and pharmacological screening of only 6% of total plant species (1).

India is called the botanical garden of the world for its rich natural resources. Over 6000 plants in India are in used in traditional, folklore and herbal medicine. The Indian system of medicine has identified 1500 medicinal plants of which 500 are commonly used (2).

Toddalia asiatica, has been in folklore use in India and China from 18th century. *T. asiatica* (Linn.) Lamk. (*Paullinia asiatica* Linn., *T. aculeata* Pers., *T. effuza* Turez), belongs to family Rutaceae. It is commonly known as Lopez root, forest pepper, wild orange tree (English); Kanchanah, Tiksnaksah, Dahana (Sanskrit); Jangli Kali Mirch, Kanch, Dahan (Hindi) Konda Kasinda, Vana Kasinda, Mulla Kasinda, Erra Kasinda, Mirapakanda, Mulla Morinda (Telugu); Milagaranai, Kattumilagu (Tamil).

Taxonomic Description

Domain : Eukaryota
Kingdom : Plantae
Subkingdom : Viridaplantae
Phylum : Tracheophyta
Subphylum : Spermatophytina
Infraphylum : Angiospermae
Class : Magnoliopsida
Subclass : Rosidae
Superorder : Rutanae.

Order : Rutales
Suborder : Rutineae
Family : Rutaceae
Subfamily : Toddalioideae
Genus : *Toddalia*
Species : *Toddalia asiatica*

DISTRIBUTION

Toddalia is native of tropical Asia from India and Sri Lanka to Malaysia; also available in Mauritius and Madagascar. It is also found in Sumatra, Java, China, Philippines, tropical Africa, Mascarene Islands. It is found almost throughout India upto an altitude of 2500 m. It is common in the Nilgiri and Palni Hills and in the shrub forests of Orissa. It is also found in Mampur, Godavari agency, Mamandur, Sunkarimetta, Tirumala Hills, Satyavedu, Karka, Bhimavaram, Balapalli, Circars areas of Andhra Pradesh.

MORPHOLOGICAL DESCRIPTION

It is an evergreen climber (woody Liana) with rambling stems up to 15 m high and 10 cm diameter. Bark of the plant is pale brown, fairly smooth with numerous conspicuous pale circular lenticels, armed with small hooked prickles about 2.5 mm long raised on old stems on the top of a conical woody pedestal up to 1.2 cm high. Blaze 2.5-7.5 mm crisp, pale yellow closely mottled with sclerotic orange portions in the outer half, turning pinkish brown on exposure. Leaves are alternate, digitately trifoliate. Petiole 1.5-3 cm long. Leaflets sessile, 5-10 cm x 1.8-3.8 cm, obovate- oblong or oblong, crenulate, shortly blunt-acuminate, base acute, glabrous, criaceous, dark shining green above with many slender parallel nerves. Inflorescences with male flowers corymbose panicles, with female flowers cymose panicles, bract scale like. Flowers polygamous, 3.8-6 mm diameter, pale greenish yellow, in axillary and terminal pubescent panicles, 2.5-6.3 cm long. Stamens 4 or 5, ovary 4 or 5 locular. Fruit orange to dark red, 7.5-12mm. diameter, subglobose, with 5 shallow grooves, yellowish, seeds dark brown, several reniform, surrounded by colorless mucilage (3-8) .

PHYTOCHEMISTRY - The root bark of *T. asiatica* is a rich source of active constituents belonging to various classes of

secondary metabolites which include benzophenanthridine, quinoline, protoberberine alkaloids, coumarins, biscoumarins, furanocoumarins, benzopyrans, terpenoids, cyclohexylamides. Literature reveals that several of these chemical constituents have been isolated and studied for their pharmacological activities.

Govindachari *et.al.* (1956) showed the identity of toddalene with the alkaloid chelerythrine (9). The other alkaloids such as 8-methoxydihydrochelerythrine, dihydronitidine and dihydroavicine were isolated from the ethanolic extract of root bark. The presence of skimmianine, norchelerythrine, γ -fagarine, aculeatin, pimpinelline, isopimpinelline, toddalolactone have also been confirmed in the root bark of the plant (10). The ethanolic extract of the root was shown to contain the dimeric coumarin, toddasin (12). The coumarins, toddanol and toddanone (13), and a dimeric benzophenanthridine alkaloid, toddalidimerine (14), were also isolated from the ethanol extract of the root extracts. Other coumarins including norbraylin, 5, 7, 8-trimethoxycoumarin, bergapten and luvangetin, and the alkaloids, robustine, dictamnine and γ -fagarine have been isolated from the chloroform extract of the stem (11). The flavonoids dihydrofisetin, diosmetin, diosmin and hesperidin were also reported in the whole plant (29).

