Pharmacognostical, Phytochemical and pharmacological perspective of *Clitoria ternatea* L

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**A B S T R A C T**

*Clitoria ternatea* L. (CT) (Family: Fabaceae) commonly known as ‘Butterfly pea’, a traditional Ayurvedic medicine, had been used for centuries as a memory enhancer, nootropic, antistress, anxiolytic, antidepressant, anticonvulsant, tranquilizing and sedative agent. A wide range of secondary metabolites including triterpenoids, flavonol glycosides, anthocyanins and steroids had been isolated from *Clitoria ternatea* Linn. Its extracts possessed a wide range of pharmacological activities including antimicrobial, antipyretic, anti-inflammatory, analgesic, diuretic, local anesthetic, anti diabetic, insecticidal, blood platelet aggregation-inhibiting and for use as a vascular smooth muscle relaxing properties. This plant had a long use in traditional Ayurvedic medicine for several diseases and the scientific studies have reconfirmed those with modern relevance. This review is an effort to explore the chemical constituents, pharmacological and toxicity studies of CT, which had long been in clinical use in Ayurvedic system of medicine along with a critical appraisal of its future ethno pharmacological potential in view of many recent findings of importance on this well known plant species.

**Keywords:** Memory enhancer, Antidepressant, Nootropic, Secondary metabolites, Local anesthetic

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1. Introduction

Clitoria Ternatea is one of four herbs traditionally used as Shankha Pushpi, an Ayurvedic medicine used to promote neurological health. It shows promise in animal models for its memory enhancing effects, and has a wide spectrum of neurological benefits (anti-depression, anxiolytic, anti-pyretic) yet for these latter claims preliminary evidence suggests it isn’t overly potent. Some other preliminary evidence suggests that it might be healthy for the liver and circulating lipoproteins, as well as possible benefit diabetics by inhibiting glucose uptake from the diet. However, these claims are much too early to guess their practical relevance on. Toxicological studies on rodents and historical usage currently. Both the water and fat soluble components appear to be bioactive and enhance memory; to get the benefits of both taking Clitoria Ternatea with meals may be needed.

Scientific name: Clitoria ternatea L.

Synonyms
Clitoria albiflora Mattei
Clitoria bracteata Poir.
Clitoria mearnsii De Wild.
Clitoria tanganiensis Micheli
Clitoria zanzibarensis Vatke

Family/tribe

Common names
butterfly-pea (Australia); blue-pea, cordofan-pea, honete (French); bläue Klitorie (German); clitoria-azul (Portuguese); azulejo, conchitis, papito, zapatico de la reina, zapotillo, conchita azul, campanilla, bandera, choroque, lupita, pito de parra, bejuco de conchitas (Spanish); cunha (Brazil).

Morphological description
C. ternatea is a vigorous, strongly persistent, herbaceous perennial legume; stems fine twining, sparsely pubescent, suberect at base, 0.5-3 m long. Leaves pinnate with 5 or 7 leaflets; petioles 1.5-3 cm long; stipules persistent, narrowly triangular, 1-6 mm long, subulate, prominently 3-nerved; rachis 1-7 cm long; stipels filiform, to 2 mm long; leaflets elliptic, ovate or nearly orbicular, 1.5-5 cm long, 0.3-3 cm wide, with apex acute or rounded, often notched, and base cuneate or rounded, both surfaces sparsely appressed pubescent. Flowers axillary, single or paired; colour ranges from white, mauve, light blue to dark blue; pedicles 4-9 mm long, twisted through 180° so that the standard is inverted. Bracteoles persistent, broadly ovate or rounded, 4-12 mm long. Calyx 1.7-2.2 cm long with a few fine hairs; tube campanulate, 0.8-1.2 cm long; lobes triangular or oblong, 0.7-1 cm long, acute or acuminate. Standard obovate, funnel-shaped, 2.5-5.5 cm long, 2-4 cm wide, notched or rounded at apex, blue with a pale yellow base, or entirely white, a few fine hairs at apex. Pods linear-oblong, flattened, 4-13 cm long, 0.8-1.2 cm wide, with margins thickened, and style persistent, sparsely pubescent when mature, pale brown, dehiscent when dry. Seeds 8-11/pod, oblong, somewhat flattened, 4.5-7 mm long, 3-4 mm wide, olive brown to almost black, shiny, often mottled, minutely pitted; 23,000 seeds/kg. Morphology can vary with different growing conditions. Cv. Milgarra, which has no significant distinguishing morphological characters, is normally towards the upper end of the size ranges of descriptions in the taxonomic literature. The picture of plants are given in the following figure: 1, 2, 3, 4

Distribution

Ecology
Soil requirements: Adapted to a wide range of soil types (from sands to heavy clays) of moderate fertility but is extremely well adapted to heavy clay alkaline soils, and especially on clay soils which are too shallow for leucaena (Leucaena leucocephala). Adapted to pH 4.5-8.7 but prefers medium to high pH. Some suggested tolerance to salinity,
but lower than, for example, siratro (Macroptilium atropurpureum).

