IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

REVIEW ARTICLE ON BUTTERFLY PEA: ITS ETHANOPHARMACOLOGICAL AND ETHANOMEDICINAL USES.

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ABSTRACT: Herbal medicine has grown over the past decades and gain popularity in developing and developed countries to cure chronic diseases or disorders. *C.pluricaulis,* an evergreen herb called *C.microphyllus Sieb.* and *C.prostratus Forsk.* it is utilized as a conventional folk remedy for a range of illnesses. In this article, we used PubMed, SciFinder, and Google Scholar to conduct electronic searches to find information about C.pluricaulis. The plant profile, phytochemistry, neuropharmacological, and toxicological information of C. pluricaulis are clarified by this thorough review. Many different in-vitro and in-vivo neuropharmacological effects, including as a boost to memory, anxiolytic, and tranquilizing properties, have been demonstrated by the crude herb and its metabolites, anti-depressants, anti-stress, neurodegenerative, anti-inflammatory, anti-oxidant, analgesic, sedative, anti-convulsant and Alzheimer's disease-reversing effects.
Secondary metabolites form *C.pluricaulis* interact with various proteins, neurosynapses, signaling pathways and serotonergic synapse which plays a crucial role in neurotransmission, Alzheimer's disease, long term depression, addictions to alcohol, cognitive disorders, psychological conditions and increasing serotonin concentration in synapses.

KEYWORDS:
Canscora decussate, Clitoria ternatea, Convolvulus pluricaulis, Evolvulus alsenoides, Shankhapushpi.

INTRODUCTION :

Clitoria ternatea commonly called as the butterfly pea of family Fabaceae and sub-family papilionaceae is a perennial leguminous twiner, which originated from the Asian tropical area and later was widely distributed in south and central America, East and West indies, India and China, where it has become naturalized[1]. The plant is also called as Aparajit in Hindi, Aparajita in Bengali, and Kokkattan in Tamil of Indian traditional medicine [2]. Its thrives in regions with full sunlight and partial shade, and its seed germination typically takes around 1-2 weeks, with flowering occurring approximately 4 weeks after germination[15]. Being a leguminous plant its roots from a symbiotic association with soil bacteria known as rhizobium which fixes atmospheric nitrogen into a plant –unstable form (a process called nitrogen-fixation), therefore this plant is used to improve soil quality through the decomposition of nitrogen-rich plant material[5]. The root part of *C.ternatea* has been used as laxative, purgative, diuretic, inflammation, indigestion, constipation, fever, arthritis,vision problems, anthelmintic[7]. Preliminary phytochemical screening of *Clitoria ternatea* revealed that the preparation contained tannis, phlebotomine, carbohydrates, anthocyanins, saponins, triterpenoids, phenols, alkaloids, flavonoids, flavonol glycoside, proteins, anthraquinone, cardiac glycosides, volatile oils and steroids[8]. The Butterfly Pea flowers contain anthocyanins, which are natural antioxidants that slow down the aging process. Prevents skin aging and help the skin. The blue hue of *Clitoria ternatea* flowers are used as an abundance of

natural coloring in the preparation of various dishes [10]. The most prominent characteristic of *Clitoria ternatea* is its petals, which appeal blue colour. The increase in the awareness of food and safety opened new area of research, with the use of naturally occuring colourants from various plant based sources being recommended as a beneficial alternative to toxic synthetic dyes[11].

Figure 1 Butterfly Pea Flower Tea

MORPHOLOGY :

The taxonomical classification of Clitoria ternatea species[15]

Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliosida
Subclass	Rosids
Order	Fabales
Family	Fabaceae
Subfamily	Papilionoideae
Genus	Clitoria
Species	Ternatea (Linnaeus)

Table 1 Taxonomical Classification

BOTANICAL CLASSIFICATION :

Shankhpushpi, scientifically known as convolvulus pluricaulis, is an evergreen plant that is associated with the family convolvulaceae. It is commonly found in India and other parts of Asia. The plant as slender stems and small white or pink flowers with a trumpet-like shape. Its leaves are oval-shaped and have a smooth texture. Shankhapushpi can grow upto 60 cm in height and thrives in warm and humid climates.

