

A Review on Phytochemical and Pharmacological Profile of *Clitoria ternatea*.

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Summary

The *Clitoria ternatea* (Papilionaceae) perennial herbaceous plant has been widely used in Ayurveda. The plant is native to tropical equatorial Asia, but has been introduced to Africa, Australia and the New World. The active chemical constituents reported from this plant are tannins, resins, starch, taraxerol and Taraxerone. *C. ternatea* has a number of uses, many of which have been verified by scientific method. In traditional medicine, the plant is used in the treatment of tubercular glands, amentia, hemicrania, burning sensation, strangury, helminthiasis, leprosy, leucoderma, elephantiasis, inflammation, vitiated conditions of pitta, bronchitis, asthma, pulmonary, tuberculosis, ascites, ulcers, ear diseases, visceromegaly and CNS disorders. The review article summarizes the chemistry and pharmacological profile of *C. ternatea*.

Key words: *Clitoria ternatea*, Phytochemistry, Pharmacological Activity.

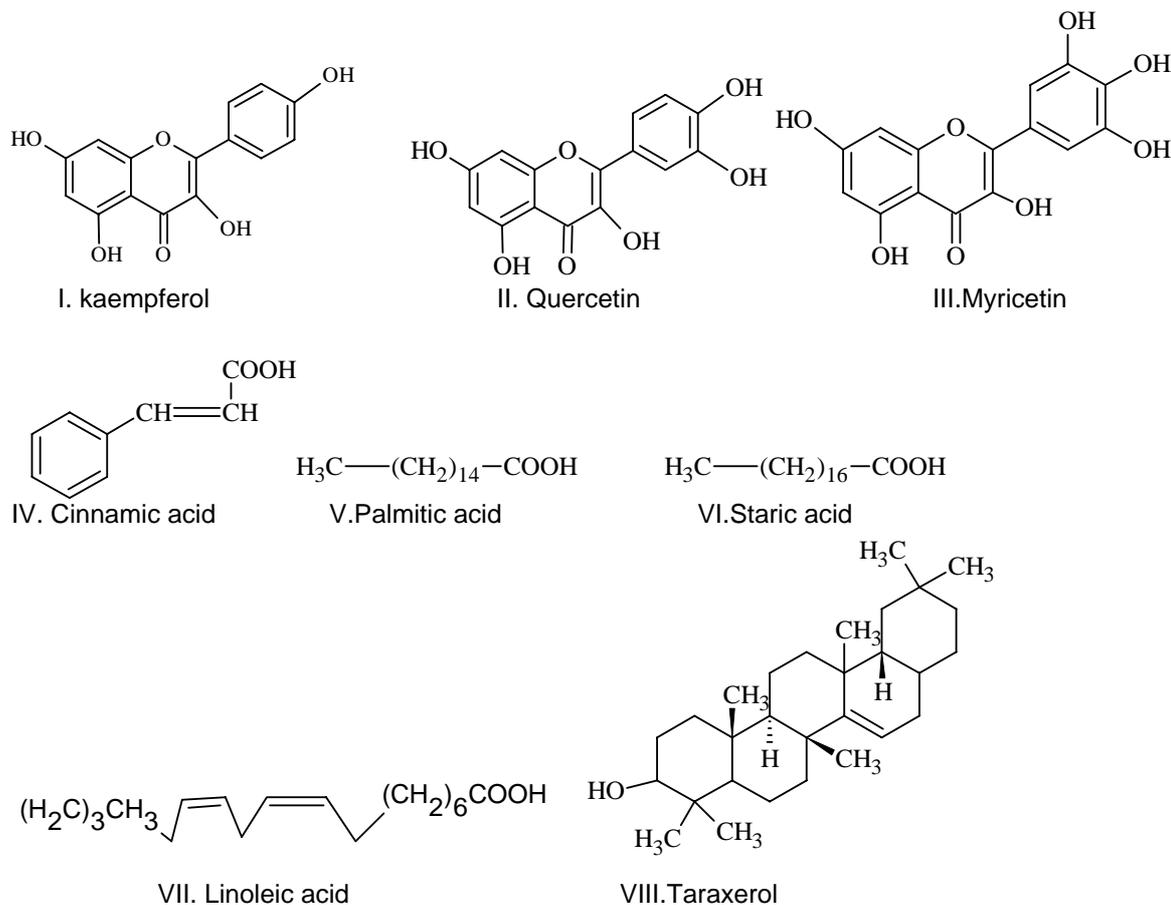
Introduction

This plant is native to tropical equatorial Asia, but has been introduced to Africa, Australia and the New World. It is a perennial herbaceous plant. Its leaves are elliptic and obtuse. It grows as a vine or creeper, doing well in moist neutral soil. The most striking feature about this plant are its vivid deep blue flowers. They are solitary, with light yellow markings. They are about 4 cm long by 3 cm wide. There are some varieties that yield white flowers. The fruits are 5 - 7 cm long, flat pods with 6 to 10 seeds in each pod. They are edible when tender. It is grown as an ornamental plant and as a revegetation species (e.g. in coal mines in Australia), requiring little care when cultivated. Its roots fix nitrogen and therefore this plant is also used to improve soil quality. The flowers are used to colour food. In animal tests the methanolic extract of *C.ternatea* roots demonstrated nootropic, anxiolytic, antidepressant, anticonvulsant and antistress activity. The active constituent(s) include Tannins, resins, Starch, Taraxerol & Taraxerone. *C. ternatea* root extracts are capable of curing whooping cough if taken orally. The extract from the white-flowered plant can cure goiter.