Ishii *et al.* (1991) have isolated coumarins - toddalenol, toddalosin, 5-methoxysuberenon, toddalene, 8-formylmettin along with benzophenanthridine alkaloids - des-N-methylchelerythrine, oxychelerythrine, arnottianamide, oxyavicine; quinoline alkaloids - N-methylflindersine, 4-methoxy-1-methyl-2-quinolone, skimmianine, integriquinolone; triterpenoid - β -amyrin and four unknown components from the root bark (18). Toddacoumalone, a mixed dimer of coumarin and quinolone (20); toddacoumaquinone, a coumarin-naphthoquinone dimer (22); toddaquinoline, a benzo[h]quinoline alkaloid (23) and

toddalosin, a biscoumarin (24) were also isolated from root bark.

Ping *et al.* (2005) have isolated the triterpenoids - 2 α ,3 α ,19 α -trihydroxy-urs-12-en-28-oic acid, 2 α ,3 α ,11 α ,19 α -tetrahydroxy-urs-12-en-28-oic acid, 2 α ,3 α ,19 α -trihydroxy-olean-11,13(18)-dien-28-oic acid and 2 α ,3 α -dihydroxy-19-oxo-18,19-seco-urs-11,13(18)-dien-28-oic acid(26). The alkaloids like N-methyl-4-hydroxy-7-methoxy-3-(2,3-epoxy-3-methylbutyl)1H-quinolin-2-one and 3-(2,3-hydroxy-3-methylbutyl)-4,7-dimethoxy-1-methyl-1H-quinolin-2-one were isolated from the dichloromethane:methanol (1:1) and methanol extracts of leaves and stems (27).

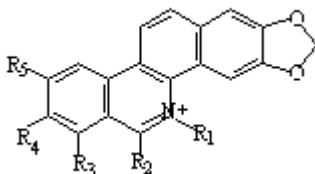
IL Tsai *et al.* (1997) have isolated toddasiatin, a dimeric coumarin and N-cyclohexylamides from the root bark and root wood. Integriamide, toddanin, (-)-isocoreximine, cyclohexylamine, peucedanol methyl ether, 2,6-dimethoxy-p-benzoquinone, haplopine,oxyterihannine and dl-lyoni-resinol have been reported from the methanolic extract of root wood (25). Ignacimuthu and Duraipandian (2007) have isolated 2,2-dimethyl-2h-benzo(h)chromen-5(6h)-one from *T. asiatica* (28).

The different terpenoids isolated from *T.asiatica* include α -pinene, β -pinene, p-cymene, d-limonene, linolyl acetate, linalool, α -thujene, α -terpineol, terpinolene, myrcene, α -borneol, bornyl acetate, camphene, eugenol, methyl chavicol, 1,8-cineol, ocimene, bisabolene, geraniol, azulene, citronellal, Δ^3 -carene, unidentified alcohol (17,46) .

Stigmasterol, β -sitosterol, lyoni-resinol, dl-syringaresinol, oxyterihannine, integriamide, peucedanol methylether, dotriacontanol, hexacosanoic acid, heptacosanoic acid, euscaphic acid, arjunic acid, benzoic acid, D-mannitol, rhamnose have been isolated and from various parts of the plant (27).

The various classes of chemical constituents isolated so far from *T. asiatica* along with their structures are shown in fig.1-11.

BENZOPHENANTHRIDINE ALKALOIDS



	R ₁	R ₂	R ₃	R ₄	R ₅
Nitidine	CH ₃	--	--	OCH ₃	OCH ₃
Chelerythrine	CH ₃	--	OCH ₃	OCH ₃	--
Norchelerythrine	--	--	OCH ₃	OCH ₃	--
Chelerythrine ψ cyanide	CH ₃	CN	OCH ₃	OCH ₃	--
Avicine	CH ₃	--	--	O-CH ₂ -O	--

