IJPSR (2024), Volume 15, Issue 8 (Review Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 20 January 2024; received in revised form, 12 April 2024; accepted, 17 May 2024; published 01 August 2024

A REVIEW ARTICLE ON ANTIOXIDANT PROFILE OF BLUE TEA POLYPHENOLS IN THE TREATMENT OF VARIOUS DISEASES

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Keywords:

Blue Tea, Antioxidants, Antimicrobial, Nootropics

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ABSTRACT: *Clitoria ternatea (Blue tea)* is a traditional medicinal plant belonging to family Fabaceae having generous amount of anthocyanins which possess majorly antioxidant properties. It contains wide range of phytoconstituents such as triterpenoids, flavanol glycosides, tannins, alkaloids, amino acids, proteins, ternatins (poly acylated anthocyanins) and carbohydrates etc. According to the data obtained from different *in-vitro* studies, this plant possess antioxidant, antimicrobial, antidiabetic, hepatoprotective, nootropic, central cholinergic, antidepressant, antianxiety, anticonvulsant, anti-inflammatory, analgesic, antipyretic, wound healing, anticancer and many other pharmacological properties. In this report various preclinical studies data revealed about the efficacy of *Clitoria ternatea* plant in the treatment of neurological, inflammatory and oxidative stress induced diseases.

INTRODUCTION: Anthocyanins are present in abundant quantities in blue tea which possess antioxidant properties and polyacylated anthocyanins also termed as ternatins [1]. It is also the powerhouse of anti-inflammatory and immune-boosting components like flavanoids, tannins and polyphenols [2]. Antioxidants present in this tea helps the body to fight against free radicals (Reactive oxygen species) which cause premature aging and are toxic for body [3]. These species generate the oxidative stress inside cells causing the damage to cellular components and resulting in cell death [4, 5, 6]. The mechanism of actions of antioxidants in biological systems to manage oxidative stress are diverse like scavenging of free radicals, oxidative enzymes inhibition, metal ions chelation, and as an antioxidant enzyme cofactor [7]. Important benefits of this blue tea are in promoting weight loss, pacifying mind, detoxifying the body, improvement in hair growth, enrich skin texture, anti-depressant, sedative property, antidiabetic as well as hepatoprotective property [8, 9]. This report highlights about the recent research on efficacy, mechanism of action of blue tea (*Clitoria ternatea*) *in-vivo* systems.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.15(8).2198-09

This article can be accessed online on www.ijpsr.com

DOI link: https://doi.org/10.13040/IJPSR.0975-8232.15(8).2198-09

Blue Tea: Blue tea is the beverage having prominent blue colour and is prepared from the *Clitoria ternatea* plant [10]. *Clitoria ternatea* belonging to family Fabaceae traditional ayurvedic medicine also known as butterfly pea, conch flower and shankapushpi. In Indian traditional medicine it is termed as Aparajit (Hindi), Kakkattan (Tamil) and Aparajita (Bengali) [11]. It is perennial twinning herbaceous plant and is widely distributed in

tropical regions of India, Malaysia, Sri Lanka, Philippines islands and Burma [12, 13]. This blue pea plant is an underutilized in Sri Lanka. The medicinal properties of this blue pea plant are well documented in traditional medicine documents but still not properly used to date. Currently there are no scientifically proven reports about the health benefits of this plant as well as of the flowers but still few products are there in the world market [14]. The novel Ternatea containing anthocyanins also termed as "ternatins" was firstly isolated in 1985 and the biosynthetic pathway of the same was postulated almost after decade [15, 16]. This plant produces pea shaped flowers having tubular calyx with free sepals five in number which are further fused about two third of their lengths [17]. Blue tea is prepared by collecting the flower petals of the blue flower pea plant (fresh and dried) and boiling some petals along with dried lemongrass (optional) in water for about 5-10 minutes. Some amount of honey should be added to this herbal concoction for sweetening purpose. This prepared blue tea can be consumed warm as well as cold and even refrigerated one. This blue tea being caffeine-free have an impressive nutritional profile as beverage [18, 19]. The analysis report of *Clitoria ternatea* leaves indicates the amount of moisture (74.5%), protein (14.9%), ash (8.7%), carbohydrate (0.1%) and crude fiber (8.5%). Various macronutrients present in the leaves are nitrogen (2.4g) present in highest quantity, potassium (1.6g), calcium (0.8g), phosphorus (0.7g), magnesium (0.6g), sodium (0.3g), iron (6.3mg), zinc (4.4mg), manganese (3.2mg) and copper (2.2 mg) for per 100 g [20]. Apart from other significant uses it has certain antipyretic properties and affects the body in similar way as paracetamol tablets used in fever, body pain as well as muscle pain with runny nose [21].

