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AYURVEDIC, PHYTOCHEMICAL AND PHARMACOLOGICAL REVIEW OF *SCHLEICHERA OLEOSA* (LOUR.) OKEN: A TRADITIONAL PLANT WITH ENORMOUS BIOLOGICAL ACTIVITY

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ABSTRACT

Schleichera oleosa (Lour) Oken., a member of Sapindaceae family, is found in South East Asia region and in sub-Himalayan tract of India. This plant is long been used in India as a folkloric plant for its enormous therapeutic effects and as livestock feeds. The plant is used in helminthiasis, acne, itching, menorrhea, malaria, dysentery, rheumatism, hair loss in Ayurveda and evaluated scientifically for anti-inflammatory, antiulcer, anticancer, antibacterial and antioxidant effects. Phenolic compounds, fatty acids, tannins, hydroxyl sterols and triterpenoids are the common active Phytoconstituents of this plant. The present study reviews the Vedic status, traditional uses, Ayurvedic properties, Phytoconstituents, chemistry and biological effects of *Schleichera oleosa* and describes as a potential plant for the source of various therapeutic agents.

KEYWORDS: *Schleichera oleosa*, folkloric plant, anti-inflammatory, antiulcer, anticancer, hydroxyl sterols and triterpenoids.

INTRODUCTION

The herbs set up resurgence and an epoch-making environment all over the globe. Herbs and herbal products today represent as safety in contrast to synthetic medicines.[1] Synthetic processes require enormous heat and pressure whereas the same contents are present in nature and can be obtained at ordinary temperature and pressure. According to the spirit of the age the herbal formulations are also set up their own positions in global market. The traditional uses of Indian medicinal plants are of long practice. It is helpful to maintain proper health

system in mankind.[2] So long the economic condition of India remains same as they are at the present and therefore, the demand of rural areas is cost effective approach towards treatment of different ailments and as a results herbs are considered as alternative treatment approach in now-a-days.[3,4]

The present paper describes the complete review of the plant *Schleichera oleosa* (Lour.) Oken. in the point of traditional importance, Vedic status and pharmacological evaluations.

METHODOLOGY

A complete literature search has been conducted for the plant *Schleichera oleosa* (Lour.) Oken. by the means of books, journals, magazines and scientific search engines. Google scholar, Researchgate, Mendely, PubMed, Science Direct, and Scopus are being used as search engines to collect the articles published related to *Schleichera oleosa* (Lour.) Oken. The ethnomedicinal, Ayurvedic, morphological, traditional, pharmacological information of *Schleichera oleosa* (Lour.) Oken. has been re-viewed and collected from 89 papers which contain original articles, review article, books chapter, website information and unpublished thesis works. The last type has not been considered for the present work. The chemical structure given in the research article has been revised and drawn using Chem Sketch freeware 8.17 (ACD Labs 8.00 release).

Vedic Status

In Vedic literature the reference of *Schleichera oleosa* was not prompt as it was mentioned as ‘Kośhamra’ in Suśhrut samhitā not in the name of ‘Kusum’.

Tumbikośhāmradantidrabantiśhyāmāsāptalānīlikā kompillaka-
Śankhinī snehastiktakatukaṣayā adhobhagadoṣaharā:
krimikaphakuṣthanilharā duṣtabraṇabiśhodhanāśhcha I
(Suśhrut samhitā: sutrasthān-45I38).[5]

The utterance of this plant in Suśhrut samhitā by Sri Dalhanacharya reveals the traditional use of it in helminthiasis, cough, leprosy and pimples. Sri Dalhanacharya described this plant as ‘Kośhamba’. In Nighantu of Dhanwantari (Dhanwantari Nighantu; āmrādibarga-6-7) the synonyms of ‘Kośhamra’ has been described as Kshudammra, Krimitaru, Lakshabriksha (as Lac insect resides on this tree), Jatudrum, Sukosh, Ghanaskandha and Suraktak. Later this plant *Schleichera oleosa* is traditionally known as Kusum.[6]

Vernacular names

In English it is popular as Lac Tree, Macassar Oil tree, Honey tree, Ceylon Oak. In local language it is commonly identified as Kosam (Hindi), Kusum (Bengali) etc. Different regional names of the plant have been given in Table No.1.[7]

Taxonomy

The plant bears the botanical name as *Schleichera oleosa* (Lour.) Oken., previously known as *Schleichera trijuga* Wild. & Klein., belongs to the family Sapindaceae. The detail plant kingdom has been given in **Table No.2.**[8]

