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ETHANOPHARMACOLOGY, PHARMACOLOGY AND PHYTOCHEMISTRY OF *Trichodesma indicum* (Linn.) R.Br.

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Abstract: *Since ancient times, people have been exploring the nature particularly plants in search of new drugs. This has resulted in the use of large number of medicinal plants with therapeutic properties to treat various diseases. For the primary health care needs, the World Health Organization (WHO) has estimated about 80% of the population of developing countries rely on traditional medicines, mostly plant drugs. Trichodesma indicum (Linn.) R.Br. belongs to the family Boraginaceae. T. indicum is traditionally used to treat arthritis, dysentery, skin disease, fever, arthalgia, as an antidote and vitiated Vata and Kapha dosha in ayurvedic system of medicine. Phytochemical investigations indicate that 23 compounds reported from the plant belong to various chemical categories. Different parts of the plant were reported for their anti-inflammatory, antimicrobial, antifungal, diuretic, antidiabetic, antioxidant, antitussive activities, dermal toxicity and metal chelating efficacy.*

Keywords: *Trichodesma indicum; Ethanopharmacology; anti-inflammatory; antidiabetic; Phytochemistry.*

Introduction: *Trichodesma indicum* (Linn.) R.Br. is commonly known as Adhahpushpi, belongs to the family Boraginaceae. It has various vernacular names like surasa (Sanskrit), chhota kulpha (Hindi), and Kazhutha thumba (Tamil). *T. indicum* is a perennial medicinal herb distributed in tropical and subtropical Asia, Africa and Australia. The herb is found as a weed throughout the greater part of India, on roadsides and stony dry wastelands [1]. In Ayurveda, the plant is useful for diseases of the eye. It is also prescribed for expulsion of the dead foetus [2]. The whole plant and root are used to treat arthritis, dysentery, skin diseases, snake-bite poisoning and fever [3]. The leaves and flowers are used as emollient and diuretic [4].The plant is useful in vitiated conditions of *vata* and *kapha*, diarrhea, arthralgia, dyspepsia, inflammations, dysentery, leprosy and skin diseases [5].

Botanical Description: *T. indicum* is an erect, spreading, branched, annual herb, about 50 cm in height, with hairs springing from tubercles. The leaves are stalk less, opposite, lanceolate, 2 to 8 centimeters long, pointed at the tip [6] and heart-shaped at the base with single pale blue flower, changing to pink or white [7].

Ethanopharmacology: Thari people of Nara Desert, Pakistan used decoction of whole plant of *T. indicum* in influenza and cough [8]. The root is pounded into a paste and is applied to reduce swellings, particularly of the joints; the extract is given to children in dysentery and fever [9, 10]. Leaves paste of *T. indicum* was used in chest problems [11]. Leaf Juice is used by Paliyar tribals in Theni district of Tamil Nadu, India in external ear pain and wounds [12]. A cold infusion of the leaves is considered depurative [4]. Root paste is applied externally to swollen joints, inflammations and superficial skin injuries [13]. In folklore medicine, the paste of the leaves of *T. indicum* along with rhizomes of *Acorus calamus* and *Allium sativum* were used for the wound healing [14].

Pharmacology

Dermal Toxicity Studies: Simple ointment base (5% each of wool fat, cetostearyl alcohol, hard paraffin and 85% of white soft paraffin) is mixed with methanol extract of the *T. indicum* at two concentrations such as 5% and 10% level. The ointment which is prepared at their 10% level did

not show any symptoms of allergic reaction, itching and erythema and hence it could be used for topical application [15].

Metal Chelating Efficacy: Synthetic chelators strongly bind to metal ions which used for iron excretion by binding to ions to produce metal chelator complex for the elimination of metals from the body. Metals have vital role in body metabolism only when in normal concentration. However severe toxicity can be induce at higher concentration. Treatment with chelating agent is an optimal method to reduce metals toxicity in organisms. Hence the chelating property of ethyl acetate extract of leaves of *T. indicum* (50 to 250µg/ml) is determined. The chelating effect of ferrous ions by the extracts was estimated in various concentrations of the different extract by adding 0.05ml of 2mM $FeCl_2$ and initiated Ferrozine (5mM). Absorbance measured spectrophotometrically at 562nm whereas EDTA is taken as standard. The result indicated that ethyl acetate extract of leaves of *T. indicum* has significant metal chelating activity [6].