TRADITIONAL USES :

Butterfly-pea flower tea is a herbal tea (caffeine free) , a drink produced with a decoction of leaves of the *C.ternatea* plant and dried lemongrass. Buttrtfly pea flower tea still has many of the therapeutic properties of the *Clitroria ternatea* as well as extracting the deep blue colour of the petals that had made the plant the popular dye for centuries. One of the important factor of the tea is the fact that it changes colour based on the values of pH of the material that was added to it, for example adding oflemon juice to the tea will change it to purple[5].
Root was used in the cause of therapy of ascetics, enlargement of abdomibal visera, sore throat and skin disease. They were not advised and were also used as purgative dueo their tendency to create gripping and soreness. Root is administred with honey as general tonic to the children for enhancing mental abilities,

developing muscles and moisturizing the skin. A further use for roots was in epilepsy. Numerous individuals utilize seeds and leave as a brain tonic for boosting memory and intelligence. For the anti dote of snake bite juices and flowers are used [10].

The herb is non-toxic and its use does not bring into being any side effects. In contrast, there is stimulating effect in strengthening of health and weight gain. According to Ayurveda concept, Rasayana therapy affects the body, mind and brings about psychic and physical improvements. This therapy prevents the effects ageing, develops intelligence within the body resistance against diseases.

It is among the most significant medhya rasayana drugs in Ayurvedic system of medicine. When taken as an astringent, the herb balances the Kapha-Vata-Pitta doshas and reduces anxiety by controlling the body's production of cortisol and adrenaline, two stress chemicals [16].

Figure 2 Clitoria ternatea in Ayurvedic medicine

CHEMICAL CONSTITUENTS :

Butterfly pea yields 25-30 tons of dry materials annually per acre in a good conditions, Due to its high calcium concentration the C.ternatea plant is used to make herbal drinks that are an excellent supplier of calcium[3].

Leaf :

The leaves have 21.5% fiber and 21.5-29% protein content, respectively. From leaves of plant clitorin and kaempferol have been seperated. The leaves also contains 3-monoglucosides, 3-rutinoside, 3-neohesperidoside, 3-o-rhamnosyl-glucoside, 3-o-rhamnosylgalactoside of kaemferol, kaemferol-3-rhamnosylo- rhamnosyl-glucoside. It also contain aparajitin and β-sitosterol. The flowers (blue in colour) contain delphinidin-3,5-diglucoside, delphinidin-3β-glucoside, and its 3 methyl derivative, malvidin,3β-glucosides, kaemferol and cynidin chloride. A lactone-aparajitin from leaves[3].

Figure 3 Leaves of clitoria ternatea plant

Root:

The roots of the plant contains taxaxerol and taxaxerone. The bark of roots contains the seresin. The root nodule contains lecine, valine, and alanine, α-amminobutyric acid, glutamic acid, arginine,ornithine, histadine, γ-amminobutyric acid[3].

Figure 4 10th leaf stage

Seed:

Along with fixed oil, tannic acid and glucose, the seed also has a cotyledon and bitter-tasting granular starch as its active ingredient. Two distinct compounds have been extracted from seeds: anthoxanthin and sitosterol. Apart from that, linoleic, strearic, palmitic and linolenic acids are produced from seed oil. Almost similar composition was discovered in the oils of blue and white-flowers.hexacosanol, cinnamicacid and neocleoprotein which shares some ammino acid sequences with insulin are also found in seeds.

The seeds are very high in protein content (15-25%). The seeds contains p-hydroxycinnamic acid, flavonol-3-glycoside, adenosine, 3,5,7,4-tetrahydroxyflavone-3-rhamnoglucoside, polypeptide, hand exacosanol. Oligosaccharides are also found in seeds. A edible colourant, delphinidin 3,3,5-triglucoside also reported in seeds lecine amounts to roughly 2.8% of the total protein that may be extracted from seed meal or 30mg of lectin/30g of *C.ternatea* seeds in contrast 9mg fetuin/30g of seeds. Tryptophan and tyrosine were also reported in seeds[3].

