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# Pharmacological importance of *Clitoria ternatea* – A review

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**Abstract:** *Clitoria ternatea* contained tannins, phlobatannin, carbohydrates, saponins, triterpenoids, phenols, flavanoids, flavonol glycosides, proteins, alkaloids, antharaquinone, anthocyanins, cardiac glycosides, Stigmast-4-ene-3,6-dione, volatile oils and steroids. The plant showed many pharmacological effects including antioxidant, hypolipidemic, anticancer, anti-inflammatory, analgesic, antipyretic, antidiabetic, CNS, antimicrobial, gastro-intestinal antiparasitic, insecticidal and many other pharmacological effects. This Review will highlight the chemical constituents and pharmacological effects of *Clitoria ternatea*.

***Keywords:*** *Clitoria ternatea, constituents, pharmacology, pharmacognosy*

## I. INTRODUCTION

A large and increasing number of patients in the world use medicinal plants and herbs for health purpose. Therefore, scientific scrutiny of their therapeutic potential, biological properties, and safety will be useful in making wise decisions about their use[1-2]. There are hundreds of significant drugs and biologically active compounds developed from the traditional medicinal plants. Plant showed wide range of pharmacological activities including antimicrobial, antioxidant, anticancer, hypolipidemic, cardiovascular, central nervous, respiratory, immunological, anti-inflammatory, analgesic antipyretic and many other pharmacological effects[3-40]. The preliminary phytochemical screening showed that *Clitoria ternatea* contained tannins, phlobatannin, carbohydrates, saponins, triterpenoids, phenols, flavanoids, flavonol glycosides, proteins, alkaloids, antharaquinone, anthocyanins, cardiac glycosides, Stigmast-4-ene-3,6-dione, volatile oils and steroids. The plant showed many pharmacological effects including antioxidant, hypolipidemic, anticancer, anti-inflammatory, analgesic, antipyretic, antidiabetic, CNS, antimicrobial, gastro-intestinal antiparasitic, insecticidal and many other pharmacological effects. This Review will highlight the chemical constituents and pharmacological effects of *Clitoria ternatea*.

**Plant profile:**

**Synonyms:**

*Clitoria albiflora* Mattei, *Clitoria bracteata* Poir., *Clitoria mearnsii* De Wild., *Clitoria tanganicensis* Micheli, *Clitoria zanzibarensis* Vatke[41].

**Taxonomic classification:**

**Kingdom**: Plantae; **Subkingdom**: Viridaeplanta; **Infrakingdom**: Streptophyta;
**Division**: Tracheophyta; **Subdivision**: Spermatophytina; **Infrodivision**: Angiospermae; **Class**: Magnoliopsida; **Superorder**: Rosanae; **Order**: Fabales;
**Family**: Fabaceae; **Genus**: Clitoria L.; **Species**: *Clitoria ternatea*[42-43].

**Common names:**

**Arabic:** Mazerion Hidi, Baslat el-Zuhoor; **Bengali** : Aparajita, **Chinese:** die dou**; English:** blue-pea, bluebellvine, butterfly-pea, cordofan-pea, Darwin-pea**; French:** honte**; German:** blaue Klitorie**; Hindi** : Aparajita, **Portuguese:** clitória-azul, clitória; **Punjabi**: Koyal; **Sanskrit**: Girikarnika, Vishnukranta; **Spanish:** conchitas papito, azulejo, zapatico de la reina, zapotillo; **Swedish:** himmelsärt; **Tamil**: Kakkanam and **Telugu** : Dintena[41,43].

**Distribution:**

The plant originated from tropical Asia and later was distributed widely to **Africa**: (Chad, Djibouti, Ethiopia, Somalia, Sudan, Sudan, Kenya, Tanzania, Uganda, Burundi, Cameroon, Gabon, Sao Tome, Zaire, Benin, Cote D'Ivoire; Gambia, Ghana, Guinea, Guinea-Bissau, Niger, Nigeria, Senegal, Sierra Leone, Togo, Angola, Malawi, Mozambique, Zambia, Zimbabwe and South Africa; **Asia:** Madagascar**,** Saudi Arabia, Yemen, Iran, Iraq, China Taiwan, Bangladesh, Bhutan, India, Nepal, Pakistan, Sri Lanka, India, Maldives, Cambodia, Laos; Myanmar, Thailand, Vietnam, Indonesia, Malaysia, Philippines and Singapore; **Australia**; **North America:** USA and Mexico; **Northwestern Pacific:** Guam, Northern Mariana Islands, Palau, **South-Central Pacific:** French Polynesia - Society Islands; **Southwestern Pacific:** Fiji, New Caledonia, Samoa, Solomon Islands, **Southern America:** Antigua, Barbuda, Aruba, Bahamas, Barbados, Cayman Islands, Cuba, Dominica, Dominican Republic, Guadeloupe, Haiti, Jamaica, Martinique, Montserrat, Netherlands Antilles, Puerto Rico, St. Kitts and Nevis, St. Vincent and Grenadines, Virgin Islands (British), Virgin Islands (U.S.), French Guiana,

Suriname, Venezuela, Brazil, Bolivia, Colombia, Ecuador - Galapagos Islands, Peru, Paraguay and Uruguay[41,44].

**Description:**

Perennial climbing or trailing herb, growing from a woody rootstock. Leaves imparipinnate with 2-4 pairs of leaflets and a terminal leaflet. Leaflets ovate to elliptic-oblong, up to 6.5 × 4 cm, mostly hairless above, pubescent below. Flowers axillary, solitary or 2 together, resupinate, large and showy, bright blue. Pod linear-oblong, 6-13 cm long, flattened, mucronate at the apex, hairless or finely pubescent[45].

**Traditional uses:**

Root was used for the treatment of ascetics, enlargement of the abdominal viscera, sore throat and skin diseases. They were also used as purgative, but because, they cause griping and tenderness, they were not recommended. Root was administered with honey and ghee as a general tonic to children for improving mental faculties, muscular strength and complexion tonics. Roots were also used in epilepsy and insanity. Seeds and leaves were widely used as a brain tonic and to promote memory and intelligence. Juice and flowers were used as an antidote for snake bite. Seeds were used in swollen joints, crushed seeds are taken with cold or boiled water for urinary problems[46-53].

**Plant parts used:**

Leaves, seeds, bark, fruits, sprouts and stems were used medicinally[54].

**Physicochemical characteristics:**

Total ash: not more than 5%, acid insoluble ash: not more than 2%, alcohol insoluble ash: not more than 5%, water soluble extractives: not more than 8%[14]. However, total ash, insoluble ash, soluble minerals, crude protein, total lipid, crude fiber and soluble carbohydrates were estimated in various plant parts (stem, flower, leaves, seeds and root) of *Clitoria ternatea* L (mg/100g dry weight). The results showed that maximum content of total ash was found in the leaves 10.93±0.29 and the minimum was recorded in the seed 3.80±0.42, insoluble ash content was highest in the leaves 3.64±0.03, followed by root 2.75±0.034, flowers 0.90±0.95, whereas there was no insoluble ash in the stem and seed. Soluble mineral content was recorded highest in stem 9.71±0.39 , followed by flowers 8.94±0.52 and leaves 7.29±0.16, while, the lowest in the seeds 3.80±0.42. Crude protein content was found highest in the seeds 43.41±0.14 followed by flowers 41.27±0.23 and leaves 33.36±0.23, whereas the lowest in the roots 14.424±0.45 . The total lipid content was highest in the stem 10.91±0.08 followed by seeds 7.78±0.11 and leaves 1.81±0.05, while, the lowest in roots 1.351±0.22. Crude fiber content was highest in the roots 40.722±0.06 followed by stem 39.68±0.27 and seeds 33.22±0.04, whereas it was lowest in the leaves 14.45±0.09. Soluble carbohydrate was observed highest in leaf 39.45±0.25 followed by root 34.003±0.74, flowers 29.18±0.15, seeds 20.79±0.08, and the lowest in stem 10.53±0.04[55].