**Moisture:** Requires summer rainfall of 500 mm over 3 months but grows best between 700-1,500 mm AAR. Drought tolerant and will survive in years which have only 400 mm rainfall and a dry season of 5-6 months or longer even if heavily grazed. Some tolerance of short term flooding but not prolonged inundation or water logging.

**Temperature:**
Warm (wet) season growth up to 2,000 m in equatorial Africa and to latitude 24ºS. Tolerates average daily temperatures down to 15ºC but not suited to districts with severe or frequent frosts. Production is limited more by low average daily temperatures or a short growing season than by light or even heavy frosts. Will regrow from stems following light frost or from the plant base after heavy frost. Essential to establish mature woody plants prior to frost, some of which will survive, depending on severity of the frost.

**Light:** Normally grown in full sunlight but moderately shade-tolerant, being used as a cover crop in coconut plantations and under rubber.

**Reproductive development:** Flowers can develop in 4-6 weeks after sowing and continue to flower while temperature and moisture are adequate. Flowering can occur throughout the year given sufficient soil moisture and frost-free conditions. Of 58 accessions planted in January at 19ºS, first flowering occurred 7-11 weeks after sowing. Subsequent flowering events overlapped pod set and fill. Predominantly self-fertile but with some out-crossing.

**Defoliation:**
Tolerant of heavy rotational grazing, but not constant heavy defoliation. Frequent trampling by cattle will damage the stems. Growing tips and axils of stems must be left to develop new leaves. Because of its high palatability it is better managed as short-term pasture under rotational grazing. Optimum cutting interval of 56 days at heights of 5 or 10 cm for total yield of DM and protein. It has persisted for 14 years and spread under heavy dry season grazing in infertile vertisols in northwestern Queensland, Australia. For persistence, must be allowed to set seed. In protein bank, cattle should be allowed to graze for only 2-3 hours each day.

**Fire:**
Temperature and duration of the fire (governed by fuel load, air temperature, soil moisture and wind) will largely decide survival of butterfly pea after fire. A hot fire has the ability to kill plants completely. Cooler fires may kill some stems, or all above ground material, in which case the plant may reshoot from surviving stems or from the plant base. Fire destroys litter, reduces cover and opens the canopy to light, which can increase the germination and establishment of both weeds and butterfly pea seedlings.

**Agronomy**
Guidelines for the establishment and management of sown pastures.

**Establishment:** Best results are achieved by planting into soil moisture (2-6 cm), in narrow rows (15-50 cm apart) at about 2-4 kg/ha for long-term pastures and about 6 kg/ha for short-term pastures to achieve plant densities of 5-10 plants/m². Excellent results can be achieved when sown as a crop using conventional planters and presswheels to achieve good soil/seed contact. For optimum yield as a green manure crop, use a seeding rate of 12 kg/ha. As a component of grass-legume pastures, can also be planted behind a blade plough or using a "crocodile seeder". Soil temperatures between 16 and 36ºC are required for good establishment. Weed competition will delay establishment but, once established, Clitoria can smother most weeds. Seed should be inoculated with Tropical Group M rhizobium. Mechanically scarify seed with a high hard seed content (>30%) when soil conditions favour immediate germination, or use unscarified seed with a high hard seed percentage when staggered germination is desired, eg. planting behind a blade plough or when using a crocodile planter. Butterfly pea establishment is considered a much lower risk on heavy textured soils because of the large seed size and greater weed tolerance than alternatives such as leucaena (Leucaena leucocephala). Use of pre-emergent herbicide such as imazethapyr, 2-8 weeks prior to sowing is desirable to achieve successful control of weeds during establishment in old cropping areas.

**Fertilizers:** Not normally used when sown on suitable soils, but P and S may be required on infertile soils.

**Compatibility (with other species):** Rapid climbing growth suggests that Clitoria will combine better with tall and tussock grasses than with creeping ones. It has been used as a leguminous mulch within elephant grass (Pennisetum purpureum) to improve the grass protein levels. When grown together, Clitoria increased total forage protein content and total DM without reducing yield of the grass. Sown as a pure stand as short-term (2-3 year) rotation with crops.