Habitat and Morphological description

The habitat of this plant species is South East Asia and India, in India it is mostly available in the sub-Himalayan tract from Jammu-Kashmir to West Bengal (Especially in Medinipur District), Orissa, Bihar, Madhya Pradesh, Punjab and somewhere in South India (Andhra Pradesh).[6] Sandy loam soil is preferable for this tree. It is a deciduous tree of approx. 20 cm high and considered to be best tree for Lac. The plant consists of paripinnate leaves having pink colour when it is young. The leaves are 8-10 cm long and being smallest at lowest pair. The bark is 10 to 12 mm thick and greyish in colour (at inside it bears red colour). The flowering season is February-March and the flowers are yellowish green in color. Male and female flowers are grown in different trees. Ripen fruits are found in April-May month which is 2.5- 3 cm long, ovoid and tastes sweet-sour when ripen. There are 1 to 2 seeds in each fruit, brown in colour and having acidic taste.[9, 10]

Traditional uses of *Schleichera oleosa*

As this plant has long been used in Ayurveda and Siddha, it has enormous traditional importance and specific folkloric uses. All the parts of these plants are used in the traditional treatment. The bark is used as astringent and the leaves are used as fodder for cattle.[11] The bark paste with water can be used to treat menorrhea, malaria and dysentery. The fruits are taken rurally as anthelmintic in Nepal Himalayan area.[12] The seed oil, *'kusum oil'*, is used in rheumatism, applied in alopecia, acne, itching and burns. The oil enhances the hair growth also. The seed oil by heating with garlic is applied over body to get relief from cold fever and the same preparation is used traditionally in ear ache in the central part of Mayurbhanj district, Orissa. The seed powder is applied in cattle for ulcer and wounds to protect them from maggots. The literature also mentioned that this plant is used traditionally as antidiabetic (**Table3**).[6,13,14,15]

Ayurvedic properties and uses of *Schleichera oleosa*

The principle of drug formulation and pharmacology in Ayurveda is largely based on the following parameters *viz. Dravya* (Substances), *Rasa* (Taste), *Guna* (Properties), *Virya* (Potency), *Vipaka* (Effect of post metabolism), *Prabhava* (Specific actions).[16] For the plant *S. oleosa Rasa* is *amla* (fruit) and *katu* (oil); *Guna* is *guru* (heavy); *Virya* is *usna* (hot potency) and *Vipaka* is katu (pungent after metabolism) (**Table 4**). In Ayurveda the seed oil is anthelmintic and appetizer and also used (2.5-5 ml) in scrotal enlargement (while taken with milk at bed time). The bark is also used to treat fever, adenitis (inflammations of gland) and different joint pains.[17]

Ayurvedic formulation of *Schleichera oleosa*

Though herbal formulations of kusum are very popular, there are very few formulations are available in global market; Nyagrodhaadi kwaatha is one of them.[11,17] Kusum oil is prepared from the seeds and the evaluation is done (like clarity, colour of soap) according to standard procedure of BIS.[18]

Phytochemical constituents of *Schleichera oleosa*

Different literatures reveal that young leaves contain gallo-tannic acid[10],crude proteins, calcium and phosphorus. The bark contains dye and tannins[11] and resins, whereas in the seed fatty oils (58-60%) are found, known as ‘macassar oil’, which contains Cyanogenetic glucoside, poisonous for human consumption, that’s why before use the oil should be purified properly. The seed oil also contains 13-19% fatty acids such as- palmitic acid, myristic acid, eicosenoic acid, eicosadienoic acid, erucic acid, stearic acid, oleic acid, arachidic acid, gadoleic acid, behanic acid, palmitoleic acid etc. Some literature reported near about 50 % of oleic acid contents and some reported 2.83-3%.[10,11,19] The oil cake is a composition of 5.57% moisture, 22.3% protein, 48-53% fat, soluble carbohydrates, soluble mineral matters, phosphoric acid and potash.[6] Estimations of Phytoconstituents among Thai wild fruits by *Kubola et al*. reported 16.41±1.73 mg/g of total phenolic contents in edible parts of *Schleichera oleosa* (Lour.) Oken., which included protocatechuic acid, *p*-hydroxy benzoic acid, vanillic acid, caffeic acid, syringic acid and *p*-coumaric acid.[20] *Pettit et al.* isolated seven hydroxylated sterols named schleicherastatins 1-7 **(Fig.1; Structure 1-*a*. to 1-*g*.)** and schleicheols 1 and 2 **(Fig.1; Structure 1-*h.* to 1-*i.*)** which inhibit cancer cell growth obtained from the dicholomethane-methanol (1:1) extract of stem bark of :*Schleichera oleosa* (Lour.) Oken. of Sri Lankan region.[21] The triterpenoids namely, taraxerone and tricadenic acid A