Wound Healing Activity: The methanolic extract of the whole plant of *T. indicum* was screened for wound healing activity in albino rats. A better healing with complete wound closure was observed in *T. indicum* ointment treated group (16 days). The neosporin treated and control groups needed 19 days and 21 days respectively for complete wound closure. The sections of the skin tissues of animals treated with *T. indicum* ointment showed the presence of strips of lining squamous epithelium which was thinned out in some places and granulation tissues were also seen. *T. indicum* treated group showed faster healing than the other treated groups based on the percentage reduction of wound area and histological assessment. It has complete rate of contraction (closure to 99.63%) when compared to other groups. The result showed that *T. indicum* has reached the granuloma tissue formation stage in wound healing activity [15].

Anti-inflammatory Activity: The chloroform extract of *T. indicum* root has been evaluated for anti-inflammatory activity against oedema produced by carrageenan, dextran, histamine and serotonin, and against formation of granulation tissues by cotton pellet in rats. The effect was compared with the activity of indomethacin, cyperoheptadine and dexamethasone against different types of inflammation. The chloroform extract at doses of 50, 100 and 200 mg/kg exhibited significant ($P< 0.001$) anti-inflammatory activity in acute and chronic inflammatory models. At 200 mg/kg, the chloroform extract showed maximum inhibition of 48.12% in carrageenan-induced paw oedema while the standard indomethacin inhibited it by 54.32% after 3hr of carrageenan injection. In the chronic inflammatory model, the chloroform extract (100 and 200 mg/kg) inhibited the granuloma weight by 15.42 and 21.12%, respectively, whereas the indomethacin and dexamethasone inhibited it by 29.29 and 34.13%, respectively. The result shows that *T.indicum* has anti-inflammatory activity [7].

Antimicrobial Activity: The *in-vitro* anti-microbial activities of the ethanol root extract of *T. indicum* and isolated compounds were evaluated by a disc diffusion test. Ethanol extract and isolated compounds n-Decanyl laurate, n-tetradecanyl laurate, n-nonacosanyl palmitate, stigmast-5-en-3b-ol-21(24)-olide, n-pentacos-9-one, n-dotriacont-9-one-13-ene, stigmast-5-en-3b-ol-23-one and lanast-5-en-3b-D-glucopyranosyl-21 (24)-olide showed varying degrees of antimicrobial activities. The ethanol extract exhibited potent growth inhibitory activity against *S. aureus, B. subtilis* and *C. albicans* with an MIC value of 19.2mg/ml. Among all the isolated compounds, lanast-5-en-3b-Dglucopyranosyl-21 (24)-olide displayed strongest antibacterial activity against *S. aureus* with MIC value of 2.4mg/ml. The results shows potential use of the ethanol extract of *T. indicum* root as well as the some of the isolated compounds in the treatment of infections associated with the studied microorganisms [7].

The methanol extract of the whole plant of *T. indicum* was screened for antibacterial screening using well diffusion method. *T. indicum* at their 10% level has more zone of inhibition than the standard Neosporin against the *E. coli,* and even though effective against all the tested organisms the zone of inhibition was comparatively less than the standard. The result showed that *T. indicum* has good antibacterial activity against the tested organisms [15].

The aerial part of ethanol *T. Indicum* posseses anti microbial activity against gram positive and gram negative becteria using Sabourad dextrose agar media. The zone of inhibition of extract range 12- 29 mm. The MIC was found in the range of 5-0.625 mg/ml. The ethanol extract was more active against gram positive becteria *S. aureus and S. subtilis* having zone of inhibition range from 24.12-26.30mm whereas aqueous extract was having strong

inhibitory effect against gram negative bacteria like *E. coli, P. aeruginosa, P. vulgaris* with zone of inhibition range from 23-28mm. The MIC was found in the range of 5 to 0.625 mg/ml. The petroleum ether and chloroform extract had inhibitory effect on tested microorganism but less as compared to ethanol and aqueous extracts [16].

The ethanol extract of aerial part of *T. indicum* possesses anti fungal activity against *A. flavons, A. niger and C. albicans* using Sabourad dextrose agar media. Ketakonazol used as a standard drug. Result showed that the aerial part of *T. indicum* possesses strong anti-fungal activity [16].

Methanolic extracts of whole plant of *T.indicum* (1000 µg/mL) on the growth of *A. niger, A. fumigatus, A. flavus and M. gypseum*. The percentage of inhibition exhibited by the methanolic extracts was found to be 43%, 33%, 15% and 6% respectively. The result showed that *T. indicum* possesses a good antifungal activity [17].

Diuretic Activity: Methanol and aqueous extract of aerial parts of *T. indicum* (150 and 300 mg/kg) were used for screening diuretic activity using Lipschitz model. The urine volume of the methanolic extract at dose of 300 mg/kg has significant diuretic activity ($p \leq 0.001$) with lipschitz value 1.25 as compared to standard (Furosemide). Urinary sodium concentration was found to be more in methanol extract but potassium was found to be more in aqueous extract. It also shows methanol extract has effect like K^+ sparing diuretics [18].