**Chemical constituents:**

The preliminary phytochemical screening showed that the plant contained tannins, phlobatannin, carbohydrates, saponins, triterpenoids, phenols, flavanoids, flavonol glycosides, proteins, alkaloids, antharaquinone, anthocyanins, cardiac glycosides, Stigmast-4-ene-3,6-dione, volatile oils and steroids[56-58].

The fatty acid content of *Clitoria ternatea* seeds includes palmitic, stearic, oleic, linoleic, and linolenic acids. Seeds also contained cinnamic acid, anthoxanthin glucoside, a highly basic small protein named finotin, water-soluble mucilage, delphinidin 3, 3', 5'-triglucoside and beta-sitosterol[59-63].

The aqueous extract of *Clitoria ternatea* flower (CTE) was investigated to determine the total phenolic compounds, flavonoid, and anthocyanin by Folin-Ciocalteu assay, $AlCl_3$ colorimetric method, and pH differential method, respectively. The results demonstrated that the content of total phenolics, flavonoids and total anthocyanins in CTE was $53 \pm 0.34$ mg gallic acid equivalents/g dried extract, $11.2 \pm 0.33$ mg catechin equivalents/g dried extract, and $1.46 \pm 0.04$ mg cyanidin-3-glucoside equivalents/g dried extract, respectively[64]. However, others found that the amount of total phenolics and flavonoids in *Clitoria ternatea* leaf extract were $358.99 \pm 6.21$ mg/g gallic acid equivalent and $123.75 \pm 2.84$ mg/g catechin equivalent, respectively[65].

The flowers contained flavonol glycosides. 3-O- (2"-O-alpharhamnosyl- 6"-O-malonyl)-beta-glucoside, 3-O-(6"-O-alpha-rhamnosyl-6"-O-malonyl)-betaglucoside and 3-O-(2",6"-di-O-alpharhamnosyl)- beta-glucoside of kaemferol, quercetin and myricetin were isolated from the petals. Delphinidin glycosides, 3-O-b-glucoside,3-O-(2"-O-a-rahmnosyl)-bglucoside, 3-O-(2"-O-a-rahmnosyl-6"-Omalonyl)- b-glucoside of delphinidin, and eight anthocyanins (ternatins C1, C2, C3, C4, C5 and D3, and preternatins A3 and C4) were also isolated from the flowers[66-68].

Three flavonol glycosides, kaempferol 3-O-(2"-O-alpha-rhamnosyl-6"-O-malonyl)-beta-glucoside, quercetin 3-O-(2"-O-alpha-rhamnosyl-6"-O-malonyl)-beta-glucoside, and myricetin 3-O-(2",6"-di-O-alpha-rhamnosyl)-beta-glucoside were isolated from the petals of *Clitoria ternatea* cv. Double Blue, together with eleven known flavonol glycosides. They were characterized as quercetin 3-(2(G)- rhamnosylrutinoside)s, kaempferol, quercetin, myricetin 3-neohesperidosides, 3-rutinosides, and 3-glucosides. In addition, the presence of myricetin 3-O-(2"-O-alpha-rhamnosyl-6"-O-malonyl)-beta-glucoside was inferred from LC/MS/MS data for crude petal extracts [69].

Flavonoids in the petals of several *Clitoria ternatea* lines with different petal colors were investigated with LC/MS/MS. Delphinidin 3-O-(2"-O-alpha-rhamnosyl-6"-O-malonyl)-beta-glucoside was newly isolated from the petals of a mauve line (wm) together with three known anthocyanins. Although ternatins, a group of 15 (poly)acylated delphinidin glucosides, were identified in all the blue petal lines. The white petal line did not contain anthocyanins[70].

Mome inositol (38.7%) and pentanal (14.3%) were isolated from the water extract of flowers of *Clitoria ternatea*, while mome inositol (33.6%), cyclohexen, 1-methyl-4-(1-methylethylideme) (7.1%), acetic acid, cyano- (6.5%) and hirsutene (5.7%) were isolated from methanolic extract of flowers of Clitoria ternatea[71].

Phytoconstituents like 1H-Cycloprop [e] azulene, 1a,2,3,5,6,7,7a,7b-octahydro-1,1,4,7-tetramethyl-,[1aR-(1aà,7à,7aá,7bà)]-[Synonyms: Varidiflorene], Pterocarpin, 6H-Benzofuro[3,2-c][1]benzopyran, 6a,11a-dihydro-3,9-dimethoxy-, (6aR-cis)- [Synonyms: Homopterocarpin], Isoparvifuran, Hexadecanoic acid, ethyl ester, Myo-Inositol, 4-C-methyl-, 1,2,3,5-Cyclohexanetetrol, (1à, 2á, 3à, 5á)-, Propane, 1,1-diethoxy- were identified from ethanol extract of the aerial part of *Clitoria ternatea*[72].

Many ternatins have been isolated from *Clitoria ternatea* flowers, and the structures have been determined as delphinidin 3-malonylG having 3'-GCG-5'-GCG, 3'-GCG-5'-GC, 3'-GCGCG-5'-GC, 3'-GCGC-5'-GCG, and 3'-GCGC-5'-GC side chains, in which G is D-glucose and C is p-coumaric acid[67,73].

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[74].

Sugar, starch, protein, phenol and lipid contents ( mg/100g) of leaf, stem and root were: sugar: 102±0.59, 112±0.30 and 120±0.35; starch: 42±0.35, 53±0.47 and 26±0.40; protein: 21±0.49, 39±0.13 and 58±0.48 ; phenol: 43±0.13, 37±0.56 and 18±0.35; lipid: 41±0.14, 18±0.35 and 16±0.40 respectively[75].

Mineral and heavy metals contents (mg/g) of *Clitoria ternatea* were included: Boron 0.0150±0.002, Magnesium 2.2306±0.134, Cadmium<0.0001, Calcium 3.0953±0.09, Manganese 0.0249±0.003 Arsenic <0.0001, Cobalt <0.0001, Molybdenum $0.0001\pm10^{-4}\times5.7$, Lead 0.002333±0.0002, Chromium 0.0007±0.0 Sodium 0.1413±0.003 Nickel 0.001267±0.0001, Cupper 0.0103±0.0004 Selenium <0.0001, Iron 0.1441±0.007, Zinc 0.5980±0.006 and Potassium 1.2506±0.235[71].