(Fig. 1; Structure 2 and 3) were isolated from the methanolic extract of the bark of this plant of Darjeeling (West Bengal, India) foothill.[22] The presence of triterpenes like lupeol, lupeol acetate, betulin and betulinic acid in alcoholic bark extract of *Schleichera oleosa* (Lour.) Oken. was confirmed by sharp peaks in HPLC (High Performance Liquid chromatography) using isopropanol and acetonitrile (1:24v/v) mobile phase with Waters Sunfire column C18, 5 µm, 4.6 × 250 mm column.[23]

Nutritional ruminant feeds and *Schleichera oleosa*

Tannins containing plants have effective use as animal feed as tannins may increase protein supply in intestine of the ruminants. Moreover, tannin serves anti-inflammatory effects in mouth and throat, anti diarrhoeal, antiparasitic and antimicrobial action which helps to maintain its importance as livestock feed for domestic animals.[24] Condensed tannin and plant protein when taken by mastication it produces insoluble condensed tannin and protein complex which is nutritionally beneficial on reaching intestine.[25] The cakes of *Schleichera oleosa* (Lour.) Oken. are used as animal feeds traditionally as it delivers enormous source of supplements for ruminants.[26]

Therapeutics benefits of *Schleichera oleosa*

Anti-inflammatory and associated analgesic activity

Inflammation is a local and protective response of tissues to the injury from several physical agents (heat, cold, mechanical trauma), chemical agents (organic and inorganic poisons), infective agents (toxins, fungi) and immunological agents, followed by healing process as a part of body defense mechanism. Though in the treatment of inflammation several synthetic agents like non-steroidal anti-inflammatory drugs (NSAIDs) of salicylates, aryl anthranilic acid, aryl propionic acid, *p*-amino phenol derivatives are used widely, but most of the drugs are having severe side-effects and not safe due to the formation of toxic metabolites, and, hence, the treatment of this ailment has been shifted to herbal based treatment. Alkaloids, glycosides, terpenoids, resins, phenolic compounds, flavonoids, steroids, fatty acids are the responsible phytoconstituents for the anti-inflammatory activity in plants.[27] The bark of the plant contains tannin, and therefore, the possible mechanism of the bark extract to exert the activity by scavenging free radicals like nitric oxide ($NO^{\cdot}$), produced by nitric oxide synthase which is the second messenger during the process of inflammation. The anti-inflammatory activity and associated analgesic activity of alcoholic extract of stem bark of *Schleichera oleosa* (Lour.) Oken. was reported against carrageenan induced paw edema and TPA (12-O-

tetradecanoylphorbol-13-acetate) induced ear edema in Wister rats and Albino mice. The extracts of 200 mg/kg and 400 mg/kg exhibited promising response against carrageenan induced paw edema indicating the significant reduction of paw volume. At higher dose, the extract showed maximum inhibition of paw edema up to 54.21% when compared to the standard. For the support of the possible mechanism behind the activity, the reduction of tissue levels of nitric oxide and malondialdehyde (MDA) were also reported. In the case of TPA-induced mouse ear edema the extract exhibited inhibition in dose dependent manner. At higher dose (400 mg/kg) the extract significantly reduced the weight of ear. Among various inflammatory mediators, *S.oleosa* mainly inhibited 5-HT (5-Hydroxy tryptamine) and PGE_2 in dose dependent manner as these agents cause inflammation via arachidonic acid mediated COX (cyclooxygenase) pathway. The results showed the inhibition of both COX-1 and COX-2 by 69.25% and 62.17% respectively.[23]

Antiulcer activity

Affecting 10% of the World Population Peptic ulcer disease becomes a major gastro-intestinal disorder now-a-days. The etiology of this disease are mainly *Helicobacter pylori* infection, NSAIDs, stress, diet etc. Flavonoids and tannins containing plants show potent antiulcer activity against animal model.[28] Tannins, which are mainly used in medicine for their astringent property, has the property to protect at the site of ulcer by precipitating micro-proteins and provide resistance against the mechanical injury and proteolytic enzymes. Some studies also exhibit the effect of tannins against *Helicobacter pylori* infection.[29] The percolated ethanolic extract of stem barks of the plant *Schleichera oleosa* (Lour.) Oken. was evaluated for antiulcer activity in Wistar albino rats at the dose of 200mg/kg against Omeprazole (2mg/kg) as standard control. The extract was found to be more effective against ulcer as it provided 60% protection against ulcer. Moreover, the extract markedly reduce total volume of gastric acid secretion, gastric acidity and Ph.[30]