**Companion species**

**Grasses:** Has been grown successfully with elephant grass (Pennisetum purpureum), and forage sorghums (Sorghum bicolor) and millets as well as Panicum maximum. Also shown with pangola (Digitaria eriantha) as a pasture, and Andropogon gayanus and Dichanthium aristatum. It has been grown successfully with Cenchrus ciliaris and Chloris gayana as a revegetation species on coal mines.

**Pests and diseases:**
Fungal leaf diseases (e.g. Cercospora, Colletotrichum, Oidium and Rhizoctonia) have been recorded in cool wet weather but rarely as a serious problem. Minor susceptibility to various leaf-eating caterpillars and grasshoppers. Most lines (variably) susceptible to root nematode Meloidyge incognita.

**Ability to spread:** Will not spread in grazed pastures. Commonly C. ternatea pastures are sown as pure legume pastures and are progressively invaded by vigorous pasture grasses as soil-N levels build up.

**Weed potential:**
Natural spread is unlikely as the plants are very palatable and the seedlings do not compete well with existing vegetation. Excellent nutritive value with high protein and digestibility (up to 80%) with nitrogen concentrations of 3.0% N for leaf and 1.5% N for whole plant. Leaf had consistently low ADF (c. 20%) and high N (c. 4%) in Queensland.
**Palatability/acceptability:** Very palatable thus requiring grazing management to persist.

**Toxicity:** Seeds are a strong purgative.

**Production potential**

- **Dry matter:** 1-15 t/ha/yr DM; cv Milgarra yielded 4,200 kg/ha DM after 4 month’s growth. Under dryland conditions in the sub-humid tropics, ley pastures of cv. Milgarra in cropping systems generally produce 2-6 t/ha/year DM.

**Animal production:**

Liveweight gains of 0.7-1.3 kg/ha/day recorded for steers grazing pure Clitoria pastures in central Queensland, Australia. In northern Australia, cattle grazing para grass (Brachiaria mutica) and C. ternatea pasture gained 0.68 kg/head/day, a higher gain than for stylo (Stylosanthes) or centro (Centrosema) mixtures with para grass.

**Genetics/breeding:**

- Diploid 2n = 16; largely self-fertile (eg. cv. Milgarra) but some accessions must be at least partially outcrossing as segregating genotypes have been identified within natural populations. Homozygous blue and white and heterozygous blue-flowering genotypes have been identified. Emasculation is easily performed with tweezers to make crosses, however no breeding programs have been conducted.

**Seed production**

Hand harvest where economical, but can achieve 700 kg/ha by mechanical harvesting methods (direct-heading). Irregular pod maturity affects best time of harvest as some pods will have shattered while flowers and green pods are still present.

**Herbicide effects**

Herbicides such as bentazone (post-emergence) and imazethapyr (post-planting) are commonly used to control weeds during early establishment in northern Australia. Invading grasses may also be controlled using selective grass killers such as fluazifop or sethoxydim.

**Strengths**

1. Easy to establish, including on heavy clays and surface-crusting soils.
2. Palatable and high nutritional value.
4. High forage and seed production.

**Limitations**

1. Requires moderate fertility soils.
2. Requires careful grazing management for persistence.
3. Generally requires replanting every 5-8 years due to increasing dominance of invading grasses.
4. Moderate tolerance of salinity and sodicity.

**Sources of Composition**

**Historical Usage**

Clitoria Ternatea, also referred to as the Butterfly Pea, is a cognitive enhancer used in Ayurveda that is also known as Shankapushpi. It is currently grown as a mixed ornamental, fodder, and medicinal plant. Clitoria Ternatea is a tropical twining herb, growing wild and also in gardens, bearing white/ink blue flowers resembling a conch-shell. The roots, leaves, and stems are all frequently used in Ayurveda, but for slightly different purposes. The roots are most widely used and are bitter, refrigerant, laxative, intellect promoting, diuretic, anthelmintic and tonic and are useful in dementia, hemicrania, burning sensation, leprosy, inflammation, leucoderma, bronchitis, asthma, pulmonary tuberculosis, ascites and fever. The seeds are cathartic, while the leaves are used in otalgia and hepatopathy. It should be noted that Shankapushpi is associated with traditional benefits, but the source is of question. Clitoria Ternatea is one of three herbs (the other two being Convolvulus pluricaulis and Evolvulus alsinoides, both from the Convolvulaceae family) that has been associated with the term Shankapushpi; all three herbs appear to have memory boosting bioactivity. Infrequently, Canescus decussata is also used. The plant that may rightfully claim the name of Shankapushpi seems to be Convolvulus pluricaulis.