**Pharmacological effects:**

**Antimicrobial effect:**

Different extracts of *Clitoria ternatea* showed inhibitory effects against *Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumonia, Bacillus subtilis, Aeromonas formicans, Aeromonas hydrophila* and *Streptococcus agalactiae*. Ethyl acetate extracts of *Clitoria ternatea* showed maximum zone of inhibition against *A. formicans* (18 mm), *A. hydrophilia* (19 mm), *B. subtilis* (19 mm) and *P. aeruginosa* (21 mm) next to that ethanol extract of *Clitoria ternatea* showed maximum zone of inhibition against *A. formicans* (18 mm) and *E. coli* (14 mm) followed by the acetone extract which showed maximum zone of inhibition against *S. agalactiae* (19 mm) and *K. pneumonia* (17 mm)[76].

Aqueous extracts of both seed and callus were prepared for evaluating the antimicrobial activity against selected pathogenic fungi and bacteria using the agar well diffusion technique. Seeds and leaf delivered calli of *Clitoria ternatea* were extracted using standardized laboratory protocol. The seed extract of *Clitoria ternatea* showed maximum zone of inhibition (22 ± 0.5 mm) against *Escherichia coli* (NCIM 2645) at 0.75 mg concentration and minimum (14 ± 1.0 mm) with *Micrococcus flavus* (NCIM 2376). The callus extract showed maximum zone of inhibition (16 ± 2.0 mm) against *Salmonella typhi*, the minimum zone of inhibition was recorded against *Escherichia coli* (NCIM 2645) and *Staphylococcus aureus* (12 ± 1.0 mm and 12 ± 0.9 mm, respectively). The seed extract of *Clitoria ternatea* showed strong antifungal activity on all the tested fungi but the callus extract exhibited marginal antifungal activity[77].

The antimicrobial activities of the methanol extracts of the leaf, stems, flower, seed and roots of *Clitoria ternatea* were tested *in vitro* against 12 bacterial species, 2 yeast species, and 3 filamentous fungi by the agar diffusion and broth dilution methods. The leaf and root extracts were found to be most effective against all of the tested organisms ($p<0.05$). The MIC (minimum inhibitory concentration), MBC (minimum bactericidal concentration) and MFC (minimum fungicidal activity) values of *C. ternatea* extracts ranged from 0.3 mg/ml to 100.00 mg/ml[56].

The antibacterial properties of *Clitoria ternatea* was investigated by agar disc and well diffusion methods. The organic solvent (petroleum ether, ethyl acetate and methanol) extracts from the leaves of *Clitoria ternatea* were tested against *Bacillus cereus*, *Staphylococcus aureus*, *Klebsiella pneumonia*, *Proteus vulgaris* and *Salmonella typhi*. The results showed promising antibacterial activity against the tested microbial pathogens. Among extracts, methanol extract was found to possess a more potent inhibitory activity when compared to the other extracts (petroleum ether and ethyl acetate)[78].

An antifungal protein with a molecular mass of 14.3 kDa was isolated from the seeds of *Clitoria ternatea*. The protein showed lytic activity against *Micrococcus luteus* and broad-spectrum, fungicidal activity, particularly against the most clinically relevant yeasts, such as *Cryptococcus neoformans, Cryptococcus albidus,*

*Cryptococcus laurentii, Candida albicans* and *Candida parapsilosis*. It also exerted an inhibitory activity on mycelial growth in several mould species including *Curvularia* sp., *Alternaria* sp., *Cladosporium* sp., *Aspergillus flavus, Aspergillus fumigatus, Aspergillus niger, Rhizopus* sp., and *Sclerotium* sp[79].

*Clitoria ternatea* leaf extract showed a favorable antifungal activity against *A. niger*, the minimum inhibition concentration was 0.8 mg/ml and minimum fungicidal concentration was 1.6 mg/ml, respectively. The leaf extract exhibited considerable antifungal activity against filamentous fungi in a dose-dependent manner with 0.4 mg/ml $IC_{50}$ value on hyphal growth of *A. niger*. The main changes observed under scanning electron microscopy after *Clitoria ternatea* extract treatment were loss of cytoplasm in fungal hyphae and the hyphal wall became markedly thinner, distorted, and resulted in cell wall disruption. In addition, conidiophore alterations were also observed when *A. niger* was treated with *Clitoria ternatea* leaf extract[80].

A single protein (finotin), was obtained from seeds of *Clitoria ternatea*. The protein finotin showed broad and potent inhibitory effect on the growth of various important fungal pathogens of plants (*Rhizoctonia solani, Fusarium solani, Colletotrichum lindemuthianum, Lasiodiplodia theobromae, Pyricularia grisea, Bipolaris oryzae* and *Colletotrichum gloeosporioides*). It also inhibited the common bean bacterial blight pathogen *Xanthomonas axonopodis pv. phaseoli*. Moreover, finotin has powerful inhibitory properties against the bean *bruchids Zabrotes subfasciatus* and *Acanthoscelides obtectus*[81].

**Antiparasitic and insecticidal effects:**

The ethanolic extract of *Clitoria ternatea* (100mg/ml) bring paralysis within 15-20 min and bring death within 28-30 min to the Indian earthworm *Pheritima posthuma*[82]. However, the anthelmintic activity of ethanolic extracts of flowers, leaves, stems and roots of *Clitoria ternatea* were also evaluated on adult Indian earthworms *Pheretima posthuma.* Results showed that roots of the *Clitoria ternatea* took less time to paralyze and death of the earthworms. Roots were further extracted successively with petroleum ether, chloroform, ethyl acetate and methanol and these extracts were screened for anthelmintic activity. Results showed that methanol extract of *Clitoria ternatea* root is the more potent[83].

The *in vitro* comparative study of anthelmintic activity of aqueous and ethanolic extracts of leaves of *Clitoria ternatea* was carried out against *Eisenia foetida* at three different concentrations (100, 50, 25 mg/ml). The study involved the determination of time of paralysis and time of death of the worms. At the concentration of 100 mg/ml both the ethanolic and the aqueous extracts showed very significant anthelmintic activities as compared to the standard drug, levamisole (0.55 mg/ml). In case of aqueous extract the time of paralysis and death time was observed as 18 ± 1.57 min and 53.33 ± 0.33 min, and in case of ethanolic extracts 12.33 ± 0.80 min and 32.33 ± 0.71min respectively[84].

The mosquito larvicidal activity of *Clitoria ternatea* was investigated against three major mosquito vectors *Aedes aegypti, Culex quinquefasciatus*, and *Anopheles stephensi*. Among the methanol extracts of *Clitoria ternatea* leaves, roots, flowers, and seeds, the seed extract was effective against the larvae of all the three species with $LC_{50}$ values 65.2, 154.5, and 54.4 ppm, for *A. stephensi, A. aegypti*, and *C. quinquefasciatus* , respectively. Among three tested plant species, *Clitoria ternatea* was showing the most promising mosquito larvicidal activity[85].

**Antiinflammatory antipyretic and analgesic effects:**

Ethanol extract of *Clitoria ternatea* root (ECTR) at doses 100, 125 and 150 mg/kg ip were evaluated for antihistaminic activity using clonidine and haloperidol induced catalepsy in mice. Results showed that chlorpheniramine maleate (CPM) and ECTR inhibit clonidine induced catalepsy significantly ($P<0.001$) when compare to control group, while CPM and ECTR fail to inhibit haloperidol induced catalepsy[86].