Antineoplastic activity

Neoplasm or cancer can be defined as an uncontrolled, abnormal, excessive and autonomous proliferation of cells which is caused by genetic disorders, heavy exposure to radiation, tobacco smoke inhalation etc. Plants active constituents like alkaloids, flavonoids, tannins, triterpenoids, polyphenols, anthocyanins, cholorogenic acids, cyanidine glycosides, quercetins have long been used to treat breast cancer, stomach cancer, colon cancer, human mammary gland carcinoma, lymphoma, melenoma in the support of their Ayurvedic uses.

These phytoconstiuents show synergistic actions along with other chemo-preventive agents to conquer the cancer cells resistance by their anti-proliferative, apoptotic and anti-metastatic actions.[31] The *in-vitro* cytotoxic assay of root extracts of *Schleichera oleosa* (Lour.) Oken. in cell lines of colon, lung, liver, CNS and Neuroblastoma was reported. A highest inhibition of 83% of methanolic extract against colon cell lines, ethyl acetate extract against CNS cell lines and aqueous extract against two types of colon cell lines were concluded by the authors.[32] Different bark extracts of the plant was evaluated for anticancer activity in same cell lines above mentioned and it was reported that ethyl acetate, methanol and aqueous extracts showed significant cytotoxic effects.[33] Isolated schleicherastatins 1-7 of stem bark of *Schleichera oleosa* (Lour.) Oken. from dicholomethane-methanol (1:1) extract showed significant cancer cell growth inhibitory effects against the murine P-388 lymphocytic leukemia and isolated schleicheols 1 and 2 showed borderline inhibitory effect against a mini-panel of human tumor cell lines. The authors have mentioned the 22- hydroxyl group of the sterols was important for the activity.[21]

Antibacterial and anti-mycotic effect

Methanolic extract of *S.oleosa*, a timber-yielding plants, was evaluated for preliminary phytochemical screening and antibacterial activity against uropathogenic bacterias. Qualitative phytochemical analysis indicated the presence of alkaloid, resin, tannin, carbohydrate, saponin, flavonoids and anthraquinones, along with, *S.oleosa* exhibited significant antibacterial activity based on minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) among twenty-one plants.[34] Tannins as a Phytoconstituents, inhibit several extracellular bacterial enzymes, affect microbial metabolism by inhibiting oxidative phosphorylation and minimize the availability of essential metal ions by formation of metal complexes.[35] Flavonoids and alkaloids are also important plant constituents for exerting antifungal and antibacterial activity. Quercetin, a flavonol, has the property to inhibit DNA gyrase.[36,37] The extracted seed oil (Kusum oil) from *Schleichera trijuga* was reported for antifungal activity and proved to be a significant member to inhibit *Candida albicans* isolated from eye-patients.[38] Triterpenoids which have been isolated from methanolic extract of outer bark of *S.oleosa* from Darjeeling foot hills, have significant effect against fungal and bacterial pathogens.[22] Though the exact mechanism of triterpenoids for inhibiting microbial growth was not fully understood but it could be hypothesized that these constituents inhibit DNA synthesis in microbes by preventing cell division.[39]

Free radical scavenging activity

Free radicals are short lived highly reactive chemicals with a single electron at its outer orbit. They can be formed during energy formation from food and oxygen in the cell or due to microbial infection, exhaustive physical activities, ozone, UV radiations, lifestyles (smoking cigarette, alcohol), pesticides.[40] Free radicals and Reactive Oxygen Species (ROS) are interrelated. During energy formation in mitochondria free radicals are formed and ROS is resulted as by-products of oxygen which has both toxic and beneficial effects to the body.[41] The benevolent effects include ATP generation, detoxification of xenobiotics, killing of microbes and cancer cell and generation of prostaglandins and leukotrines via cyclo-oxygenase and lipo-oxygenase pathway. Oxidative stresses, lipid peroxidation, oxidative damage to DNA (DNA modifications, strand break, DNA-protein cross linking) oxidation of proteins are the baneful effects of free radical formation. Oxidative stress is the result of an unfavourable imbalance between free radical production and antioxidant defense. Oxidative stress has an important effect on human health as is associated with cardiac diseases, inflammatory diseases and neurological disorders. ˙OH and ˙H react with sensitive C4-C5 double bond of pyrimidine of DNA causing oxidative damage.[42,43] Plant constituents like alkaloids, flavonoids, tannins, sesquiterpene have been reported for having their antioxidant activity. The hydroxyl group of flavonoids can donate hydrogen to form stable flavonoids radical by their metal-ion chelating and antiradical properties.[44] Sesquiterpene lactone and alkaloids were also been studied for Fe^{2+}- chelating activity and antiradical properties to evaluate possible mechanism of antioxidant activities.[45]