Antidiabetic Activity: *In-vitro* anti-diabetic activity of whole plant of hydro-alcoholic extract of *T. indicum* was studied using the glucose uptake model in rodent skeletal muscle cells (L-6 cells) involved in glucose utilization. The drug extract showed percentage growth inhibition value of 500 µg/ml and showed average glucose uptake ($P<0.05$) with percentage of glucose uptake of 91.03±10.12 over the control. The result shows the hydro-alcoloholic extract of *T. indicum* exhibited moderate antidiabetic activity [19].

Antioxidant Activity: The hydro-alchoholic extract of whole plant of *T. indicum* was screened for its *in-vitro* antioxidant activity using 2,2-Diphenly1-picryl hydrazyl assay, Scavenging of Nitric oxide, Superoxide radical methods, Total antioxidant capacity of the extract and reducing power assay. The extract of *T. indicum* showed good antioxidant properties against 2,2-Diphenly1-picryl hydrazyl radical with low IC_{50} values 135µg/ml. Nitric oxide and superoxide radical exhibited poor scavenging properties with IC_{50} value of > 1000µg/ml. The total antioxidant activity which expressed equivalent to Ascorbic acid has 225.28 mg per gm of dried extract. The extract of *T. indicum* exhibited significant antioxidant activity [19].

The chloroform and ethyl acetate extract of the roots of *T. indicum* exhibits strong inhibition against DPPH radicals. Ethanol extract of the leaves, fruits and roots of *T. indicum* showed significant ABTS radical scavenging activity and petroleum ether extract of the leaves was found to possess potent superoxide scavenging activity. The maximum nitric oxide scavenging activity was found to be exhibited by the benzene fruit extract of *T. indicum*. Ethyl acetate and benzene extract of the leaf of *T. indicum* reveals the significant activity of hydroxyl radical scavenging activity. The results showed that T. indicum have great potential of free radical scavenging activity [20].

The antioxidant effect of leaves of *T. indicum* of different extract was studied using DPPH, phosphomolybdenum, metal chelating and hydroxyl radical scavenging assay. The extracts are then subjected to phytochemical screening which showed the presence of flavonoids, terpenoids and tannins in ethyl acetate extract of the plant. *T. indicum* could be considered as a significant source of natural antioxidants. The IC_{50} values for the hexane, ethyl acetate and methanol extracts were observed to be 171.65, 140.57 and 156.56µg/ml, respectively. Based on the results obtained, the ethyl acetate extract possessed major radical scavenging potential when compared to the hexane and methanol extracts [6].

The methanol extract of the whole plant of *T. indicum* (Linn.) was screened for its *in-vitro* antioxidant utilizing Nitric oxide scavenging activity assay and reducing power assay. The methanolic extract had maximum scavenging capacity and it was found to be 76.21 ± 0.34% and standard ascorbic acid had 80.03 ± 1.97 % and the IC_{50} was found to be 130.04 µg/ mL and 84.64 µg/ mL for methanolic extract and standard respectively. The absorbance of the extract was 0.346 ± 0.010 while the ascorbic acid had 0.443 ± 0.001. The antioxidant potency can also be expressed in terms of ascorbic acid equivalent and it was found to be 0.747g/g of extract. The result showed that the methanolic extract of *T. indicum* has good antioxidant

activity against nitric oxide scavenging and reducing power assay [15].

Anti-tussive Activity: The oral administration methanol extract of whole plants of *T. indicum* has been investigated on sulphur dioxide induced cough reflex by the method of Miyagoshi *et al.* (1986) [21], Saha *et al*. (1997) [22] and Murugesan *et al.* (2000) [23] in swiss albino mice. The 100-200 mg/kg body weight extract has demonstrated significant ($p < 0.001$) inhibition in frequency of cough when compared with control group. The effect persisted up to 90 min of administration and also comparable to the standard (Codeine phosphate).The activity possessed by 100 mg/kg at 30 minutes was lesser than that of other increasing doses in all the experimental duration. The result of the present study provides pharmacological confirmation in support of folklore claims as an anti-tussive agent [24].