The methanol extract of blue flowered variety of *Clitoria ternatea* root (MECTR), was evaluated for its anti-pyretic potential on normal body temperature and yeast-induced pyrexia in albino rats. Yeast suspension (10 ml/kg bw) increased rectal temperature after 19 hours of subcutaneous injection. The extract, at doses of (200, 300 and 400 mg/kg bw, po), produced significant reduction in normal body temperature and yeast-provoked elevated temperature in a dose-dependent manner. The effect extended up to 5 hours after the drug administration. The anti-pyretic effect of the extract was comparable to that of paracetamol (150 mg/kg bw, po)[87].

*Clitoria ternatea* roots methanol extract, 200-400 mg/kg orally, to rats was found to inhibit both the rat paw oedema caused by carrageenin and vascular permeability induced by acetic acid in rats. Moreover, the extract exhibited a significant inhibition in yeast-induced pyrexia in rats. In the acetic acid-induced writhing response, the extract markedly reduced the number of writhings at doses of 200 and 400 mg/kg po in mice[88].

The analgesic and anti-inflammatory activity of *Clitoria ternatea* flower extract were carried out in rats (carrageenan paw edema) and mice (hot plate). The petroleum ether (60-80◦C) extract possessed significant anti inflammatory and analgesic properties[89].

The analgesic activities of the methanolic extract of *Clitoria ternatea* Linn. leaves were examined at the doses of 200 and 400 mg/kg of body weight on mice. The analgesic activities were investigated using acetic acid induced writhing test. The plant extract's Central Nervous System (CNS) depressant activity was evaluated by

using hole cross and open field tests. Acetic acid induced writhing test revealed that the extract at the lower dose inhibited 82.67% and at the higher dose produced a maximum of 87.87% inhibition of writhing that is comparable to the reference drug, diclofenac sodium. The results of CNS depressant activity showed that the extract decreased the dose dependent motor activity and exploratory behavior of mice in hole cross and open field test. The number of field crossed in open field test and hole crossed in hole cross test decreased as time approached[90]. On the other hand, the possible mechanism underlying the antinociceptive action of methanolic extracts of *Clitoria ternatea* leaf and root was studied using several antinociception models. The different antinociception models such as hot plate, tail-flick and formalin tests were used along with naloxone (a non-selective opioid antagonist) to establish the antinociceptive activity of both leaf and root extracts. Both *Clitoria ternatea* leaf and root extracts markedly demonstrated antinociceptive action in experimental animals. Results of formalin test showed that the antinociceptive activity of the extracts may be mediated at both central and peripheral level. Moreover, the results of hot plate and tail-flick tests further confirmed that *Clitoria ternatea* root extract mediated antinociceptive activity centrally at supraspinal and spinal levels whereas, the *Clitoria ternatea* leaf extract's antinociceptive activity is mediated centrally at supraspinal level only. The authors believe that the opioid receptors are probably involved in antinociceptive activity of both *Clitoria ternatea* root extract[91].

**Anticancer effect:**

The *in vitro* cytotoxic effect of petroleum ether and ethanolic flower extracts (10, 50, 100, 200, 500 µg/ml) of *Clitoria ternatea* was studied using trypan blue dye exclusion method. Both extracts exhibited significant dose dependent cell cytotoxic activity. For petroleum ether extract the concentration 10 µg/ml showed 8% reduction in cell count, however, 100% reduction was observed at 500µg/ml. In case of ethanolic extract, 10 µg/ml concentration possessed 1.33 % reduction in cell count, while, at 500µg/ml 80 % reduction in cell count was observed[92].

The cytotoxicity of the aqueous and methanol extracts of the flowers of *Clitoria ternatea* was evaluated on six types of normal and cancer-origin cell lines. These included the hormone-dependent breast cancer cell line (MCF-7), non-hormone-dependent breast cancer cell line (MDA-MB-231), human ovary cancer cell line (Caov-3), human cervical cancer cell line (Hela), human liver cancer cell line (HepG2) and human foreskin fibroblast cell line (Hs27). The anti-proliferation activities of the extracts were examined by employing colorimetric MTT (3-(4,5-dimethylthiazol-2-yl) 2,5 diphenyltetrazolium bromide) assay through time periods of 24, 48 and 72 hours. Results showed that the water extracted of *Clitoria ternatea* had significant effects ($p<0.05$) against MCF-7 with an $IC_{50}$ value of 175.35 µg/ml[65].

The crude methanol extract of leaves, seeds and stem-bark of *Clitoria ternatea* demonstrated a significant cytotoxic activity in a brine shrimp lethality bioassay test. The $LC_{50}$ values of the crude methanol extract of leaves, seeds and stem-bark were 25.82, 110.92 and 179.89 µgm/ml respectively. Crude methanol extract and methanol fraction of leaves showed a very promising cytotoxic activity[93].

The ethanolic extract of *Clitoria ternatea* . was evaluated for its *in vitro* cytotoxic and antioxidant activities. The extract showed potent cytotoxic activity in trypan blue dye exclusion method using DLA cell lines with $EC_{50}$ value of 305µg/ml and exhibited a dose dependent decrease in cell count for all the concentrations tested (0.0196-10 µg/ml)[94].

The anticancer activity of *Clitoria ternatea* was evaluated in Dalton's lymphoma (DLA) bearing mice. Tumour was induced in mice by the intraperitoneal injection of DLA cells. After 24 hours of tumour inoculation, methanol extract of *Clitoria ternatea* (MECT) was administered at doses of 100 and 200mg/kg body weight for 14 consecutive days. The effect of MECT was assessed using *in vitro* cytotoxicity, survival time, peritoneal cell count, hematological studies and antioxidant parameters. Treatment with MECT decreased tumour volume, packed cell volume and viable count. It also increased the non-viable cell count and mean survival time, thereby increasing the life span of EAC bearing mice. Hematological profile reverted to more or less normal levels in the treated group[95].

**Antioxidant effects:**

The different solvent extracts of *Clitoria ternatea* leaf were assessed for their *in vitro* free radical scavenging potential by 1,1-diphenyl-2-picryl-hydrazyl (DPPH) radical scavenging assay. All extracts exhibited potent *in vitro* free radical scavenging activity that increased with extract concentrations. The methanol extract was found to be the most potent, followed by the chloroform and petroleum ether extracts[96].

Petrolem ether, chloroform and methanol extracts of roots of blue and white flowered varieties of *Clitoria ternatea* were studied for their antioxidant potential. DPPH free radical scavenging assay, reducing power assay, hydroxyl radical scavenging assay were used for evaluation of antioxidant potential. Petrolem ether, chloroform and methanol extracts of roots of blue and white flowered varieties of *Clitoria ternatea* (CT) significantly inhibited the DPPH free radical at concentrations ranging from 50-600 mu g/ml. Petroleum ether, chloroform and methanol extracts of roots of blue flowered variety of CT showed highest inhibition (49.11, 35.42 and

70.67% at 600 mug/ ml), respectively. Petroleum ether, chloroform and methanol extracts of roots of white flowered variety of (CT) showed highest inhibition (54.48, 39.21 and 78.13% at 600 mu g/ml), respectively. Methanol extracts of blue and white flowered varieties of CT showed a very powerful antioxidant activity in DPPH radical-scavenging assay. Methanol extracts of CT also showed significant reductive ability as well as hydroxyl radical scavenging activity. Methanol extract of white flowered variety of CT showed more significant antioxidant activity as compared to blue flowered variety of CT. All the concentrations of methanol extract of CT (MECT) showed antioxidant activity when compared to control ($p<0.001$)[97-98].