Its roots are used in ayurveda Indian medicine. Roots useful in ophthalmopathy, tubercular glands, amentia, hemicrania, burning sensation, strangury, helminthiasis, leprosy, leucoderma, elephantiasis, inflammation, vitiated conditions of pitta, bronchitis, asthma, pulmonary, tuberculosis, ascites, ulcers, ear diseases, visceromegaly and fevers. They are administered with honey and ghee as a general tonic to children for improving mental faculties, muscular strength and complexion and in epilepsy and insanity. Leaves are useful in otalgia, hepatopathy and eruptions. Seeds are useful in visceralgia. Roots and leaves are useful in the treating bodyaches, infections, urinogenital disorders, as anthelmintic, and antidote to animal stings.

Chemical constituent:

Sr.no	Plant Parts used	Chemical constituent
1.	Flowers	Major flavonol glycosides, 3-O- (2"-O-alpha-rhamnosyl-6"-O-malonyl)-beta-glucoside, 3-O-(6"-O-alpha-rhamnosyl-6"-O-malonyl)-beta-glucoside and 3-O-(2",6"-di-O-alpha-rhamnosyl)-beta-glucoside of kaemferol (I), quercetin (II) and myricetin (III) were isolated from the petals ^{1,2} minor delphinidin glycosides, 3-O-b-glucoside,3-O-(2"-O-a-rahmnosyl)-b-glucoside, 3-O-(2"-O-a-rahmnosyl-6"-O-malonyl)-b-glucoside of delphinidin ¹ .Eight anthocyanins (ternatins C1,C2,C3,C4,C5 and D3, and preternatins A3 and C4) were also isolated from the flowers ^{2, 3} Six ternatins from the flowers were partly characterized as highly acylated dephinidin derivatives ⁴ . Deacylternatin was determined asdelphinidin3, 3', 5'-tri-O-b-D glucopyranoside. ⁴ White petals do not contain anthocyanins. ⁵ There are low levels of condensed tannins (0-2.48 mg catechin/g) and protein precipitable polyphenols (0.16-0.77 mg tannic acid/g) in the raw mature seeds. ⁶ contain little calcium (1.9 mg/100 g) ⁷
2.	Seeds	Contain a highly basic small protein named finotin ⁸ .contain fixed Oil. Cinnamic acid, palmitic (IV), stearic (V), oleic (VI), linoleic (VII), linoleic acids and an anthoxanthin glucoside
3.	Root bark	Contains Tannin and Resin Taraxerol (VIII) and tataxerone .