**Taxonomically speaking**, the above four plants all share the same class (Magnoliopsida) and Clitoria Ternatea separates itself at the level of sub-class (belonging to Rosidae, while the other three belong to Asteridae); Canescus decussata then separates into the Gentianales order while the remaining two plants keep identical orders (Solanales) and families (Convolvulaceae) [8, 10]. 'Historically used' as a brain booster, but its historical reports are inherently going to be confounded with three other herbs since they have been used interchangeably when the 'true' Shankapushpi is not available.

**Composition**

Benefits have been seen with both the water and ethanolic components, so there are likely multiple bioactive compounds (in regards to brain boosting); the known components of Clitoria Ternatea are: Taraxerol [11, 12], Anthocyanin compounds based on Delphinidin called Ternatins [13, 14], Steroids, undisclosed [15] but possible related to stig mast-4-ene-3,6-dione [16], Flavonoids, undisclosed [15], Glycosides, undisclosed in one study [15] and those based on Kaempferol and Quercetin in another study [17], Saponins, undisclosed [15], Carbohydrates in the seeds and leaves, mostly water-soluble mucilage, flutulene, and oligosaccharides [9, 18]. A fatty acid composition consisting mostly of Palmitic, Stearic, Oleic, and Linoleic acids [9]. A biopesticide called Finotin [4], Trypsin inhibitors (unidentified) in the seeds [4]. Total phenolic content of Clitoria Ternatea is approximately 1.9 mg/g (0.2%) gallic acid equivalents (GAE); relatively low compared to other herbs [19]. Composition of Clitoria Ternatea is still not too well known.

**2. Neurology and the Brain**

**Memory:** In young rat pups, 50 or 100mg/kg of the water extract of Clitoria Ternatea was able to increase memory over the course of 30 days. Higher doses of the ethanolic extract (300mg/kg) have also been found to be effective, with the root extract being seemingly more potent.
than the aerial (leaf and stem) extract [21]. A subsequent comparative study found 100mg/kg Clitoria Ternatea (water extract) insignificantly different than 50mg/kg Piracetam after 9 days of treatment, despite no apparent effects of Clitoria after the first day (with Piracetam being effective after the first dose); suggestive of a loading effect of Clitoria similar to Bacopa monnieri [6]. One in vivo study noted higher cholinergic function after oral administration of Clitoria Ternatea, suggesting the mechanism for memory enhancement is via acetylcholine [21]. Other studies have also noted increases in acetylcholine localized to the hippocampus using 100mg/kg of a water extract [7]. This latter study assessed both neonatal (6 day old) and adult (60 day old) rats and found increases in hippocampal acetylcholine to 130% and 262% of baseline values, respectively, with more efficacy in older rats. The authors suspected an increase in acetylcholine synthetic enzymes due to earlier work on dendritic arborization [22] being indicative of enhanced protein synthesis in neurons [7].

When rats are subject to electroshock stress (to induce cholinergic amnesia) a higher degree of memory retention is seen with Clitoria roots relative to aerial parts, and insignificant differences exist between the potency of 300mg/kg or 500mg/kg Clitoria Ternatea and 54mg/kg Pyritinol when looking at acetylcholine content of the brain; Pyritinol led to an increase in acetycholinesterase activity in the Midbrain while higher doses of the root extract led to increases in the cortex and decreases in the Medulla; 300mg/kg had no effect on acetycholinesterase [21]. Preliminary animal evidence suggests that it has the memory enhancing effects that have been attributed to it historically, and comparative analysis' put it at a similar potency in animals to some common Nootropic compounds.

**Anxiety and Depression:**
Clitoria Ternatea appears to possess both anxiolytic and anti-depressive actions, of moderate to weak potency relative to control drugs (Diazepam, Fluoxetine) [6]. In tests doses of 30-400mg/kg it showed dose-dependence, however, Clitoria was also able to reduce the biological effects of stress on rats when taken at 400mg/kg, as assessed by stress-induced ulcers. High doses of Clitoria may be adaptogenic [6]. Appears to possess stress reducing effects, but may not be overly potent in doing so; lack of evidence anyways.

**Interactions with Glucose Metabolism**
Absorption: In vitro studies on carbohydrate enzymes found that Clitoria was able to inhibit the intestinal glucosidase enzymes (IC50 of 3.15+/−0.19 mg/ml) against intestinal sucrase (IC50 4.41+/−0.15 mg/ml) and pancreatic alpha-amylase (IC50 4.05+/−0.32 mg/ml) [23]. The pancreatic alpha-amylase inhibition was additive with the herb Hibiscus sabdariffa [23].