***Clitoria ternatea* Plant:** This plant is classified under the kingdom Plantae, phylum Tracheophyta, class Magnoliopsida and belonging to family Fabaceae [22]. It is perennial climber (approximately 2-3m in height) and commonly known by names such as blue flower pea or butterfly pea [23]. This plant is native to Malaysia and franchised almost all over the world majorly in Sri Lanka. This plant can be grown well in neutral and moist soils. It contain dark blue or white colour flowers which are those parts of the plant which have predominant vital phytochemicals. These phytochemicals have valuable medicinal properties and also found in variable proportions in the other parts of plant as in roots, leaves, seeds and bark [24]. In Sri Lanka two common names used for this plant in Sinhala language are 'Ela-katarolu' (white flowers) and 'nil-katarolu' (blue flowers) based on the colour of petal. In 1981, studies done by Jayaweera indicates that this plant is grown in Sri Lanka to be used as an ornamental plant as well as traditional medicinal plant. Blue flowers are found in two varieties as bearing either an enlarged keel petal or a normal keel petal [25]. It can be grown in full sunlight as well as in shaded area and seed germination take place in about 1-2 weeks while time required for flowering is for about 4 weeks [26, 27]. The leaves are bijugate having 5-7 leaflets, elliptic-oblong shape with length range 2.5-5.0 cm and width range of 2.0-3.2 cm. They are having flat linear beaked seed pods with length in range of 5-7 cm. The shape of seed is oval and color is yellowish brown or blackish with length and width range of 4.5-7.0 mm and 3-4 mm respectively. It is having taproot system connected with many slender lateral roots [28, 29].

Phytochemical Composition of Blue Tea: From ancient times roots, leaves and seeds are the reported parts of plant that are used. Major phytoconstituents present in plant are pentacyclic triterpenoids known as taraxerone and taraxerol.

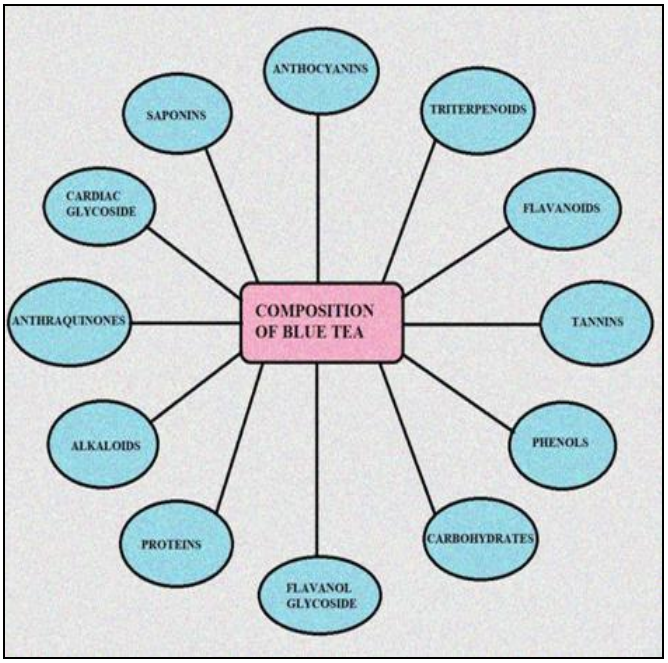

FIG. 1: PHYTOCONSTITUENTS IN BLUE TEA

The new sensitive, simple, precise and selective technique like High performance liquid chromatography (HPLC) has been used for the determination of taraxerol in plant and which is being performed using Thin Layer Chromatography aluminium plates

Roots: Pentacyclic triterpenoids like taraxerone and taraxerol are majorly isolated from roots of the plant [30, 31, 32]. The roots of the plant forms nodules which have high amount of growth substance for plant such as indole acetic acid and nodules of roots also contain free amino acids and amides such as valine, glycine, alanine, leucine, γ-aminobutyric acid, γ-methyleneglutamic acid, γ-aminobutyric acid, α-aminobutyric acid, glutamic acid, aspartic acid, arginine, histidine and ornithine [33, 34]. Bark of roots also contains starchand flavanol glycoside, resin and tannins [35].