The antioxidant activity of the leaves as well as blue and white flowers of *Clitoria ternatea* was investigated. They exhibited significant antioxidant activity and the sample from the blue flower bearing plant showed better scavenging activity [99].

The antioxidant activity and protective ability of *Clitoria ternatea* flower petal extract (CTE) was investigated. CTE showed antioxidant activity as measured by oxygen radical absorbance capacity (ORAC) method and 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay. CTE (400 µg/ml) remarkably protected erythrocytes against AAPH-induced hemolysis at 4 h of incubation. Moreover, CTE (400 µg/ml) reduced membrane lipid peroxidation and protein carbonyl group formation and prevented the reduction of glutathione concentration in AAPH-induced oxidation of erythrocytes. The AAPH-induced morphological alteration of erythrocytes from a smooth discoid to an echinocytic form was effectively protected by CTE[100].

The antioxidant effects and apoptotic study of the leaves of *Clitoria ternatea* was studied using the yeast cell. The yeast cells were isolated from the sugar factory effluents and the yeast cell DNA was isolated. The leaves extract from different solvents were tested for their scavenging activity against the stable free radical DPPH (2, 2'-diphenyl-1-picryl hydrazyl) in dot plot rapid screening assay method and quantified using a spectrophotometric assay method. Oxidative damage was induced *in vitro* by treating yeast DNA and analyse the effects of the leaf extracts. Genomic DNA samples were isolated from YBD broth culture. DPPH scavenging activity was highly elicited by the methanol extract of *Clitoria ternatea.* The *Clitoria ternatea* leaf extracts treatment effectively decreased the extent of DNA damage[101].

The potential antioxidant activity of *Clitoria ternatea* extracts and an extract containing eye gel formulation was investigated. Aqueous extracts were shown to have stronger antioxidant activity (as measured by DPPH scavenging activity) than ethanol extracts ($IC_{50}$ values were 1 mg/ml and 4 mg/ml, respectively). Aqueous extracts incorporated into an eye gel formulation were also shown to retain this activity, however, it was significantly less than a commercial antiwrinkle cream included for comparison. The total phenolic content was 1.9 mg/g extract as gallic acid equivalents[102].

The antioxidant property of methanolic extract (ME) of *Clitoria ternatea* leaf was investigated by employing an *in vitro* antioxidant assay. The hepatoprotective effect against paracetamol-induced liver toxicity in mice of ME of *Clitoria ternatea* leaf was also studied. Activity was measured by monitoring the levels of aspartate aminotransferase, alanine aminotransferase and billirubin along with histopathological analysis. The antioxidant activity of *Clitoria ternatea* leaf extract was 67.85% at a concentration of 1 mg/ml and was also concentration dependant, with an $IC_{50}$ value of 420 µg/ml. The results of the paracetamol-induced liver toxicity experiments showed that mice treated with the ME of *Clitoria ternatea* leaf (200 mg/kg) showed a significant decrease in ALT, AST, and bilirubin levels, which were all elevated in the paracetamol group ($p<0.01$). *Clitoria ternatea* leaf extract therapy also showed a protective effects against histopathological alterations [65].

**Antidiabetic effect:**

The hypoglycemic effects of methanol, water, petroleum ether and chloroform extract of *Clitoria ternatea* leaves were evaluated in Streptozotocin induced diabetic rats for acute and subacute effects. The extract of *Clitoria ternatea* ( 200 and 400 mg/kg) significantly reduced blood glucose level in Streptozotocin induced diabetic rats. 400mg/kg possessed significant hypoglycemic effect, 200 mg/kg also decreased glucose level but not as 400mg/kg. The result of acute effect of the methanol extract , showed that 200 and 400 mg/kg exerted a very similar effect, but at the initial stage at the 30 min, 200mg/kg showed a fine decrease in blood glucose level. Subacute activity showed that on the long term use of extract the dose 200 mg/kg is much better to control the blood glucose level than the 400 mg/kg dose[103].

The hypoglycemic effects of methanol extract of *Clitoria ternatea* leaves (200 and 400 mg/kg) was investigated in alloxan induced diabetic rats. The extract of *Clitoria ternatea* significantly ($P<0.001$) reduced blood glucose level in alloxan induced diabetic rats twelve hours after administration[104].

The hypoglycemic effects of the aqueous extract of *Clitoria ternatea* leaves and flowers ( 50-500mg/kg) were investigated in alloxan-induced diabetes in rats. The aqueous extracts of *Clitoria ternatea* leaves and flowers (400 mg/kg bw) significantly ($P<0.05$) reduced serum glucose, glycosylated hemoglobin and the activities of gluconeogenic enzyme, glucose-6- phosphatase, but increased serum insulin, liver and skeletal muscle glycogen and the activity of the glycolytic enzyme, glucokinase. For all the biochemical tests performed, the leaf extract-treated rat showed essentially the same profile as those treated with the flower extract[105-106].

The effect of combined leaf extracts of *Clitoria ternatea* (CTL) and *Trichosanthes dioica* (TDL) was evaluated on the streptozotocin (STZ) induced diabetic Wistar rats. The results revealed that the combined extracts significantly decreased ($p<0.05$) serum glucose after the 28-days treatment[107].

Encephalopathy is a major complication in juvenile diabetes mellitus which cripples the potential physiomorphological growth and development in early childhood. The alcoholic extract of roots of *Clitoria ternatea* was evaluated in preventing the possible complications related to brain hippocampal area CA3 and pancreatic tissue in juvenile diabetic rat experimental models. The diabetes was induced in 22 days (post natal) Wistar rats by giving intra peritoneal injection of Streptozotocin at a dose of 60 mg/kg body weight. After the confirmation of diabetic state, the treatment with oral administration of alcoholic root extract of *Clitoria ternatea* at a dose of 100 mg/kg bw/ day, was started immediately and continued for one month duration. At the end of 30 days treatment, the animals were sacrified, brain and pancreatic tissues were collected for gross and histological studies. On microscopy the brain tissue showed homogenous architecture, the hippocampal CA3 region neurons showed gross viable changes in the cell morphology. On the other hand, pancreatic tissue showed reduction in the cell with hypertrophy along with relatively less inflammatory changes in the islet cells of Langerhans of animals treated by alcoholic extract of roots of *Clitoria ternatea*. The authors concluded that alcoholic root extract of herb *Clitoria ternatea* significantly prevented the complications related to brain hippocampal area CA3 and pancreatic tissue in juvenile diabetic rat experimental models[108].

The effect of alcoholic root extract of *Clitoria ternatea* on the neurons of frontal cortex and dentate gyrus was studied in young diabetic rats. The diabetes was induced in 22 days (postnatal) Wistar rats by giving intraperitoneal injection of Streptozotocin at a dose of 60mg/kg body weight. Daily single oral treatment of 100 mg/kg bw of alcoholic root extract of *Clitoria ternatea* was started and continued for a month. At the end of treatment, the animals were sacrificed and brain tissue was subjected to histopathological studies. The preventive effect of the alcoholic root extract of *Clitoria ternatea* was confirmed by significant increase of viable neurons and the significant effect on the morphology of neurons of frontal cortex and dentate gyrus[109].