Pharmacology

Central Nervous System effects

Clitoria ternatea showed a wide spectrum of central nervous system activities i.e. nootropic, anxiolytic, anti-stress, antidepressant and anti-convulsant.⁹ *C.ternatea* methanolic extract showed nootropic effects (facilitation of intellectual performance, learning and memory) as it decreased the time required for rats to occupy the central platform in the elevated plus maze and increased the discrimination index in object recognition tests⁹. The plant exhibited weak anxiolytic activity by increasing the occupancy of rats in the open arm of the exploratory maze and the lit box of the light/dark exploratory test, and antidepressant activity as it decreased the immobility time in the tail suspension test. The methanolic extract reduced stress-induced ulcers and decreased the convulsing actions of pentylenetetrazol and maximum electroshock. Cognitive abilities were improved without the production of sedation and behavioral toxicity.⁹ Oral intubation of rats for 30 days with the aqueous root extract (100 mg/kg) led to improved learning and memory.¹⁰ In neonatal and young adult rats, this led to significant increases in acetylcholine content in the hippocampus, pointing to a neurochemical basis for the improvement in learning and memory.¹⁰ The memory enhancing property of the root extract was also shown by its ability to improve retention and spatial learning performance in behavioral tests.¹⁰

Alcoholic root extracts (300 & 500 mg/kg doses orally) were more effective than the aerial parts in attenuating memory deficits in rats and this was associated with increased levels of rat brain acetylcholine and acetyl cholinesterase.^{11,12} Relationships of these effects with inhibition of acetyl cholinesterase activity were not established, cortical acetyl cholinesterase activity was actually found to be increased.¹² There was also an increase in the functional growth of the neurons of the amygdala.¹³

Anti-inflammatory, analgesic and antipyretic activities

The methanol root extract (200-400 mg/kg) given orally reduced normal body temperature and yeast-induced pyrexia in rats in a dose-dependent manner.^{14,15} The antipyretic effect of the extract was comparable to that of an oral dose of paracetamol (150 mg/kg).¹⁴ Rat paw edema induced by carrageenin and vascular permeability induced by acetic acid were inhibited by the both doses of the methanol extract. The extract also markedly reduced the number of writhing responses in the acetic acid-induced writhing response test.¹⁵ Anti-inflammatory, analgesic and antipyretic activities of the plant were attributed to its flavonoid content.¹⁵

Antifungal

A highly basic small protein, finotin, was also isolated from the seeds. This protein has broad antifungal activity.

Larvicidal activity¹⁶

Leaves: Screening of natural products for mosquito larvicidal activity against three major mosquito vectors *Aedes aegypti*, *Culex quinquefasciatus*, and *Anopheles stephensi* resulted in the identification of three potential plant extracts viz., *Saraca indica/asoca*, *Nyctanthes arbor-tristis*, and *C.ternatea* for mosquito larval control. In the case of *S. indica/asoca*, the petroleum ether extract of the leaves and the chloroform extract of the bark were effective against the larvae of *C. quinquefasciatus* with respective LC₅₀ values 228.9 and 291.5 ppm. The LC₅₀ values of chloroform extract of *N. arbor-tristis* leaves were 303.2, 518.2, and 420.2 ppm against *A. aegypti*, *A. stephensi*, and *C. quinquefasciatus*, respectively. The methanol and chloroform extracts of flowers of *N. arbor-tristis* showed larvicidal activity against larvae of *A. stephensi* with the respective LC₅₀ values of 244.4 and 747.7 ppm. Among the methanol extracts of *C. ternatea* leaves, roots, flowers, and seeds, the seed extract was effective against the larvae of all the three species with LC₅₀ values 65.2, 154.5, and 54.4 ppm, respectively, for *A. stephensi*, *A. aegypti*, and *C. quinquefasciatus*. Among the three plant species studied for mosquito larvicidal activity, *C. ternatea* was showing the most promising mosquito larvicidal activity. The phytochemical analysis of the promising methanolic extract of the seed extract was positive for carbohydrates, saponins, terpenoids, tannins, and proteins. In conclusion, bioassay-guided fractionation of effective extracts may result in identification of a useful molecule for the control of mosquito vectors.

Proteolytic activity¹⁷⁻²⁰

The activities of endopeptidases (hemoglobin pH 3.5 and azocasein pH 6.0), carboxypeptidase (CBZ-Phe-Ala pH 5.2), and arylamidases (LPA 7.0 and BAPA 7.6) were assayed in extracts of cotyledons and axis of resting and germinating seeds of *Clitoria ternatea* L. All the activities were low in resting seeds but the endopeptidases at pH 3.5 and the arylamidase at 7.0 were high in cotyledons.