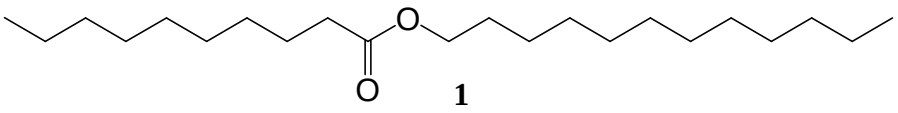
Antimiotic and Antiproliferative: The dried aerial part of chloroform and ethanolic extract of *T. indicum* was evaluated for Antimiotic and antiproliferative activity. *In-vitro* antimiotic activity in *allium sepa* root and antiproliferative activity using the yeast model and five human cell lines (MCF-7, HOP-62, MOLT-4, HCT-15 and PRO) was determined. The miotic index for chloroform and ethanolic extract was found to be 12.01±1.34 and 12.99±0.25 mg/mL respectively. The IC50 value in the antiproliferative assay was found to be 30.14-35.36 mg/mL for chloroform and ethanolic extracts respectively.both extract showed significant antimiotic and antiproliferative when compared to the standard methotreaxate, vincreastine and adriamycin. Ethanolic extracts strong inhibition MCF-7 and MOLT-4 cell lines at concentration of <30µg/mL [25].

Antidiarrheal Activity: Anti-diarrhoeal activity of ethanolic extract of root of *T. indicum* was estimated in castor oil induced diarrhea in rats. The frequency of defecation and the weight of faecal material were noted up to 4 h. The ethanolic extract of root of *T.indicum* The extract significantly inhibited the castor oil-induced diarrhea and decrease propulsion of charcoal meal through gastrointestinal tract. It also reduced the castor oil-induced small intestinal fluid accumulation. The ethanolic extract of root of *T.indicum* has significantly activity and substantiates the use of this herbal remedy as nonspecific treatment of diarrhea in folk medicine [26].

Antipyretic Activity: Ethanolic extract of root of *T. indicum* was evaluated for its antipyretic potential on normal body temperature and yeast-induced pyrexia in albino rats in wistar rats. The extract (100, 200 and 400 mg/kg) produced dose related fall in rectal temperature at room temperature. The extract also produced a dose related fall in rectal temperature in rats for up to 3 h after its administration. Yeast suspension (10 mg·kg−1) increased rectal temperature 19 h after subcutaneous injection. In yeast induced pyrexia, the extract significantly ($P < 0.05$) reduced rectal temperature for up to 4 h after its administration in a dose dependent manner and the efficacy was similar to that of aspirin (standard drug) [7].

Analgesic Activity: Analgesic effect of alcoholic extract of root of *T. indicum* was performed in Wistar rats of either sex by chemical (acetic acid and formalin) and thermal (tail - immersion) pain models in mice, using classical standard drugs. The ethanolic extract (400 mg/kg) exhibited maximum inhibition of 67.99 ± 4.63% in acetic acid - induced abdominal constrictions in mice in comparison with indomethacin produced 74.96 ± 4.21% of inhibition. In tail immersion methods pentazocine (5 mg/kg), an analgesic narcotic drug, was used as positive control. In the tail immersion method, the extract at dose 400 mg/kg showed significant ($P < 0.001$) difference between pre-treatment and post-treatment latency time to heat stimulus. At 400 mg/ kg the ethanol extract exhibited maximum inhibition of 19.71+3.99 % in the formalin –induced licking during the first phase. The ethanol extract (400mg/kg) also inhibited (49.53 ± 2.25 %) of the late phase (15-30 min) of the formalin-induced licking. Indomethacin had no effect on the first phase, but it produced a reduction (55.32 ± 1.12%) of the second phase at 10 mg/kg [7].

Phytochemistry: Phytochemical investigation on *T. indicum* led to the isolation of n-decanyl laurate (1), n-tetradecanyl laurate (2), n-nonacosanyl palmitate (3), stigmast-5-en-3β-ol-21(24)-olide (4), n-pentacos-9-one (5), n-dotriacont-9-one-13-ene (6), stigmast-5-en-3β-ol-23-one (7) lanast-5 en-3β-D-glucopyranosyl-21 (24)-olide (8) [7]. Some of the chemical constituents of the plant have been identified as non-steroidal compounds; hexacosane (9), ethyl hexacosanoate (10) 21, 24-hexacosadienoic acid (11) ethyl esters from leaves [27] oleic (12), linoleic (13), palmatic (14), stearic (15) linolenic acid (16) from seed oil [27]. The plant also contains monocrotolin (17), suspinine (18), lupeol (19) [14] amylin (20), Hexcosane (21) [2] catechin (22), gallic acid (23), β-sitosterol (24) [6].