The inhibitory effect of the aqueous extract of *Clitoria ternatea* flower (CTE) was studied on fructose-induced formation of advanced glycation end products (AGEs) and protein oxidation. Inhibition of AGE formation is the imperative approach for alleviating diabetic complications. The various concentrations of CTE were incubated with BSA and fructose at 37°C for 28 days. The formation of fluorescent AGEs, the level of fructosamine, protein carbonyl content, and thiol group were measured. The *in vitro* antioxidant activity was measured by the 1,1-diphenyl 2-picrylhydrazyl (DPPH) scavenging activity, trolox equivalent antioxidant capacity (TEAC), ferric reducing antioxidant power (FRAP), hydroxyl radical scavenging activity (HRSA), superoxide radical scavenging activity (SRSA), and ferrous ion chelating power (FICP). The results demonstrated that CTE (0.25-1.00 mg/ml) significantly inhibited the formation of AGEs in a concentration-dependent manner. CTE also markedly reduced the levels of fructosamine and the oxidation of protein by decreasing protein carbonyl content and preventing free thiol depletion. In the DPPH radical scavenging activity and SRSA, CTE had the $IC_{50}$ values of $0.47 \pm 0.01$ mg/ml and $0.58 \pm 0.04$ mg/ml respectively. Furthermore, the FRAP and TEAC values of CTE were $0.38 \pm 0.01$ mmol FeSO4 equivalents/mg dried extract and $0.17 \pm 0.01$ mg trolox equivalents/mg dried extract. However, CTE showed weak scavenging activity on hydroxyl radical and a weak antioxidant iron chelator. As conclusion, the results showed that CTE has strong antiglycation and antioxidant properties and might have therapeutic potentials in the prevention of AGE-mediated diabetic complications[64].

The pancreatic regeneration potential of diferent fractions of the ethanol extract of the aerial parts of *Clitoria ternatea* L. was studied. The antidiabetic and antihyperlipidemic potential was evaluated in streptozotocin-induced diabetic rats and correlated with its *in vivo* and *in vitro* antioxidant activity. The extract and its fractions were initially screened for acute and sub-chronic antidiabetic activity in the dose range of 100-200 mg/kg. The most potent extract and fractions were further evaluated for pancreatic β-cells regeneration activity along with antioxidant and antihyperlipidemic activity. The most significant pancreatic regeneration activity, antidiabetic and antihyperlipidemic activity was shown by ethanol extract and butanol soluble fraction at a dose level of 200 mg/kg[110].

**Central nervous effect:**

Seeds and leaves of *Clitoria ternatea* have been widely used as brain tonic and believed to promote memory and intelligence. The activity of *Clitoria ternatea* in Alzheimer's disease was studied to investigate its efficacy and to identify the major bioactive constituent attributing the activity. The result showed that the aqueous extract of *Clitoria ternatea* was beneficial in Alzheimer's disease through many mechanisms. The isolated compounds may act as a lead compounds for identifying new derivatives which could use for improving memory[42].

Shankhpushpi, a well-known drug in Ayurveda, is extensively used for different central nervous system (CNS) effects especially memory enhancement. Different plants were used under the name shankhpushpi in different regions of India, leading to an uncertainty regarding its true source. Plants commonly used under the name shankhpushpi are: *Convolvulus pluricaulis* Chois., *Evolvulus alsinoides* Linn., both from Convolvulaceae, and *Clitoria ternatea* Linn. (Leguminosae). The memory-enhancing activity of these three plants was investigated.

Anxiolytic, antidepressant and CNS-depressant activities of these three plants were also evaluated and compared. The nootropic activity of the aqueous methanol extract of each plant was tested using elevated plus-maze (EPM) and step-down models. Anxiolytic, antidepressant and CNS-depressant studies were evaluated using EPM, Porsolts swim despair and actophotometer models. *Clitoria ternatea* extract (CTE) showed maximum memory-enhancing and anxiolytic activity ($p<0.001$) at 200 and 100 mg/kg, respectively. Amongst the three plants, *Clitoria ternatea* extract (CTE) showed significant ($p<0.05$) antidepressant activity. All the three plants showed CNS-depressant action at higher dose levels[111].

Treatment with 100 mg/kg of *Clitoria ternatea* aqueous root extract (CTR) for 30 days in neonatal and young adult rats, significantly increased acetylcholine (ACh) content in their hippocampi as compared to age matched controls. Increase in ACh contents in their hippocampus may represent the neurochemical basis for their improved learning and memory[112].

For the studying of the mechanisms of memory enhancement of the *Clitoria ternatea* aqueous root extract, young adult (60 day old) Wistar rats of either sex were orally intubated with 50 and 100 mg/kg bw of aqueous root extract of *Clitoria ternatea* (CTR) for 30 days, along with age-matched saline controls. These rats were then subjected to passive avoidance tests and the results showed a significant increase in passive avoidance learning and retention. The amygdala of these rats were processed for Golgi staining and the stained neurons were traced using a camera lucida and analysed. The results showed a significant increase in dendritic intersections, branching points and dendritic processes arising from the soma of amygdaloid neurons in CTR treated rats especially in the 100 mg/kg group of rats compared with age-matched saline controls [113].

The effectiveness of alcoholic extracts of aerial and root parts of *Clitoria ternatea* at 300 and 500 mg/kg doses orally was studied in attenuating electroshock-induced amnesia in rats. Extracts at 300 mg/kg dose produced significant memory retention, and the root parts were found to be more effective. In order to delineate the possible mechanism through which *Clitoria ternatea* elicited the anti-amnesic effects, its influence on central cholinergic activity was studied by estimating the acetylcholine content of the whole brain and acetylcholinesterase activity at different regions of the rat brain (cerebral cortex, midbrain, medulla oblongata and cerebellum). The results showed that *Clitoria ternatea* extracts increase rat brain acetylcholine content and acetyl cholinesterase activity, in a similar fashion to the standard cerebro- protective drug, Pyritinol[114].

The spectrum of activity of the methanolic extract of *Clitoria ternatea* (CT) on the CNS was determined. The CT was studied for its effect on cognitive behavior, anxiety, depression, stress and convulsions induced by pentylenetetrazol (PTZ) and maximum electroshock (MES). To explain these effects, the effect of CT was also studied on behavior mediated by dopamine (DA), noradrenaline, serotonin and acetylcholine. The extract decreased time required to occupy the central platform (transfer latency, TL) in the elevated plus maze (EPM) and increased discrimination index in the object recognition test, indicating nootropic activity. The extract was more active in the object recognition test than in the EPM. The extract increased occupancy in the open arm of EPM by 160% and in the lit box of the light/dark exploration test by 157%, indicating its anxiolytic activity. It decreased the duration of immobility in tail suspension test (suggesting its antidepressant activity), reduced stress-induced ulcers and reduced the convulsing action of PTZ and MES. The extract exhibited tendency to reduce the intensity of behavior mediated via serotonin and acetylcholine. The effect on DA- and noradrenaline-mediated behavior was not significant. Accordingly, the extract possessed nootropic, anxiolytic, antidepressant, anticonvulsant and antistress activity[115].