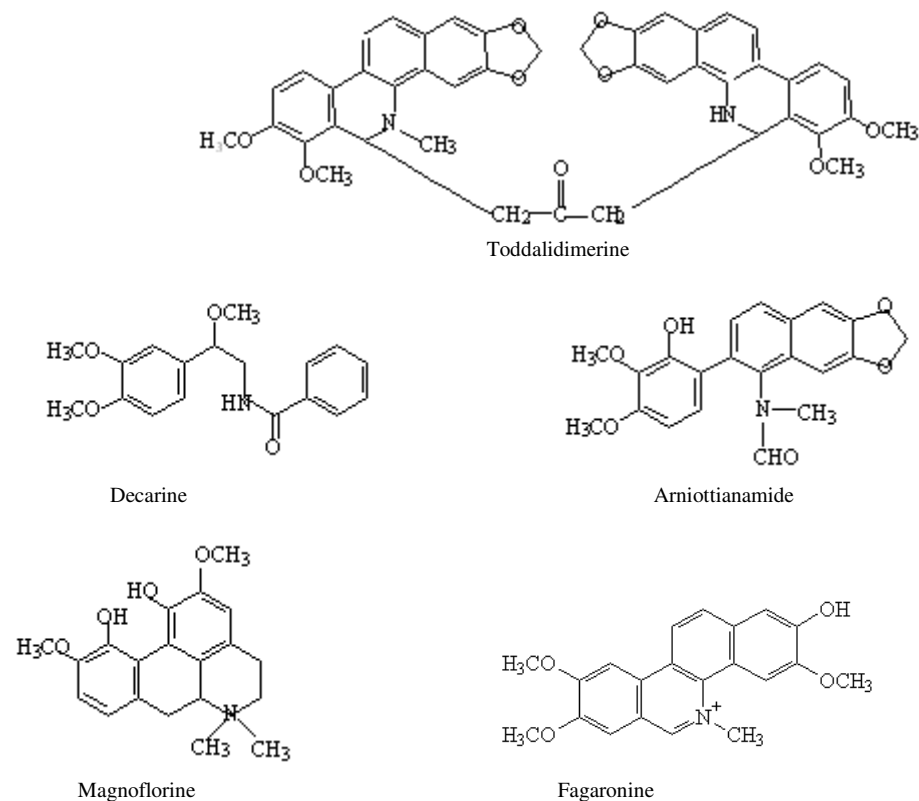
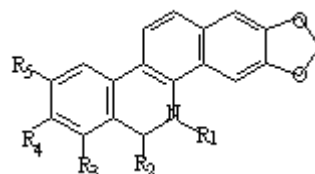


Fig.1

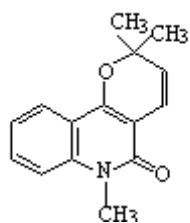
DIHYDROBENZOPHENANTHRIDINE ALKALOIDS



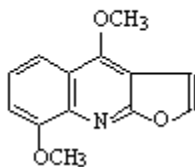
	R ₁	R ₂	R ₃	R ₄	R ₅
Dihydrontidine	CH ₃	--	--	OCH ₃	OCH ₃
Oxynitidine	CH ₃	= 0	--	OCH ₃	OCH ₃
Dihydrochelerythrine	CH ₃	--	OCH ₃	OCH ₃	--
Oxychelerythrine	CH ₃	= 0	OCH ₃	OCH ₃	--
8-hydroxydihydrochelerythrine	CH ₃	OH	OCH ₃	OCH ₃	--
8-methoxydihydrochelerythrine	CH ₃	OCH ₃	OCH ₃	OCH ₃	--
8-acetyldihydrochelerythrine	CH ₃	CH ₂ -COCH ₃	OCH ₃	OCH ₃	--
Dihydroavicine	CH ₃	--	--	O-CH ₂ -O	
Oxyavicine	CH ₃	= 0	--	O-CH ₂ -O	

Fig.2

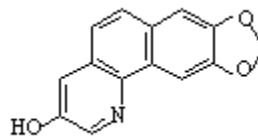
QUINOLINE ALKALOIDS



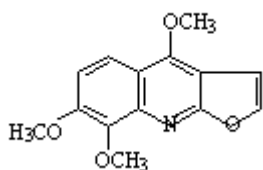
N-methyl flindersine



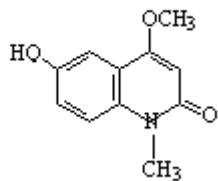
Haplopine



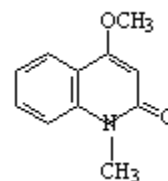
Toddaquinoline



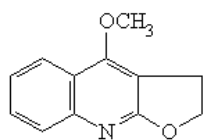
Skimmianine



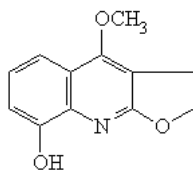
Integriquinolone



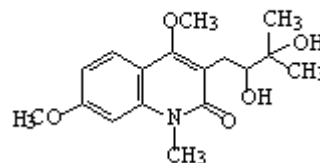
4-methoxy-1-methyl-2-quinolone



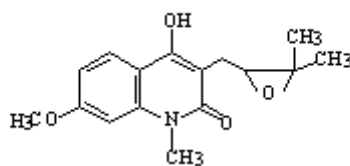
Dictamnine



Robustine



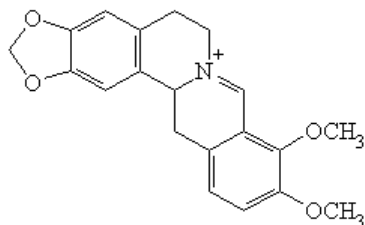
3(2,3-dihydroxy-3-methyl-butyl)-4,7-dihydroxy-1-methyl-1H-quinolin-2-one