The activities of carboxypeptidase and the arylamidases increased in cotyledons reaching a maximum at the day 9, while the endopeptidases showed an increase at the day 3 followed by a decrease. In the axial tissue the endopeptidases and carboxypeptidase activities showed an increase until the day 9 followed by a decrease and the arylamidases were low. The increase of acidic endopeptidase and carboxypeptidase activities in germinating cotyledons has been suggested as an indication of their participation in the degradation of the storage proteins.

Antihyperglycemic and antihyperlipidemic ²¹⁻²⁵

Leaves and flowers extract on alloxan-induced diabetic rats. The effect of aqueous extract of *C. ternatea* leaves and flowers on serum glucose, glycosylated hemoglobin, insulin, total cholesterol, triglycerides, HDL-cholesterol, protein, urea, creatinine were examined in control and extract treated diabetic rats. Glycogen was examined both in the liver and skeletal muscles of control and extract treated diabetic rats, whereas, the activity of glycolytic enzyme glucokinase and gluconeogenic enzyme glucose-6-phosphatase was examined in the liver. Oral administration of aqueous extract of *C. ternatea* leaves (400 mg/kg body weight) and flowers (400 mg/kg body weight) for 84 days significantly reduced serum glucose, glycosylated hemoglobin, total cholesterol, triglycerides, urea, creatinine and the activity of gluconeogenic enzyme glucose-6-phosphatase, but increased serum insulin, HDL-cholesterol, protein, liver and skeletal muscle glycogen content and the activity of glycolytic enzyme glucokinase. For all the above biochemical parameters investigated, *C. ternatea* leaves treated rat showed a little better activity than *C. ternatea* flowers treated diabetic rats. The present investigation suggests that *C. ternatea* leaves and flowers extract exhibit antihyperglycaemic and antihyperlipidaemic effects and consequently may alleviate liver and renal damage associated with alloxan-induced diabetes mellitus in rats.

Conclusions

C. ternatea is traditionally very important plant having many important pharmacological activities like antileprosy, anti-inflammatory, anthelmintic, immunomodulatory, antiasthmatic, antidepressant and anti-convulsant, analgesic, antipyretic, antifungal, proteolytic, antihyperglycemic and antihyperlipidemic property. Many important phytoconstituents responsible for the activity were isolated. This proves therapeutic importance of the plant. Such type of systematic information about the plant is useful for the researchers.

References

1. Kogawa K, Kazuma K, Kato N, Noda N and Suzuki M. Biosynthesis of malonylated flavonoid glycosides on the basis of malonyltransferase activity in the petals of *Clitoria ternatea*, *Journal of Plant Physiology*. 2006 5; 2(6): 374-379
2. Terahara N, Oda M, Matsui T, Osajima Y, Saito N, Toki K, Honda T. Five new anthocyanins, ternatins A3, B4, B3, B2, and D2, from *Clitoria ternatea* flowers. *J Nat Prod*. 1996; 59(2): 139-44
3. Terahara N, Toki K, Saito N, Honda T, Matsui T, Osajima Y. Eight new anthocyanins, ternatins C1-C5 and D3 and preternatins A3 and C4 from young *Clitoria ternatea* flowers. *J Nat Prod*. 1998; 61(11): 1361-7