Neonatal rat pups (7 days old) were intubated with either 50 mg/kg body weight or 100 mg/kg body weight of aqueous root extract of *Clitoria ternatea* (CTR) for 30 days. These rats were then subjected to open field, two compartment passive avoidance and spatial learning (T-Maze) tests (i) immediately after the treatment and (ii) 30 days after the treatment, along with age matched normal and saline control rats. Results showed no change in open field behaviour, but revealed improvement of retention and spatial learning performance at both time points of behavioural tests, indicating the memory enhancing property of CTR which implicates a permanent change in the brain of CTR treated rats[116].

The effectiveness of *Clitoria ternatea* in the treatment of obsessive-compulsive was carried out experimentally. The influence of ethanolic extract of *Clitorea ternatea* was evaluated in marble-burying behavior in mice. The results revealed that ethanolic extract of *Clitorea ternatea* (EECT) (100, 200 and 400mg/kg) reduced the marble burying behavior in mice. It was clear that EECT exhibited significant anti-compulsive effect in marble-burying behavior test in mice and the effect may be attributed to enhanced serotonergic function and might have influence on 5-HT reuptake[117].

The effect of aqueous and hydroalcoholic extracts of *Clitoria ternatea* on biochemical and behavioral parameters related to cognitive impairment was studied *in vitro* and *in vivo*. *In vitro* free radical scavenging and enzyme-inhibitory (cholinesterase, glycogen synthase kinase-3-β, rho kinase, prolyl endopeptidase, catechol-O-methyl transferase, and lipoxygenase) activities of aqueous and hydroalcoholic extracts of *Clitoria ternatea* plant were evaluated. Based on *in vitro* results, hydroalcoholic extract of *Clitoria ternatea* (100, 300, and 500 mg/kg, po) was selected for evaluation in intracerebroventricularly injected streptozotocin (STZ)-induced

cognitive impairment in male Wistar rats. Behavioral assessment was performed at baseline and on the 14th, 21st, and 28th days after STZ injection using elevated plus maze, passive avoidance, Morris water maze, and photoactometer. Oxidative stress parameters (malondialdehyde, reduced glutathione, nitric oxide levels, and superoxide dismutase activity), cholinesterase activity, and rho kinase (ROCK II) expression were studied in cerebral cortex and hippocampus of rats' brain at the end of the study. The hydroalcoholic extract possessed significantly more *in vitro* antioxidant and enzyme-inhibitory activities as compared to aqueous extract. The hydroalcoholic extract of *Clitoria ternatea* prevented STZ-induced cognitive impairment dose dependently, by reducing oxidative stress, cholinesterase activity, and ROCK II expression. The authors concluded that *in vitro* and *in vivo* results suggest the potential of hydroalcoholic extract of *Clitoria ternatea* for treatment of cognitive deficit in neurological disorders[118].

A Perment polyherbal Ayurvedic formulation that contains equal parts of *Clitoria ternatea*, *Withania somnifera* Dun., *Asparagus racemosus* Linn., *Bacopa monniera* Linn., is used clinically as mood elevators. The behavioural effects and the possible mode of action of Perment was studied in stress induced depressive model. Chronic unpredictable mild stress (CUMS) was used to induce depression in rats. Open field exploratory behaviour, elevated plus maze, social interaction and behavioural despair tests were used to assess behaviour. Plasma noradrenaline, serotonin, corticosterone and brain/adrenal corticosterone levels were measured to support the behavioural effects of Perment. Exposure to CUMS for 21 days caused anxiety and depression in rats, as indicated by significant decrease in locomotor activity in the open field exploratory behaviour test and increased immobility period in the behavioural despair test. Perment predominantly exhibited antidepressant action than anxiolytic activity. Furthermore, Perment increased the plasma noradrenaline and serotonin levels in stressed rats. No significant alteration in the brain corticosterone level in stressed rats was observed with Perment treatment. However the adrenal corticosterone level was decreased with Perment. It can be concluded that the Perment formulation exhibited synergistic activity, has a significant antidepressant and anxiolytic activity, which may be mediated through adrenergic and serotonergic system activation[119].

**Gastrointestinal effect:**

The antiulcer potential of aqueous and ethanolic extracts of *Clitoria ternatea* was evaluated in different experimentally induced ulcer models in rats. Ethanolic extract (200 and 400 mg/kg) and aqueous extract (200 and 400 mg/kg) of whole plant were examined in pylorus ligation and indomethacin induced gastric ulcer in rats. Various parameters like volume of gastric acid secretion, pH, total acidity, ulcer index and antioxidant parameters were determined and compared between extracts, standard and vehicle control group following ulcer induction. Among different dose of alcoholic extract, high dose showed significant antiulcer activity in pylorus ligation and indomethacin induced ulceration [57].

**Hypolipidemic effect:**

The anti-hyperlipidemic effect of *Clitoria ternatea* L. was studied in experimentally induced hyperlipidemia in rats. The poloxamer 407-induced acute hyperlipidemia and diet-induced hyperlipidemia models were used in this investigation. Oral administration of the hydroalcoholic extract of the roots and seeds of *Clitoria ternatea* resulted in a significant ($p < 0.05$) reduction of serum total cholesterol, triglycerides, very low-density lipoprotein cholesterol, and low-density lipoprotein cholesterol levels. The atherogenic index and the HDL/LDL ratio were also normalized after treatment in diet-induced hyperlipidemic rats. The effects were compared with atorvastatin (50 mg/kg, po) and gemfibrozil (50 mg/kg, po)[120].

**Antihistaminic and antiasthmatic effect:**

Ethanol extract of *Clitoria ternatea* root (ECTR) was evaluated for antiasthmatic activity using milk induced leucocytosis and eosinophilia in mice, egg albumin induced mast cell degranulations in rats and passive cutaneous anaphylaxis in rats at doses (100-150 mg/kg ip). The results showed that ECTR significantly decreases milk induced leucocytosis and eosinophilia, protected against egg albumin induced degranulations of mast cells in mice and inhibited area of blue dye leakage in passive cutaneous anaphylaxis in rats[121].

The antiasthmatic activity of ethanol extract of *Clitoria ternatea* roots was evaluated in histamine aerosol induced bronchospasm in Wister rats. The ethanolic extract of *Clitoria ternatea* (400 mg/kg, po) showed 47.45 % protection against histamine induced bronchoconstriction in rats. The results showed that aqueous extract of *C. tenatea* has not only bronchodilating activity but also decreases bronchial hyperreactivity by decreasing the infiltration of inflammatory cells in the airway and inhibition of release of histamine like mediators from the mast cell by stabilizing it [122].

**Immunomodulatory activity:**

The immunomodulatory activity of *Clitoria ternatea* seed and root extracts was investigated, the effects on humoral immune response were investigated in SRBCs-sensitized rats, while, the effects on cell medicated immunity were studied by measuring delayed type hypersensitivity (DTH) response in SRBC-sensitized rats. Neutrophil recruiting and phagocytosis were measured by studying neutrophil adhesion and carbon clearance method respectively. Furthermore the effects on hematological parameters were also studied. *Clitoria ternatea* seed and root extracts showed significant immunosupressive effects as evident from significant decrease in

primary and secondary antibody titers in SRBCs-sensitized rats, paw thickness in DTH response, and neutrophil adhesion and *in vitro* phagocytosis. The immunomodulatory effects of *Clitoria ternatea* on humoral, cell mediated and non-specific immune response could be attributed to decreased immune cell sensitization, immune cell presentation and phagocytosis. The authors concluded that the anti-inflammatory and antioxidant properties of plant might be playing major role in immunomodulatory activity[123].