**Interactions with Cardiac Health**
Lipids and Lipoproteins:
In a model of experimentally induced hyperlipidemia (via poloxamer 407 in one study, diet-induced in the other), Clitoria Ternatea was able to suppress triglycerides and total cholesterol (at 500mg/kg) to a similar extent as the statin atorvastatin (50mg/kg) and Gemfibrozil (50mg/kg) although no group brought levels back down to control value [24]. Both seeds and the root extract reduced Triglycerides, although only the root was able to reduce total cholesterol. Since benefit was also seen with poloxamer 407, it was concluded that the benefits on triglycerides were seen through activating lipoprotein lipase (LPL) [24]. Clitoria Ternatea was also associated with increased fecal cholesterol content (indicative of inhibiting absorption of cholesterol) but did not influence HMG-CoA activity [24]. This study finally concluded an improvement in the artherogenic index and the HDL: LDL ratio, with a decrease in lipid peroxidation associated with Clitoria Ternatea [24].

**Diuresis:** Clitoria Ternatea has been used traditionally as a diuretic, which has been confirmed in dogs [25] but has not been investigated further.

**Immunity and Inflammation**
Asthma: The ethanolic extract of Clitoria Ternatea has been shown in one mouse study to possess anti-asthmatic effects as assessed by passive cutaneous anaphylaxis [15] In this test, there was no significant difference between 100, 125, and 150mg/kg bodyweight Clitoria Ternatea and it was equally effective as 50mg/kg Dexamethasone in regards to suppression of leukocytes and Eosinophils [15].

**Interactions with Hormones**
Estrogen: Components of Clitoria Ternatea (aerial parts) have failed to induce appreciable estrogenicity in a yeast assay on both estrogen receptors subtypes [26].

**Nutrient-Nutrient Interactions**
Perment: Perment is a brand name for 500mg of four herbs of Ayurveda in equal (125mg) parts; Bacopa monnieri, Ashwagandha, Clitoria ternatea, and Asparagus racemosus; touted to be synergistic with each other in at least one (independent) study [27]. In an animal model of Chronic unpredictable manageable stress (which effectively induces anxiety and depression), the Perment ratio was administered at 75, 150, and 300mg/kg bodyweight for 21 days alongside stressors was able to negate stress-eating (no dose-response), was about as potent than Diazepam (2mg/kg) at normalizing neurotransmitter levels, and less potent at reducing Anxiet [27]. Perment appeared to be more catered towards anti-depressive effects than anti-anxiety effects in this study, and no evidence was put forward for synergism between the molecules [27].

**Safety and Toxicity**
One study assessing oral toxicity and using doses up to 3000 mg/kg bodyweight failed to notice any salient toxicological signs or deaths with this dose, using concentrated ethnicolic extracts of the aerial parts (11:1) and roots (6:4:1) [21].

**3. Results and Discussion**
This plant’s root is specially used for leucoderma. It is also considered as Visahara. Brhat Trayi texts do not come across the term Aparãjita. Externally uses of this plant are: it alleviates swelling and pain, it has haemostatic action hence it is used in piles specially bleeding piles. Piles are cleaned with the decoction and the paste of whole plant is applied over it. Leaf juice is used as nasal drops in headache. Oil boiled with dhamasa is used for massage in
rheumatoid arthritis. Decoction is used for gargling in stomatitis and for cleaning wounds. It prevents pus formation. Internally it is used in the treatment of deases of various organs and systems which are given below:

**Nervous system:** It has a tranquilizing effect on the brain hence it is used in symptoms like syncope, vertigo and brain weakness.

**Digestive system:** It is an antiemetic, antidyspeptic, mild-laxative and cholagogue. Therefore it is used in emesis, dyspepsia, constipation jaundice and piles. Kapha and pitta work together in the lower part of the stomach. It is used in healing ulcers of pylorus duodenum etc.

**Circulatory system:**
Being haemostatic and blood purifier, it is useful in haemorrhagic disorders and vatarakta. Hot infusion of dhamasa is given to prevent small pox.

**Respiratory system:**
It is used in common cold, cough, asthma as it acts as an expectorant and reduces the irritation of respiratory organs. Besides this, whole plant is used for smoking. Decoction is used for gargling in throat manifestations

**Mansavaha srotas:** Dhamasa is applied over neck stiffness.

4. Conclusion
In conclusion, we report here, that plant had a long use in traditional Ayurvedic medicine for several diseases and the scientific studies have reconfirmed those with modern relevance. This review is an effort to explore the chemical constituents, pharmacological and toxicity studies of CT, which had long been in clinical use in Ayurvedic system of medicine along with a critical appraisal of its future ethno pharmacological potential in view of many recent findings of importance on this well known plant species.

5. References