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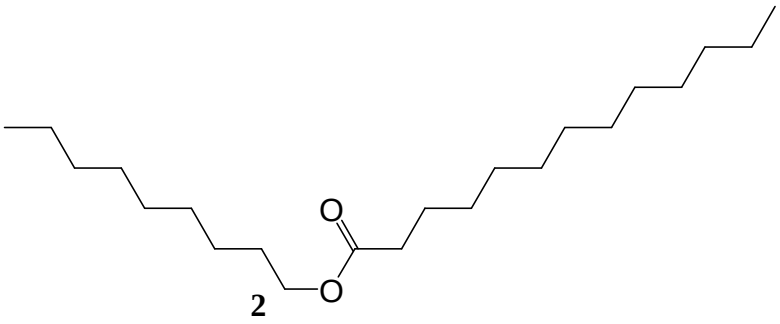

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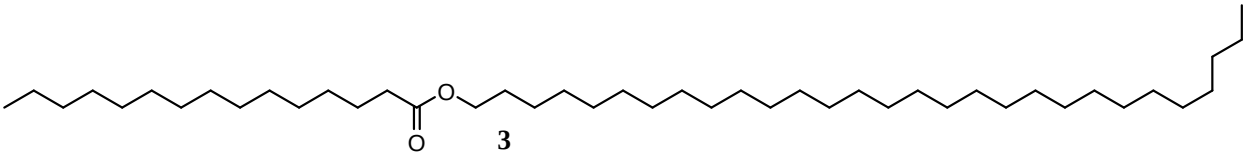

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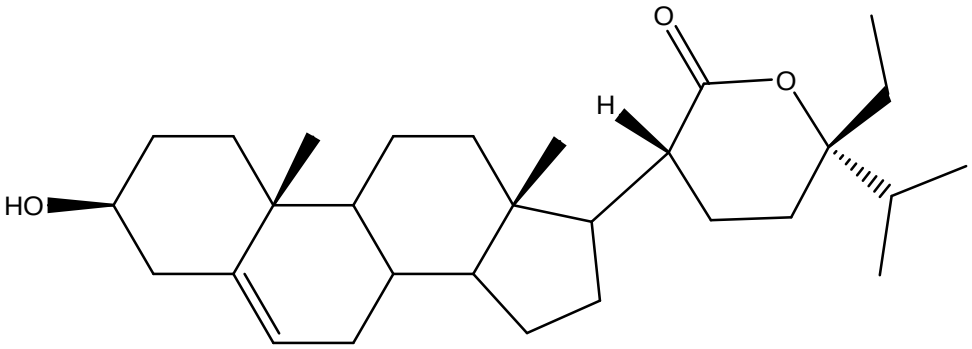

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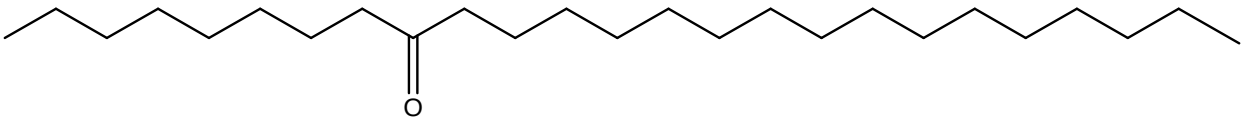

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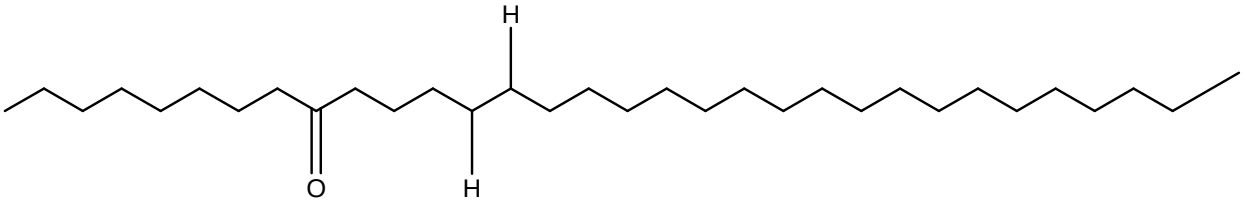