Figure 5 Seeds of Clitoria ternatea plant

Flower:

Two acyl moieties were determined as E-4-0-β-D-glucopyranosyl-p-coumaric acid and 6-0-malonyl-D-glucopyranose. Other six ternatins A1,A2,B1,B2,D1 and D2 in *C.ternatea* flower are separated by reverse phase High Performance Liquid Chromatography (HPLC). The white flower yield only kaeferol. Petals of *C. ternatea L*. contain some flavonol glycosides isolated are kaempferol 3-O-(200-O-a-rhamnosyl-600-o-malonyl)-b-glucoside; quercetin 3-O-(200-O-arhanmnosyl-600-O-malonyl)-b-glucoside; myricetin 3-2G-rhamnosylrutinoside; quercetin 3-2G-rhamnosylrutinoside. Flower also contain kaempferol3-2G-rhamnosylrutinosude; kaempferol 3-rutinoside; quercetin 3-glucoside; myricetin 3-glucoside. Cyanine chloride and kaempferol are identified from the flowers. Seperation of Six acylated anthocyanins A,B,C,D,E and F by the petals of blue flowers has been done with the partial characterization of kaempferol and its 3-glucosides, robinin, quercetin and 3-glucoside. Blue flowers of C.ternatea plant also contain lobelinins, which has the 3,5,3,5-tetraglucoside substituted pattern. Deacylternatin is also discovered in the blue flower petals[3].

Figure 6 Clitoria ternatea Flower

PHARMACOLOGICAL ACTIVITIES :

Anthelmintic activity :

Anthelmintic avtivity was found in ethanolic and water based extract of *C.ternatea* leaves at the dos of 100mg/ml.This was performed at three different concentrations(100,50,25mg/ml) of ethanol-based extracts, utilizing *Eisenia foetida*, in turn. The primary goal of the study was to compare the anthelmintic activity of c.ternatea leaf extracts in-vitro using both water-based and ethanol-based extracts. For this reason, the research required timing the worms' paralysis (P) and death (D). While determination of both extracts, the time of paralysis (P) and death (D) time of aqueous extract was reported as 18±1.57 and 53.33 ± 0.33 and in case of ethanolic extracts 12.33±0.80 and 32.33±0.71 respectively. At last, the anthelmintic activity of ethanol-based extract of *C.ternatea* was found more efficacious than water-based extract of *C.ternatea*[3].

Anti Diabetic activity :

Anti diabetic activity of ethanolic extracts was evaluated in rats. Rats fed with ethanol-based extracts of flowers for three weeks significantly lowerd serum sugar level in experimentally induced diabetics due to inhibition of the galactosides and glucosides activities but no inhibition of fructosidase activity was observed.

The hypoglycemic properties of methanol, water, and petroleum ether and chloroform extract *Clitoria ternatea* leaves were evaluated in streptozotocin-induced diabetics rats foracute and subacute effects.The extracts of *Clitoria ternatea* (200-400 mg/kg) significantly reduced the hyperglycemic effect in streptozotocin-induced diabetic rats,400mg/kg possessed significant hypoglycemic effects, 200mg/kg also decreased glucose level but not as 400mg/kg. The methanol extract's acute action resulted in nearly similar effects for200-400mg/kg; however, after the 30-minute mark, 200mg/kg caused a little drop in blood glucose levels. Subacute activity

showed that on the long term use of extract the dose 200mg/kg is much better to control the blood glucose level than the 400mg/kg dose.

For all the biochemical tests, the leaf extract – treated rat essentially shown the same profile as those treated with the flower extracts.

The anti diabetic and anti hyperlipidemic potential was evaluated in streptozotocin-developed diabetic rats and co related either its in-vitro and in-vivo antioxidant activity. The extracts and parts was initially screened for acute and subchronic anti diabetic activity in the dose range of 100-200mg/kg.