Leaves: Leaves majorly contain four types of Kaempferol glycosides I, II, III and IV such as Kaempferol-3-glucoside (I), Kaempferol-3-rutinoside (II), Kaempferol-3-neophesperidoside (III) and Kaempferol-3-orhamnosyl glucoside (also named as Clitorin) and they were identified using Ultra Violet, Mass Spectrometry and Protein Magnetic Resonance [36]. These leaves also contain asparajitin, β-sitosterol, essential oil, mucilage and colouring-matter. Further composition of mucilage contains anhydropentosan, anhydrogalacton and methylpentos an and also an alkaloid [37, 38].

Seeds: The seeds contain active principle compound bitter acid resin and fixed oil, glucose, tannic acid and also a toxic alkaloid. They also contain cotyledon which is bitter in taste as well as full with the presence of granular starch. Sitosterol (γ-sitosterol and β-sitosterol) and anthoxanthin are the two chemicals that are isolated from seeds. The composition of blue-flowered and white-flowered varieties is almost identical. Seeds also contain cinnamic acid, hexacosanol, and a nucleoprotein with an amino acid sequence similar to insulin, delphinidin-3,3,5-triglucoside, a phenol glycoside, ethyl D-galactopyranoside, 3,5,7,4-tetrahydroxy-flavone-3-rhamoglycoside, an alkaloid, p-hydroxycinnamic acid polypeptide, 6% ash and highly basic protein known as finotin. Different oils are yielded by seed-oil like stearic, linoleic, palmitic, oleic and linoleic acids [39, 40, 41, 42].

Flowers: Young flowers contain minor delphinidin glycosides and eight major anthocyanins (ternatins C1, C2, C3, C4, C5 and D3 and also preternatins A3 and C4). It was also determined that flowers contain five new anthocyanins (ternatins A3, B3, B4, B2 and D2) [43].

Malonylated flavanol glycosides are also isolated from petals of plant with different petal colours [44]. The flowers also contain kaempferol 3-2G-rhamnosylrutinoside; kaempferol 3-neohesperidoside; quercetin-3-neohesperidoside; myricetin-3-neohesperidoside; kaempferol 3-rutinoside; quercetin-3-rutinoside; myricetin 3-rutinoside; kaempferol-3-glucoside; quercetin-3-glucoside; myricetin-3-glucoside. White flowers only yield kaempferol [45]. While blue flowers also contain lobelinins having 3,5,3’,5’-tetraglucoside substituted pattern and also reported that it contains deacylternatin [46].

Pharmacological Properties:

Antioxidant Activity: Free radicals cause the cell damage acting as major contributor to aging of cells that further lead to degenerative diseases such as cardiovascular diseases, cancer, brain dysfunction and immunity system decline. Reactive oxygen species (ROS) play a significant role in progression or even the initiation of many severe diseases such as inflammatory injury and atherosclerosis [47].

Antioxidants act as free radical scavengers, freely inhibits lipid peroxidation as well as radical-mediated processes, therefore they protect the human body from some disease caused by the reaction of radical. Many substances suggested to act as an antioxidant. Various phenolic antioxidants such as flavonoids, Tannins, coumarins, xanthenes, *etc*. Procyanidins have recently been shown to do this Scavenging radicals based on dose-dependent action [48]. Some antioxidants are themselves free radicals, donating electrons for stabilization and neutralization of dangerous free radicals. Other antioxidants counteract these molecules that form free radicals, destroy them before they start their effect of oxidative damage [49]. Using the 1,1-diphenyl-2-picryl-hydrazyl (DPPH) radical scavenging experiment, the various solvent extracts of *Clitoria ternatea* leaf were evaluated for their *in-vitro* free radical scavenging capacity.