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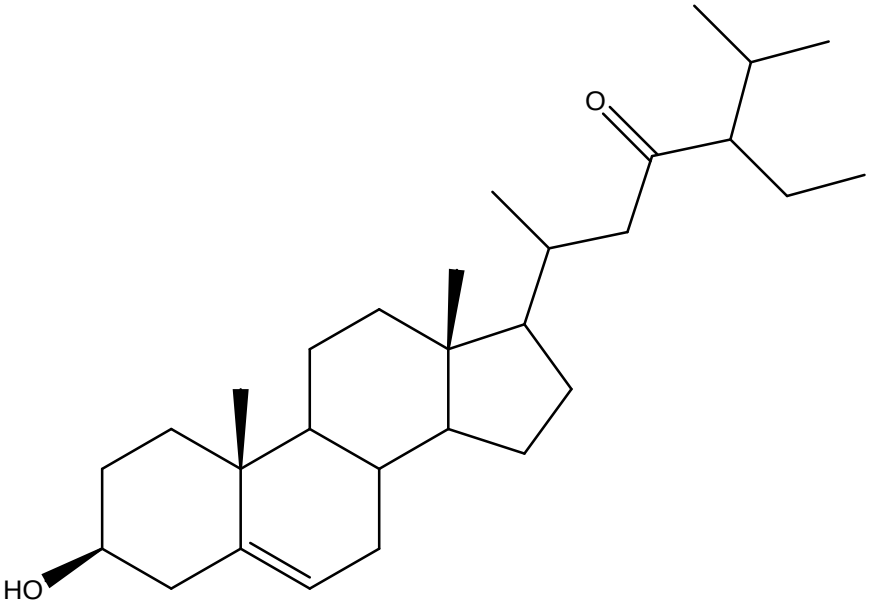

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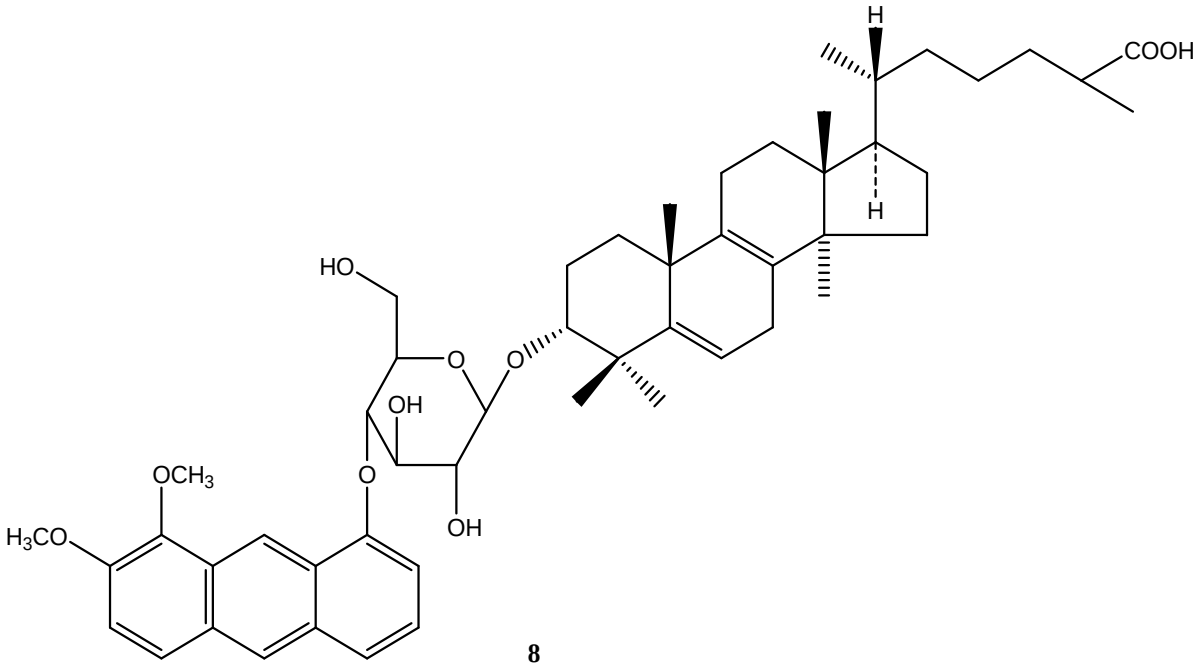

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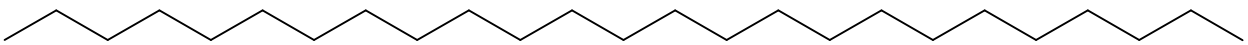

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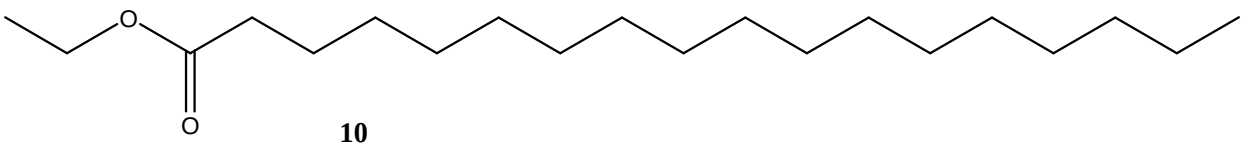