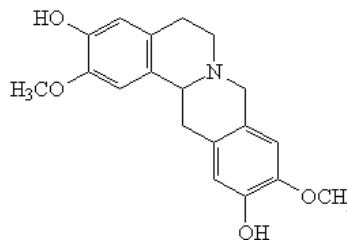
N-methyl-4-hydroxy-7-methoxy-3-(2,3-epoxy-3-methyl-butyl)-1H-quinolin-2-one

Fig.3

PROTOBERBERINE ALKALOIDS



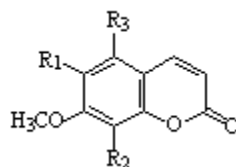
Berberine



Isocoreximine

Fig.4

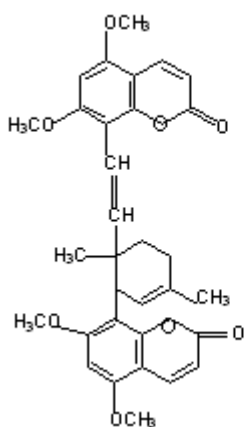
COUMARINS



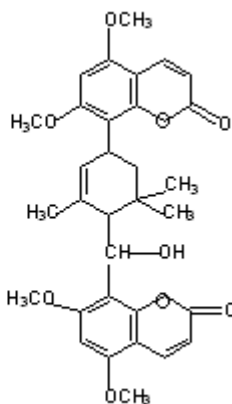
	R ₁	R ₂	R ₃
5,7,8-trimethoxy-coumarin	--	OCH ₃	OCH ₃
Toddaolactone	$\text{---CH}_2\text{-CH-C}\begin{matrix} \text{CH}_3 \\ \text{OH} \\ \text{CH}_3 \end{matrix}$	--	OCH ₃
Aculeatin	$\text{CH}_2\text{-CH-O-C}\begin{matrix} \text{CH}_3 \\ \text{CH}_3 \end{matrix}$	--	OCH ₃
Toddanol	$\text{-CH}_2\text{-CH-OH-CH=CH}_2$	--	OCH ₃
Toddanone	$\text{-CH}_2\text{-CH=O-CH(CH}_3)_2$	--	OCH ₃
Toddaculin	$\text{-CH}_2\text{-CH=CH(CH}_3)_2$	--	OCH ₃
Suberosin	$\text{-CH}_2\text{-CH=CH(CH}_3)_2$	--	--
5-methoxy-suberenone	-CH=CH-C(=O)CH_3	--	OCH ₃
Coumurrayin	--	$\text{-CH}_2\text{-CH=CH(CH}_3)_2$	OCH ₃
Coumurrenol	--	$\text{-CH=CH-C}\begin{matrix} \text{CH}_3 \\ \text{OH} \\ \text{CH}_3 \end{matrix}$	OCH ₃
8-(3,3-dimethyl allyl)-6,7-dimethoxy-coumarin	OCH ₃	$\text{-CH}_2\text{-CH=CH(CH}_3)_2$	--
Toddalenol	$\text{-CH=CH-C}\begin{matrix} \text{CH}_3 \\ \text{OH} \\ \text{CH}_3 \end{matrix}$	--	OCH ₃
Toddalenone	--	-CH=CH-C(=O)CH_3	OCH ₃
6-(2-hydroxy-3-methoxy-3-methyl-butyl)-5,7-dimethoxy-coumarin	$\text{CH}_2\text{-CH-C}\begin{matrix} \text{CH}_3 \\ \text{OCH}_3 \\ \text{CH}_3 \end{matrix}$ OH	--	OCH ₃
6-(3-chloro-2-hydroxy-3-methyl-butyl)-5,7-dimethoxy-coumarin	$\text{-CH}_2\text{-CH}_2\text{-CH-C}\begin{matrix} \text{CH}_3 \\ \text{Cl} \\ \text{CH}_3 \end{matrix}$ OH	--	OCH ₃
Limettin	--	--	OCH ₃
6-formyl limettin	CHO	--	OCH ₃
8-formyl limettin	--	CHO	OCH ₃
7-methoxy-coumarin	--	--	--