4. Terahara N, Saito N, Honda T, Toki K and Osajima Y. Further structural elucidation of the anthocyanin deacylternatin, from *Clitoria ternatea*. *Phytochemistry*. 1990; 29(11): 3686-3687
5. Kazuma K, Noda, N and Suzuki M. Flavonoid composition related to petal color in different lines of *Clitoria ternatea*. *Phytochemistry*. 2003; 64: 1133-1139
6. Laurena AC, Revilleza Ma JR and Mendoza EMT. Polyphenols, phytate, cyanogenic glycosides and trypsin inhibitor activity of several Phillipine indigenous food legumes. *Journal of Food Composition and Analysis*. 1994; 7(3): 194-202
7. Chin CO. Direct analysis of plant minerals and comparison of extraction processes using ICP-AES. *Food Chemistry*. 1992; 45: 145-149
8. Kelemu S, Cardona C and Segura G. Antimicrobial and insecticidal protein isolated from seeds of *Clitoria ternatea*, a tropical forage legume. *Plant Biochemistry and Physiology*. 2004; 42: 867-873
9. Jain NN, Ohal CC, Shroff, RH, Bhutada RH, Somani RS, Kasture VS and Kasture SB. *Clitoria ternatea* and the CNS. *Pharmacology, Biochemistry and Behaviour*. 2003; 75: 529-536
10. Rai KS, Murthy KD, Karanth KS, Nalini K, Rao MS and Srinivasan KK. *Clitoria ternatea* root extract enhances acetylcholine content in rat hippocampus . *Fitoterapia* . 2002; 73: 685-689
11. Taranalli AD and Cheeramkuzhy TC. Influence of *Clitoria Ternatea* Extracts on Memory and Central Cholinergic Activity in Rats . *Pharmaceutical Biology (Formerly International Journal of Pharmacognosy)*. 2000; 38(1): 51-56
12. Howes MR and Houghton PJ. Plants used in Chinese and Indian traditional medicine for improvement of memory and cognitive function. *Phytother Res*. 2003; 17(1): 1-18
13. Rai KS, Murthy KD, Rao MS and Karanth KS. Altered dendritic arborization of amygdala neurons in young adult rats orally intubated with *Clitoria ternatea* aqueous root extract. *Phytother Res*. 2005; 19(7): 592 – 598
14. Parimaladevi B, Boominathan R and Mandal SC. Evaluation of antipyretic potential of *Clitoria ternatea* L extract in rats. *Phytomedicine*. 2004; 11: 323-326
15. Parimaladevi B, Boominathan R and Mandal SC. Anti-inflammatory, analgesic and antipyretic properties of *Clitoria ternatea* root. *Fitoterapia*. 2003; 74: 345-349
16. Nisha Mathew, M. G. Anitha, T. S. L. Bala, S. M. Sivakumar, R. Narmadha and M. Kalyanasundaram , Larvicidal activity of *Saraca indica*, *Nyctanthes arbor-tristis* , and *Clitoria ternatea* extracts against three mosquito vector species, *parasitology research*, Nov. 2008, 104: 1017-1025
17. Ainouz, I.L.; Benevides, N.M.B. & Freitas, A.L.P. Proteolytic activities in seeds of *Vigna unguiculata* (L.) Walp. *Biologia Plantarum (Praha)*, 1981, 23(2): 133-140,
18. Azevedo, A.R. Estudio del valor nutritivo del heno de cunha (*Clitoria ternatea* L.) en cuatro periodos derecoleccion. Madrid, 1980. 203-205.
19. Bradford, M.M. A rapid sensitive method for the quantition of microgram quantities of protein utilizing the principle of protein-dye binding. *Analytical Biochemistry*, 1976,72:248-254.
20. Charney, J. & Tomarelli, R.M. A colorimetric method for determination of the proteolytic activity of duodenal juice. *Journal of Biological Chemistry*, 1947 171:501-505.

21. Alarcon-Aguilara FJ, Jimenez-Estrada M, Reyes-Chilpa R, Roman-Ramos R Hypoglycemic effects of extracts and fractions from *Psacalium decompositum* in healthy and alloxan diabetic mice. *J. Ethnopharmacol.* 2000, 72: 21-27.
22. Al-Shamaony L, Al-Khazraji SM, Twaij HAA Hypoglycemic effect of *Artemisia herba alba*. II. effect of a valuable extract on some blood glucose parameters in diabetic animals. *J. Ethnopharmacol.* 1994. 43: 167-171.
23. Anuradha K, Hota D, Pandhi P. Investigation of central mechanism of insulin-induced hypoglycemic convulsions in mice. *Indian J. Exp. Biol.* 2004, 42: 368-372.
24. Arise RO, Malomo SO, Adebayo JO, Igunnu A. Effects of aqueous extract of Eucalyptus globules on lipid peroxidation and selected enzymes of rat liver. *J. Med. Plant Res.* 2009, 077-081.
25. Baginsky ES, Foa PP, Zak B. Methods of enzymatic analysis, second edition, Bergmeyer HU and Gawehn K 5th edition, Academic Press, New York 1992. 2; 876-880.

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