**Diuretic and anti urolithiasis effect:**

*Clitoria ternatea* roots or their extract in 95% alcohol showed no significant diuretic or natriuretic effect in dogs when administered orally in non-toxic dose. Intravenous doses of the extract led to a moderate increase in the excretion of sodium and potassium in the urine, but at the same time, it showed signs of kidney damage[124].

The inhibition of *in vitro* calcium oxalate crystal (a common major component of most urinary stones) formation by various extract of *Clitoria ternatea* was investigates by titrimetric method. The inhibitory potency of alcoholic extract of *Clitoria ternatea* was found to be comparable to that of Cystone (a proprietary drug for dissolving kidney stones). Alcoholic extract of leaves of *Clitoria ternatea* showed higher calcium oxalate crystallization inhibition (72.99±1.2%) *in vitro* in comparison with cystone (90.55±1.27%) in terms of formation of calcium oxalate precipitation [125].

**Wound healing effect:**

The wound healing activity of *Clitoria ternatea* seed and root extracts was investigated using excision, incision and dead-space models in rats. *Clitoria ternatea* seed and root extracts significantly improved wound healing in excision, incision and dead-space models when administered orally by gavage as well as applied topically as ointment. These effects were comparable to that of cotrimoxazole ointment. The finding of the study also showed that *Clitoria ternatea* affected all three phases: inflammatory, proliferative and remodeling phases of wound healing[126].

The wound healing potential of standardized *Clitoria ternatea* leaf extract in terms of different enzymatic models, which are mostly associated with skin wound, was evaluated. The methanol extract and fractions were screened for its hyaluronidase, elastase, and matrix metalloproteinase-1 (MMP-1) inhibitory activity compared with standard oleanolic acid. The activity was rationalized through reverse phase high performance liquid chromatography (RP-HPLC) standardization of the extract and fractions with respect to its isolated biomarker taraxerol (yield 5.27% w/w). The extract showed significant ($P < 0.001$) hyaluronidase ($IC_{50}$) 18.08 ± 0.46 µg/ml) and MMP-1 ($P < 0.05$) inhibition, but the elastase inhibition was insignificant ($IC_{50}$ 42.68 ± 0.46 µg/ml). Among the fractions, ethyl acetate fraction showed significant ($P < 0.001$) inhibition of hyaluronidase ($IC_{50}$ 28.01 ± 0.48 µg/ml) and MMP-1 ($P < 0.01$). The HPLC analysis revealed that the extract and the ethyl acetate fraction are enriched with taraxerol (5.32% w/w and 4.55% w/w, respectively) [127].

## II. PROTECTIVE EFFECTS

Petroleum ether, chloroform, and methanol extracts of roots of blue and white flowered varieties of *Clitoria ternatea* (CT) were studied for their hepatoprotective potential against carbon tetrachloride ($CCl_4$) induced hepatotoxicity in rats. The hepatoprotective activity was assessed using various biochemical parameters like serum glutamate oxaloacetate transaminase, serum glutamate pyruvate transaminase, serum alkaline phosphatase and total bilirubin along with histopathological studies of liver tissues. The substantially elevated serum enzymatic levels of serum transaminases, alkaline phosphatase and total bilirubin were significantly restored towards normalization with the treatment of CT. The biochemical improvement were confirmed by histopathological examination of liver sections[128].

The nephroprotective and antioxidant activities of the ethanol extract of the aerial parts of *Clitoria ternatea* were evaluated in acetaminophen induced toxicity in rats. Biochemical studies showed that there was an increase in the levels of serum urea and creatinine along with an increase in the body weight and reduction in the levels of uric acid in acetaminophen induced groups. These values were retrieved significantly by treatment with *Clitoria ternatea* extracts at two different doses. The antioxidant studies reveal that the levels of renal SOD, CAT, GSH and GPx in the APAP treated animals were increased significantly along with a reduced MDA content in *Clitoria ternatea* ethanol extract treated groups. Histopathological changes also reveal the protective nature of the *Clitoria ternatea* extract against acetaminophen induced necrotic damage of renal tissues[72].

The protective effect of *Clitoria ternatea* (CT) flower extracts with antioxidant activity were studied in male reproductive parameters including sperm concentration, serum testosterone level, histopathology of the testis, and testicular tyrosine phosphorylation levels in testicular damage in rats induced with ketoconazole (KET). The antioxidant activity of CT flower extracts was determined using 2,2-diphenyl-1-picrylhydrazyl (DPPH) and ferric reducing antioxidant power (FRAP) assays. Male rats were treated with CT flower extracts (10, 50, or 100 mg/kg BW) or distilled water via a gastric tube for 28 days (preventive period: Days 1-21) and testicular damage induced by KET (100 mg/kg bw) via intraperitoneal injection for 7 days (induction period: Days 22-28). After the experiment, all animals were examined for the weights of the testis, epididymis, vas deferens and

seminal vesicle, serum testosterone levels, sperm concentration, histological structures and diameter of testis, and testicular tyrosine phosphorylation levels by immunoblotting. The CT flower extracts had capabilities for DPPH scavenging and high reducing power. At 100 mg/kg bw, the extract had no toxic effects on the male reproductive system. Significantly, in CT+KET groups, CT flower extracts (50 and 100 mg/kg BW) alleviated the reduction of reproductive organ weight parameters, testosterone levels, and sperm concentration. In addition, CT flower extracts gave protection from testicular damage in KET-induced rats. Moreover, in the CT100+KET group, CT flower extracts significantly enhanced the expression of a testicular 50-kDa tyrosine phosphorylated protein compared with that of other groups[(129)].

## III. SIDE EFFECTS AND TOXICITY

$LD_{50}$ of ethanol extract of *Clitoria ternatea* root was more than 1,300 mg/kg in mice[(81)]. Acute oral toxicity study showed that there was no mortality up to 3000mg/kg in mice[(130)].

After single dose 1000 mg/kg in rats, no death or any other disorders up to 72 h[(86)]. The extract wass found safe even at the dose of 2000 mg/kg body weight in rats[(49)]. There was no mortality observed at doses up to 2 g/kg (po) of the ethanol extract of the aerial parts of *Clitoria ternatea* in rats. During observation, the animals exhibited decreased mobility but no signs of convulsions or loss of writhing reflex. This result indicates that *Clitoria ternatea* has a low toxicity profile[(110)].

The mutagenic effect of the aqueous extract of *Clitoria ternatea* Linn was assessed by three test methods, *Bacillus subtilis* rec assay, *Salmonella typhimurium* Ames' test and micronucleus test. The aqueous extract gave negative results, no mutagenic activities in both bacterial and mammalian cells[(131)].

## IV. CONCLUSION

The paper reviewed *Clitoria ternatea* as promising medicinal plant with wide range of pharmacological activities which could be utilized in several medical applications because of its effectiveness and safety.

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