Fig.5

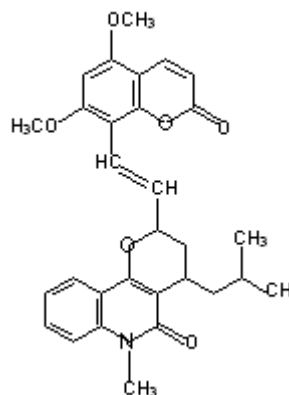
BISCOUMARINS



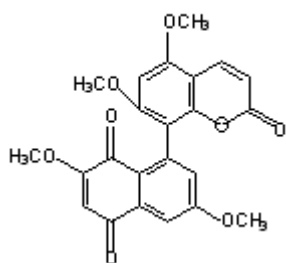
Toddasin



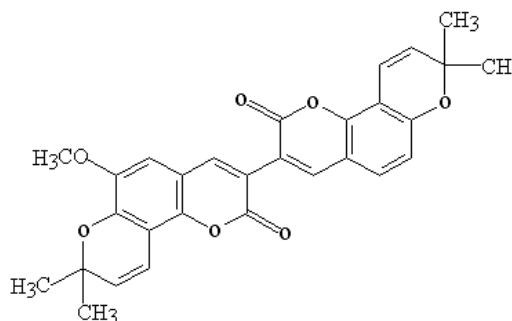
Toddalosin



Toddacoumalone



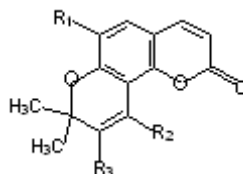
Toddacoumaquinone



Toddasiatin

Fig.6

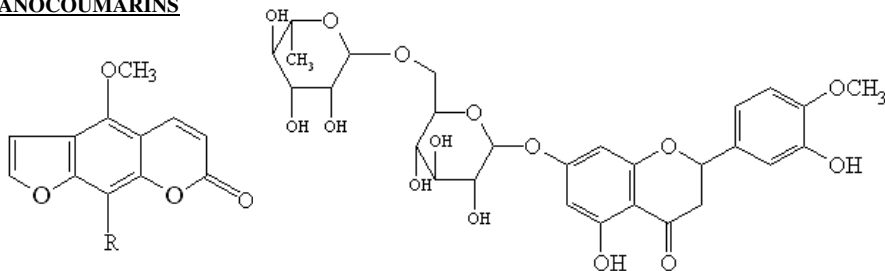
PYRANOCOUMARINS



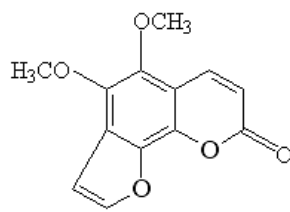
	R ₁	R ₂	R ₃
Braylin	OCH ₃	--	--
Norbraylin	OH	--	--
Luvangetin	--	OCH ₃	--
Toddanin	OCH ₃	H	OH

Fig.7

FURANOCOUMARINS



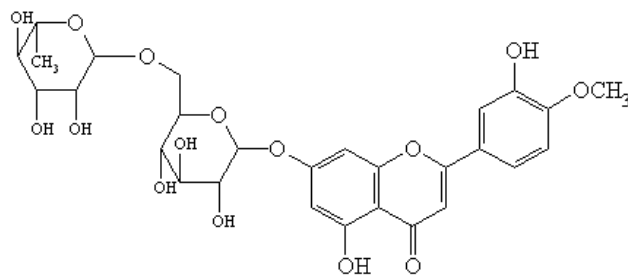
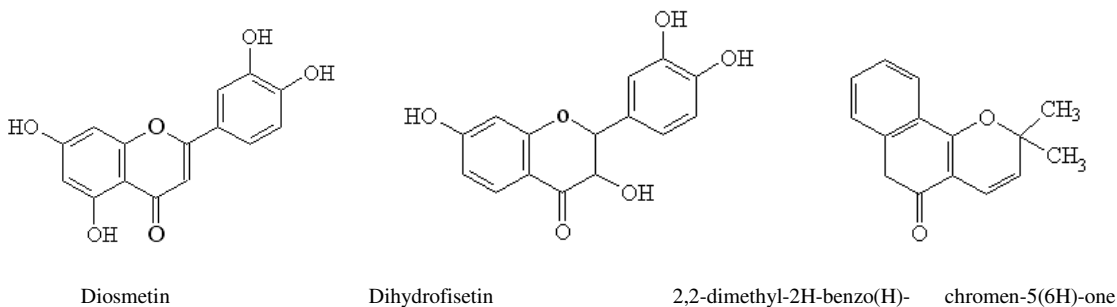
	R
Bergapten	--
Isopimpinellin	OCH ₃
Phellopterin	$-\text{OCH}_2\text{CH}=\text{CH}\begin{matrix} \text{CH}_3 \\ \text{CH}_3 \end{matrix}$