Root extracts of *Schleichera oleosa* (Lour.) Oken. was assayed for free radical scavenging activity with Fenton's reaction generated ˙OH in site-specific and non-site specific deoxyribose degradation assay. Ethyl acetate extract (67.72%) and methanolic extract (83.38%) exhibited maximum activity in site-specific and non-site specific assay respectively at 100µg/ml concentration, therefore, the extracts were more potential in metal-ion chelation and in support of result the authors performed plasmid nicking assay to confirm the prevention of DNA damage.[32] Methanolic bark extract of the plant showed maximum inhibitory activity (94.29%) in site-specific assay and in non-site specific assay ethyl acetate fraction was established as more potent candidature in dose dependent manner.[33] The ethanolic extract of the bark was also reported having significant free radical scavenging activity which was assayed by DPPH (2,2-diphenyl-1-picrylhydrazyl), hydrogen peroxide and nitric oxide scavenging methods.[46]

Conclusion and future aspect

The present review of the plant *Schleichera oleosa* reveals that from the ancient time the plant has been used traditionally to treat different ailments as well as livestock feeds. The study on different phytochemical constituents of different plant parts has been tabulated **(Table 5)** and presence of phenolic compounds, tannins, fatty acids, resins, hydroxyl-sterols, triterpenoids have been reported. The significant therapeutic effects of the plant and responsible constituents for the activity have been discussed; therefore, an idea of possible mechanism for the activities are established **(Table 6)**. Along with the pharmacological effect, the plant *Schleichera oleosa* has an impact on environmental green chemistry approach as the non-edible oil from the plant has used in bio-diesel production.[47] The present article deals the complete information of the plant *Schleichera oleosa* and surely will help the researcher to study the molecular level mechanism for different activities.

Table 1: Vernacular names of *Schelichera oleosa* (Lour.) Oken.

English:	Ceylon oak, Lac Tree, Macassar Oil Tree
Hindi:	Kausum, Kosumb, Kusum
Kannada:	Akota
Marathi:	Kasimb
Tamil:	Arakku
Telugu:	Pusuku
Bengali:	Kusum

Table 2: Plant kingdom of *Schelichera oleosa* (Lour.) Oken.

Rank	**Scientific name**
Kingdom	Plantae
Subkingdom	Tracheobionta
Superdivision	Spermatophyta
Division	Magnoliophyta
Class	Magnoliopsida
Subclass	Rosidae
Order	Sapindales
Family	Sapindaceae
Genus	*Schelichera* Wilid.
Species	*Schelichera oleosa* (Lour.) Oken

Table 3: Traditional and Ayurvedic uses of *Schelichera oleosa* (Lour.) Oken.

Parts	Traditional and Ayurvedic Uses
Leaves	Food stock for ruminants
Bark	Astringent, Menorrhea, Malaria, Dysentery , Febrifuge, used in Adenitis, Lumbago, Notalgia and Arthralgia
Fruit	Anthelmintic
Seed oil	Rheumatism, alopecia, acne, itching, burns, promotes hair growth, cooking and lighting, cold fever and Ear ache (with garlic), Appetizer, scrotal enlargement, anthelmintic
Seed powder	Wounds of cattle
Aerial part	CNS stimulant
Whole plant	Antidiabetic

Table 4: Ayurvedic properties of *Schelichera oleosa* (Lour.) Oken.

Category	Properties
Rasa	*Amla* (Fruit), *Katu, Tikta,Kasaaya* (Oil)
Guna	*Guru*
Virya	*Usna*
Vipaka	*Katu*
Dosakarma	*Kapha Pitta shaamaka*

Table 5: Major phytoconstituents present in different parts of *Schelichera oleosa* (Lour.) Oken.