The study revealed that the *C.ternatea* leaves and flowers extract possess anti-hyperglycaemic and anti-hyperlipidaemic effects and consequently may reduce liver and renal damage associated with alloxan-induced diabetic mellitus in rats. Anti-hyperlipidemic effect of *C.ternatea L*. and *V.mungo L*. (Fabaceae) on preliminary developed hyperlipidemia in rats by poloxamer 407- induced acute hyperlipidemia and deit – induced hyperlipidemia models was studied and results showed that the mixture of water and alcohol lysates of the roots and the seeds of *C.ternatea* and the hydroalcoholic extracts of the seeds of *V.mungo* results in a significant ($P<0.05$) reduction of triglycerides, very low density lipoprotein cholesterol,and low density lipoprotein cholesterol level. The atherogenic index (AI) and the high density (HDL) / low density lipoprotein (LDL) ratio were normalized after treatment in diet-induced hyperlipidemic rats[5].

Anti-inflammatory activity, Anti-pyretic activity and analgesic activity :

Leaf and flower extract of *C.ternatea* has been identified as having an inflammatory activity. Petroleum based ether lysates and ethanol reported in the pain relieving activity that ethanol treated lysates showed up to 1.5-2 hrs. of long lasting effect. Flavonoids were important for anti-inflammatory, analgesic and anti-pyretic activity in *C.ternatea*. The methanolic extract of *C.ternatea* root T 200, 300 and 400mg/kg body weight doses. The yeast provoked increased the temperature dose-dependent and decrease the body temperature to normal. The narcotics drugs treat the inflammatory and pain condition, which are mostly costly and have adverse effects. Natural drugs, especially from *C.ternatea*, can be an option for providing cheaper and feasible drugs[13].

Another study reported that carrageenan induced rat paw oedema and acetic acid-induced vascular permeability in rats were considerable reduced after oral administration of methanolic root extract of *C.ternatea*. The extract's anti-pyretic efficacy found to be comparable to paracetamol. Recently, *C.ternatea* leaf extract have been linked to analgesic properties[14].

Antidepressant activity :

The methanol based extract of *C.ternatea* at the doses of 100 and 400 mg/kg, p.o has shown antidepressants effect in tail-suspension test in mice. The extract of CT significantly decreased the duration of motionlessness at doses 100 and 400 mg/kg. The reduction in the duration of motionlessness was greater in 400mg/kg of *C.ternatea* in contrast to fluoxetine, 10mg/kg, i.p. The another study anti-depressants effects of ethanol-based extract of *C.ternatea* roots was also resulted at the doses of 150 nd 300mg/kg. The results from previous study indicated that two compounds, (Z)-9,17-octadecadienal and n-hexadacanoic acid isolated from root of CT can serve as potential lead molecules for developing noval selective MAO-A inhibitors which can give herbal remedy for the treatment of psychiatric disorders including the depression and ansiety[7].

Neuro-pharmacological activity :

C.ternatea has been reported to have neuroprotective effects, which may be linked to have its anti-oxidant and anti-inflammatory activities. It has shown promise in preventing the neurodegenerative disorders and increasing cognitive fuction[15]. *C.ternatea* is reported to be a good brain tonic drug mainly used in the treatment of mental wellness. Studies reported IP administration of alcohol extract of steam, flower, leave and fruit of *C.ternatea* to rats and mice, has been reported to produce sedative action and reduced alertness. The root parts of *C.ternatea* at 300-500mg/kg in rats in diminishing electroshock-induced amnesia, increase acetylcholine content and acetylcholinestarase activity in the different regions of the brains, viz, cerebral cortex, midbrain, medulla oblongata and cerebellum[12] .