Pimpinellin

Fig.8

BENZOPYRANONES

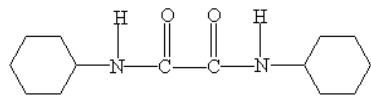


Diosmin

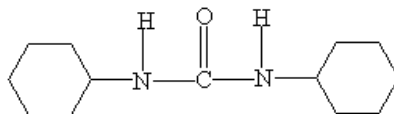
Hesperidin

Fig.9

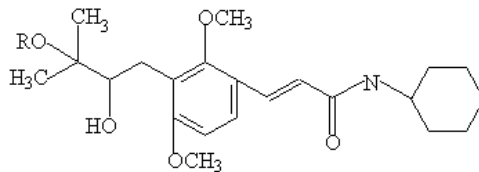
CYCLOHEXYLAMIDES



N,N'-dicyclohexyloxamide



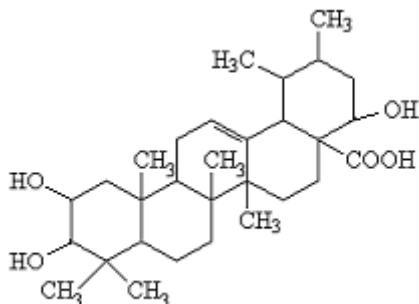
N,N'-dicyclohexyl urea



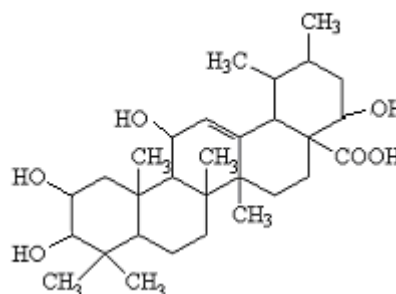
Toddaliamide : R= H
Methyl Toddaliamide R= CH₃

Fig.10

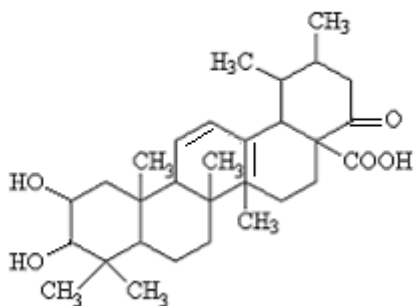
TRITERPENOIDS



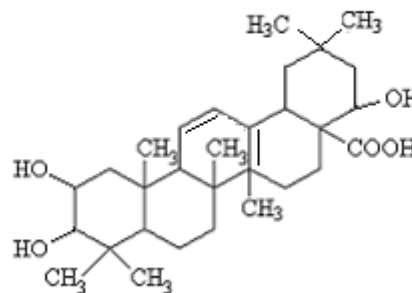
2,3,19-trihydroxy-urs-12-en-28-oic acid



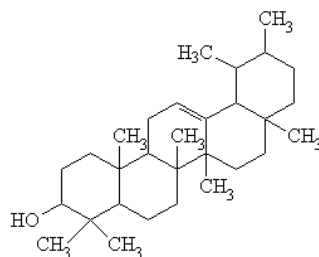
2,3,11,19-tetrahydroxy-urs-12-en-28-oic acid



2,3-dihydroxy-19-oxo-18,19-seco-urs-12-en-28-oic acid



2,3,19-trihydroxy-olean-11,13(18)-11,13(18)-dien-28-oic acid



β-amyrin

Fig.11

PHARMACOLOGY

Folklore uses

The plant is well known for its antipyretic property. All parts of the plant have characteristic pungent taste. It is used in sprains, contusions, intercostal neuralgia, cough, malaria, dysentery, gastralgia, poisonous snake bites and furuncle infections. Fresh bark of the root is used in the treatment of hill fever. The root is used as dental analgesic. It is also used in odontalgia, paralysis, intermittent fevers, dyspepsia, colic, flatulence, bronchitis, nausea, wounds, filthy ulcers, epilepsy, gonorrhoea, constitutional debility, convalescence after febrile and exhausting diseases, blood motions and arthritis. The root bark is bitter, astringent, acrid, digestive, carminative, constipating, diaphoretic, expectorant, antibacterial, vulnerary, aromatic, tonic, stimulant, antiperiodic, antidiarrhoeal, antipyretic and diuretic. Fresh leaves are eaten raw for pain in the bowel. The leaves are burnt and the ash is used as tooth powder and in decayed teeth. The flowers are useful as an external application in wasp-stings. The unripe fruit is rubbed down with oil to make a stimulant liniment for arthritis. The fruits are used for cough and throat pain. The roots and leaves are boiled and used orally or inhalation for common cold and cough. Apart from these the fruits are also used for culinary purposes in the form of pickles (3-8, 30-33).