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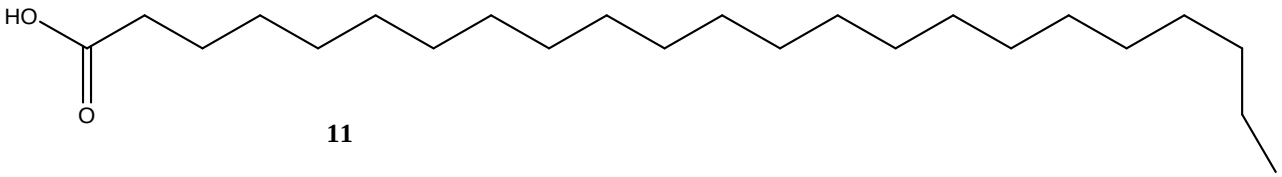

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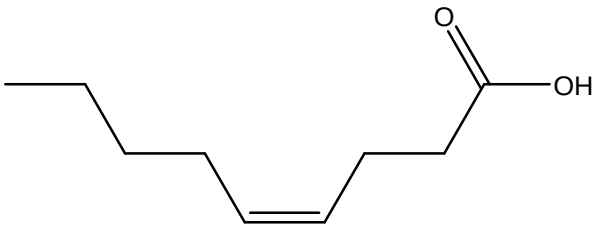

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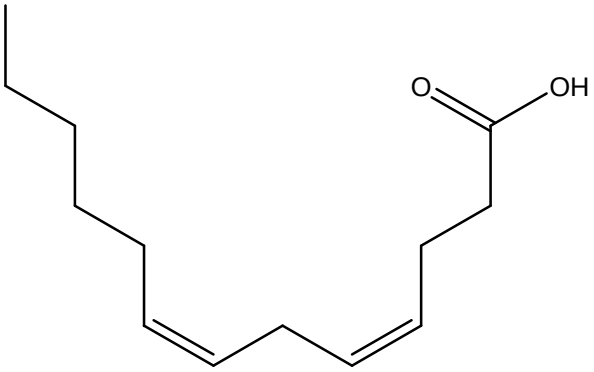

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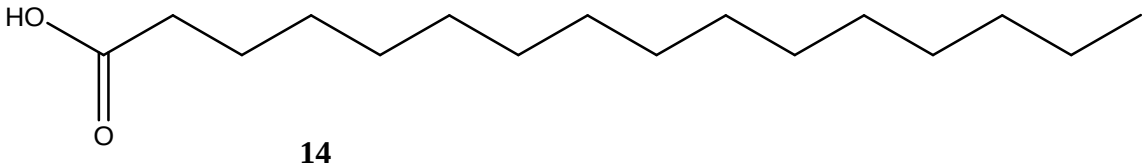

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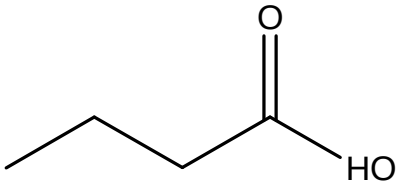

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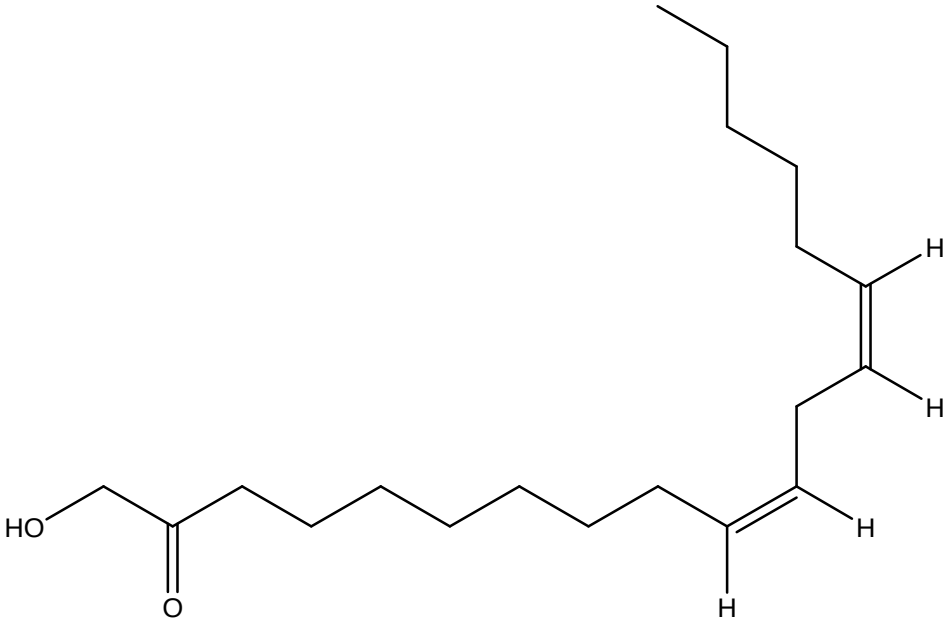