Plant parts	Phytoconstituents
Leaves	*Gallo-tannic acid, Crude Protein, Calcium, Phosphorus*[10]
Bark	*Dye, Tannins, Resin,*[11] *Hydroxy- Sterols,*[21] *Triterpenoids*[22,,23]
Seed	*Fatty Acids,*[19] *Cyanogenic glucoside, Protein, Fat, Carbohydrate, Phosphoric acids, Potash*[6]
Fruits	*Protocatechuic acid, p-hydroxy benzoic acid, Vanillic acid, Caffeic acid, Syringic acid, p-coumaric acid*[20]

Table 6: Possible mechanisms for therapeutic effects of *Schelichera oleosa* (Lour.) Oken.

Therapeutic Activity	Possible Mechanism
Anti-inflammatory effect	*Reduction of Nitric oxide, MDA, 5-HT and* PGE_2[23]
Antiulcer activity	*Precipitate micro-proteins at the site of ulcer to protect, Resistance against proteolytic enzymes and action against H.pylori.*[29]
Anticancer activity	*Anti-proliferative effect to resist uncontrolled cell proliferation, Inhibit evasion of apoptosis and metastasis.*[31]
Antimicrobial activity	*Inhibit bacterial enzyme, Inhibit oxidative phosphorylation, Inhibition of DNA gyrase,*[36,,37] *prevent cell division to inhibit DNA synthesis*[39]
Antioxidant activity	*Metal-chelating complex, Antiradical activity and Inhibition of free radical generation*[44,,45]

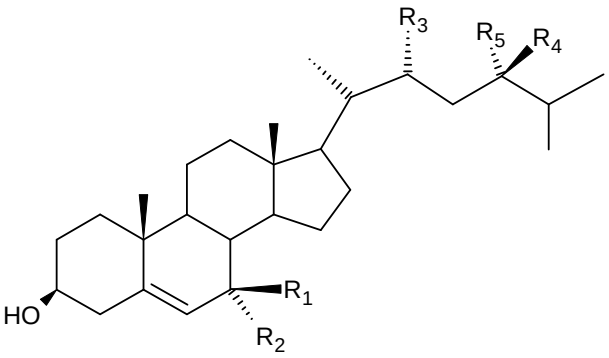


Figure 1: Isolated phytochemical constituents from *Schelichera oleosa* (Lour.) Oken.

Structure 1

1-*a*. Schleicherastatins 1; R_1= OCH_3; R_2= H; R_3= OH; R_4= C_2H_5; R_5= H

1-*b*. Schleicherastatins 2; R_1= H; R_2= OCH_3; R_3= OH; R_4= C_2H_5; R_5= H

1-*c*. Schleicherastatins 3; R_1= OCH_3; R_2= H; R_3= OH; R_4= CH_3; R_5= H

1-*d*. Schleicherastatins 4; R_1= OCH_3; R_2= H; R_3= OH; R_4= H; R_5= CH_3

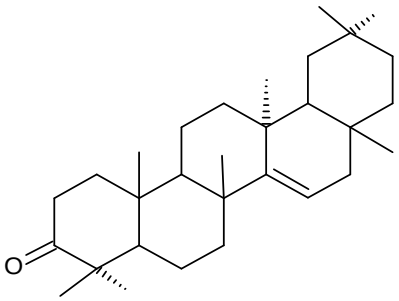
1-*e*. Schleicherastatins 5; R_1= O; R_2= O; R_3= OH; R_4= C_2H_5; R_5= H

1-*f*. Schleicherastatins 6; R_1= O; R_2= O; R_3= OH; R_4= CH3; R_5= H

1-*g*. Schleicherastatins 7; R_1= O; R_2= O; R_3= OH; R_4= H; R_5= CH_3

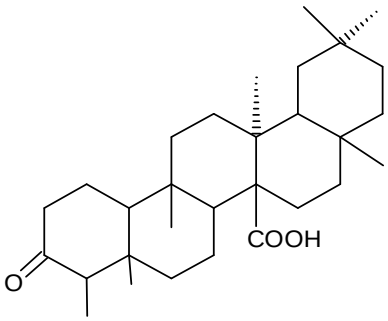
1-*h*. Schleicheols 1; R_1= OCH_3; R_2= H; R_3= H; R_4= C_2H_5; R_5= H

1-*i*. Schleicheols 2; R_1= H; R_2= OCH_3; R_3= H; R_4= C_2H_5; R_5= H



Structure 2

Taraxerone



Structure 3

Tricadenic acid

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