Anti-HIV activity

Bioassay-directed fractionation of *T. asiatica* extract resulted that nitidine and magnoflorine inhibited human lymphoblastoid cell killing by HIV-1 in *in vitro* XTT- based anti-HIV assay (34,35).

Antimalarial activity

The root bark of the plant was fractionated using ethyl acetate, dichloromethane, methanol, water and was studied for *in vitro* antimalarial activity against chloroquine-susceptible strains (K67, K39, M24, UPA, SL/D6, HB3) and chloroquine-resistant strains (ItD12, FCR3, FCB, V1/S) of *Plasmodium falciparum* and compared with nitidine. It was found that the methanolic extract showed highest activity and nitidine was two orders of magnitude more potent than the crude extract (36-38).

The antiplasmodial activity of the crude extract was attributed to 5,7-dimethoxy-8-(3'-hydroxy-3'-methyl-1'-butene)-coumarin which was isolated from bioactivity-guided fractionation of the ethyl acetate extract of the plant (39).

Antiplatelet aggregation activity

The methanolic extract of the wood was studied for *in vitro* antiplatelet aggregation activity using turbidimetric method. It was observed that chelerythrine was an inhibitor of thromboxane formation, phosphoinositide breakdown on rabbit platelet aggregation and ATP release reaction. 2,6-Dimethoxy-*p*-benzoquinone inhibited platelet aggregation induced by collagen and platelet aggregation factor (PAF). Apart from these braylin and four other compounds were strong inhibitors of platelet aggregation induced by 100 µg arachidonic acid. It was also observed that 7-substituted (except OH) or 7,8-disubstituted natural coumarins have more antiplatelet aggregation activity *in vitro* (40).

Antipyretic activity

The ethanolic extract of whole plant and the root was studied for antipyretic activity in yeast induced hyperthermic test model *in vitro* using female albino rats in a dose of 60 mg/kg. The rectal temperature was recorded at various time points using Shan laboratory digital telethermometer. It was found that it possesses a significant antipyretic activity which was comparable with that of paracetamol (41).

Anti-inflammatory activity

The volatile oil of the leaves obtained by steam distillation was studied on the exudative and proliferative phases of the inflammatory reactions using carrageenin induced paw edema and cotton pellets granuloma in male albino rats. The rats were given 0.2, 0.4, 0.8 and 1.6 ml/kg of oil obtained from the leaves and was found to be safe up to a maximum dose of 1.6 ml/kg. It was found that the activity was comparable with that of ketorolac tromethamine. The anti-inflammatory effect of the oil was attributed to inhibition of histamine, kinin and prostaglandin. It also showed effect in cotton pellets granuloma due to suppression of the proliferation phase of inflammation which involves the proliferation of macrophages, neutrophils and fibroblasts. The oil was also found to be very safe as it did not show any toxic manifestations even upon continuous administration for 10 days (42).

Analgesic activity

The crude alkaloids were studied for their pharmacological actions and toxicity in rats and found that they had analgesic activity showing decrease in body distortions in rats. They also showed anti-inflammatory action and inhibited the auricle swelling caused by xylol; joint swelling caused by agar and leucocyte migration caused by sodium carboxy methyl cellulose. The effects of alkaloids on hepatic function were observed by testing the contents of ALT, AST in serum and calculating the liver index. It was observed that the alkaloids did not cause any injury to the liver even after long term administration (43).

Antiviral activity

T. asiatica extract was studied for antiviral activity against Influenza type A virus (H1N1, H5N1) using 3-(4,5-dimethylthiazol-2yl)-5-(3-carboxymethoxy phenyl)-2-(4-sulfophenyl)-2H-tetrazolium (MTS) assay for virus induced cytopathic effect (CPE) and further it was subjected to quantitative real time polymerase chain reaction (PCR) to quantify reduction of H1N1 virus genomic RNA. It was found that the extract had potent antiviral activity with EC50 of 4.7 mg/L in MTS assay and 0.9 mg/L in PCR assay. It also showed antiviral activity with co-treatment of influenza virus infection, it was observed that it remained effective even when administered 24 hrs before and after the initiation of infection (44, 45).