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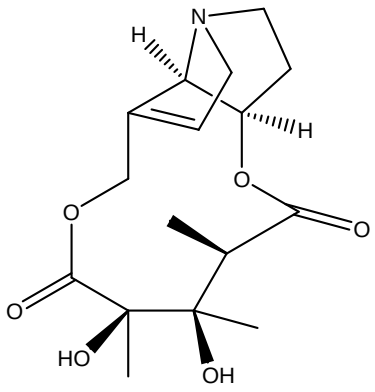

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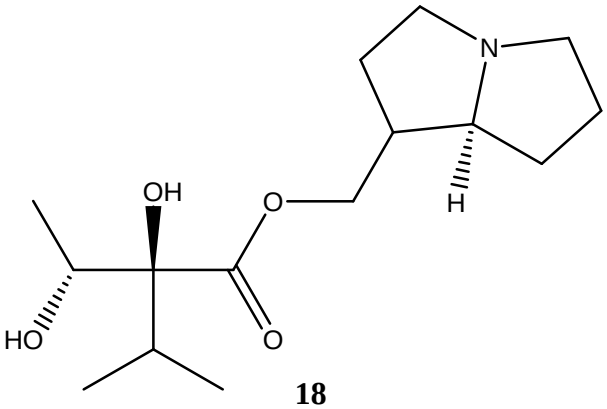

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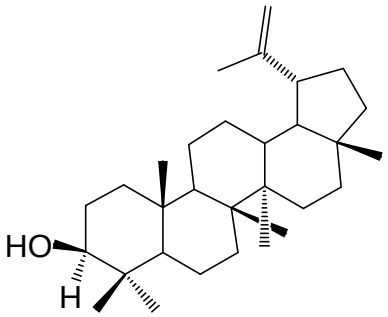

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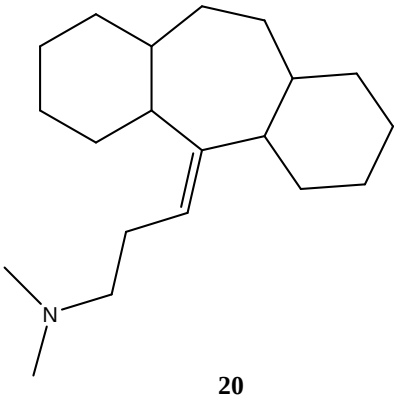

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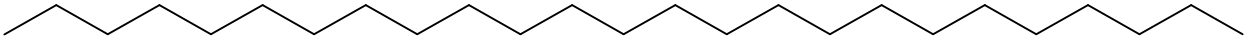

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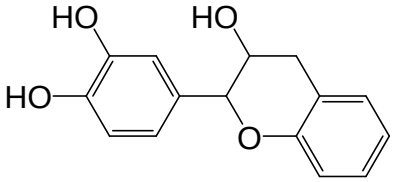

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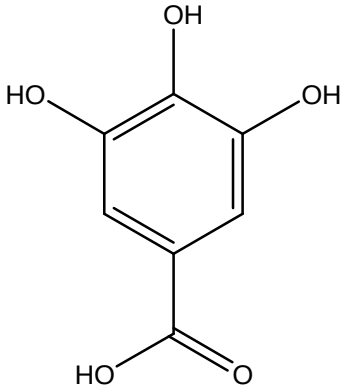

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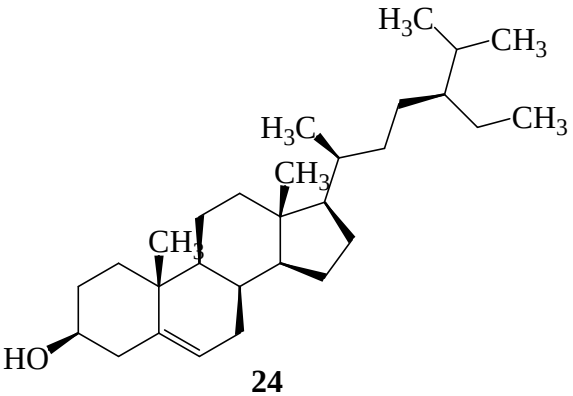

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Conclusion: *T. indicum* is an important medicinal plant mentioned in the ancient literature of traditional Indian medicine. *T. indicum*, having potential medicinal values and most widely cultivated species of the family Boraginaceae. Various parts of the plant have been used for human medication. The exciting findings of the previous studies must provoke the researchers for determining other pharmacological profile. This review summarizes some important pharmacological studies on *T. indicum* and more emphasizes on the phytochemical investigations

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