Anti-convulsant activity :

An imbalance between excitatory and inhibitory neurotransmitter caused seizures. The drugs which boost the GABA levels in brain, may possess anti-convulsant activity in the experimental models of seizures. The maximal electroshock (MES) is the validated model for screening of antiepilectic drugs in the generalized tonic-lonic seizures. The methanol-based extract of the arial parts of CT shown anticonvulsant activity at dose of 100mg/kg, p.o in both pentylenetertazole(PTZ) and MES developed seizures in mice delaying the onset of

convulsions and reducing the duration of tonic hind limb extention, respectively. These results suggest the potential of CT as an antiepileptic drug, however extract of arial part of CT was not effective against PTZ and MES induced seizures in rats[7].

Anti-oxidant activity :

Antioxidants acts as radical scavengers, inhibit lipid peroxidation and the other free radical-medicated processess, and therefore they protect the human body from several diseases attributed to the reactions of radical. Various phenol-based antioxidants such as tannis, coumarins, xanthenes and more recently procyanidins have been introduced to scrounge radical in a dose-dependant manner and therefore are viewed as pathologies. Phenolic compunds are the large and diverse group of phytochemicals, which include many different families of aromatic secondary metabolites in plants. They are known to exert various physiological effects in humans, such as inhibiting platelet aggression, reducing the risk of coronary heart disease and cancer and preventing oxidative damage of lipid and low density lipoprotein. Phenolic compounds have strong in-vitro & in-vivo anti-oxidant activities associated with their ability to scrounge free radical, breaks radical chain reactions and chelate metals[2].

Nootropic activity :

From the resulted studies, it was looked into the ethanol extract of *C.pluricaulis* and its ethyl acetate and water-based parts has nootropic activity. 2 doses of 100-200 mg/kg/p.o of ethyl acetate and water-based parts are given to rats in distinct groups. Both the doses of *C.pluricaulis* found to be effective for memory and learning in rats. This activity assessed active & passive avoidance paradigms using Cook and Weidley's pole climbing apparatus and elevated plus-maze as models. One more study was done to find out nootropic property of Shankhpushpi. 3 plants i.e. *C.pluricaulis*, *C.ternatea*, *Evolvulusalsinoides* were evaluated for the nootropic activity using Porsolt's swim despair, RPM and actophotometer models. The results showed that all 3 plants possess anxiolytic, CNS-depressants & nootropic activity but *C.pluricaulis* plant shown a true source for memory enhancement[19].

Several studies have reported improvement in cognitive performance when *C.ternatea* extracts were administrated to experimental animals. In one study, rats orally dosed with ethanol extracts derived from *C.ternatea* roots or aerial tissues were showed to deplete electric shock-induced amnesia better than controls. In a separate study, 48 hrs. and 30 days after receiving an oral dosage of water based *C.ternatea* root extract, neonatal rats demonstrated increased spatial learning skill and memory retention[9].

Anti-microbial activity :

By employing the leaf- disc method and feeding deterrent using Spilosoma Oblique Walker as the test insect, the *C.pluricaulis* plant was bio-assayed . A new compound, 29-oxodotriacontanol was isolated from chloroform fraction of the plant which found to be significant antifeedant constituent where as another compound, tetratriacontanoic acid was discovered 1st time in this plant[19]. The antimicrobial screening was evaluated against Extended Spectrum Beta Lactamase (ESBL) producing *Salmonella enteritidis*, *Salmonella typhimurium*, *Klesiella pneumonia*, Enteropathogenic *E.coli*, Uro-pathogenic *E.coli*, and *Pseudomonas aureginosa* isolated from patients with urinary tract infection and acute gastroenteritis. Disc diffusion method was used to test the above mentioned extracts for their activity. Water, methanolic & chloroform extract of *C.ternatea* flower was showed activity against uropathogenic *Escherichia coli*, Enteropathogenic *Escherichia coli*, Enterotoxigenic *Escherichia coli*, *Salmonella typhimurium*, *Klesiella pneumonia* and *Pseudomonas aureginosa*. Methonol extract of *C.ternatea* exhibits comparatively high as compared with aqueous and chloroform extracts. The zone of inhibition produced by water, chloroform & methanolic extracts at a conc. of 4mg/disc was found 12mm, 16 to 26mm and 14 to 18mm respectively while hexane & petroleum ether extracts did not show any activity[3].

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