Antimicrobial activity

The essential oil of the leaves was studied for its antimicrobial and antifungal activities by disc diffusion method and was found to be effective against *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella newport* and *Staphylococcus aureus*, *Aspergillus fumigatus*, *Aspergillus niger*, *Microsporum gypsum* and *Rhizopus stolonifer* up to 1:20 dilution. The activity was

several orders of magnitude larger than that of penicillin and tetracycline (46).

Wound healing activity

The different extracts of stem bark were studied for their antimicrobial effects on *S. aureus*, *E. coli*, *C. albicans* by excision and also by incision wound models with uninfected and infected wounds. It was proved that the extracts exhibit antibacterial activity against *S. aureus* and *E. coli*, but none was effective against *C. albicans*. There was almost complete healing on the 12th post wounding day in both excision and incision wound healing models containing *S. aureus*, *E. coli*. The degree of wound contraction of the extracts were in order of petroleum ether > chloroform > acetone > ethanol > aqueous extract. The wound healing property was comparable with that of nitrofurazone (47).

Spasmolytic activity

The crude ethanolic extract of the aerial parts was determined for spasmolytic activity by studying its ability to inhibit contractions induced by a sub-maximal concentration of spasmogens like barium chloride, acetyl choline, histamine and nicotine in guinea pig ileum. The extract inhibited barium chloride induced contraction by 15% & 70%, acetylcholine by 10% & 55%, histamine by 8% & 44% and nicotine by 10% & 78% at 10 & 50 µg/mL concentrations. The inhibition was higher when compared with that of papaverine. The coumarins toddalactone and toddanone which were isolated from the active fraction did not show spasmolytic activity up to a dose of 50 µg/mL. The traditional use of the plant extract/fraction for the treatment of colic pains suggests that combination of constituents may be responsible for the activity (48).

Antifeedant activity

Aqueous leaf extracts of *T. asiatica* were screened for antifeedant activity on young tomato leaves against the sixth instar larvae of *Helicoverpa armigera* by applying 0.2, 0.4, 0.6, 0.8, 1.0 percent aqueous extract on young tomato leaves and was observed that a high mortality rate of 86.1% at 1.0 percent concentration. The consumption index, relative growth rate, approximate digestibility, efficiency of conversion of ingested food, efficiency of conversion of digested food and mortality rate were measured. There was reduction in the rate of food consumption and growth which may be due to the presence of toxic chemicals like alkaloids. The extract was recommended to be used as a bio-pesticide which is eco-friendly, pollution free and easily degradable (49). In another study the methanolic extract was tested for mortal activity on the third instar larvae of *Plutella xylostella* (Black diamond moth) by topical application and spraying method and was found to be effective in producing mortality (50).

Effect on Cardiac function

The effect of aqueous extract of *T. asiatica* was studied on cardiac function and hemodynamics of acute myocardial ischemia in New Zealand rabbits, by high positioned double ligation of anterior left descending coronary artery. It was found that there was decreased ventricle work and consumption of oxygen of acute ischemic myocardium improving the diastolic function of myocardium and cardiac output (51).

Anticancer activity

Ethanolic extract of the dried stem chips of *T. asiatica* was studied for *in vitro* cytotoxicity on various cell lines using Fluorescence Activated Cell Sorter (FACS) analysis, RNA extraction and gene expression analysis morphological observations and statistical analysis and measurement of Caspase-3 activity. Dihydroneitidine exhibited highly specific cytotoxicity to human lung carcinoma (A549) cells and induced specific apoptotic cell death by regulating the cell cycle related genes (CDK2; CCNE), and up-regulated the cell death related genes specifically in tumor cells. The tumor selective cytotoxicity was in contrast to camptothecin where dihydroneitidine revealed specific accumulation within the cytosolic organelle but not in the nuclei of adenocarcinoma. Dihydroneitidine also showed selective cytotoxicity to lung adenocarcinoma but not to normal lung (WI-38) cells (52).

Skin whitening property

The methanolic extract of the dried root of *T. asiatica* was studied for skin whitening property in the form of a milky lotion and as a solid foundation. It was found to have suppressive effect on the melanin production, without affecting cell proliferation, and has a superior whitening effect similar to arbutin in lightening and whitening pigmentation after sunburn, blemishes, freckles, liver spots and it was also superior in safety (53).

CONCLUSIONS

People increasingly are willing to self-doctor their medicinal needs by investigating and using herbs and herbal preparations. Modern day medicine is directly or indirectly derived from plant sources, so it would be wrong to conclude that plants offer no further potential for treatment or cure of major diseases like AIDS, cancer, diabetes, etc. The therapeutic claims over *T. asiatica* must be evaluated for efficacy and safety in order to raise confidence in using the plant for various diseases.

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