With increasing extract concentrations, all extracts showed strong *in-vitro* free radical scavenging activity. The most potent extract was found to be methanol extract, further followed by chloroform and petroleum ether extracts [50].

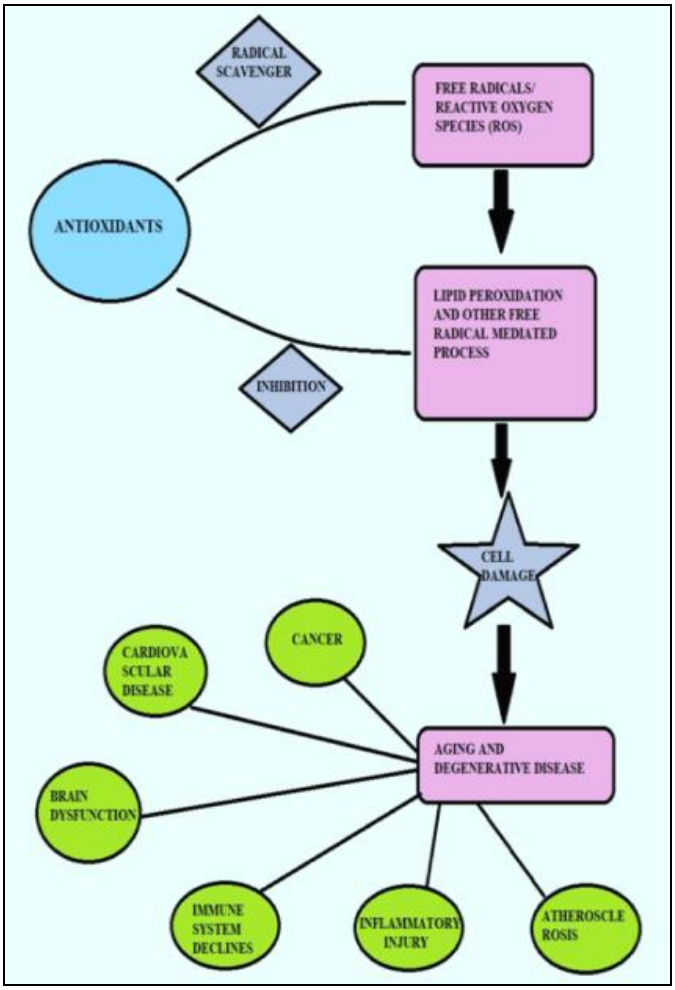

FIG. 2: ANTIOXIDANT ACTION WITH DIFFERENT PHARMACOLOGICAL ACTIVITIES

The investigational studies were performed on leaves as well as on both the white and blue colour flowered *Clitoria ternatea* plant for their antioxidant activity. The findings indicate that *Clitoria ternatea* leaves and flowers have strong antioxidant activity. It was discovered that the blue flower yielding plant have increased antioxidant activity. Consequently, they can be employed to treat conditions caused by free radicals and to fight oxidative stress [51]. The yeast cell was used to investigate the antioxidant properties and apoptotic research of *Clitoria ternatea* leaves. The yeast cells and yeast cell DNA were separated from the effluents of the sugar factory. In a dot plot quick screening assay method, the leaves extract from various solvents was tested for its scavenging ability against the stable free radical DPPH (2, 2'-diphenyl-1-picryl hydrazyl), and its concentration was determined using a spectrophotometric assay method. By treating yeast DNA, oxidative damage was created *in-vitro*, and the effects of leaf extracts were examined. Samples of genomic DNA were taken from the YBD broth culture. The methanol extract of *Clitoria ternatea* strongly induced DPPH scavenging activity. The use of *Clitoria ternatea* leaf extracts successfully reduced the level of DNA damage [52, 53].

Antimicrobial Activity: Antimicrobial chemotherapy is increasingly being questioned because of development of pathogenic strains which exhibits higher levels of antibiotic resistance and there are multiple mechanisms being involved in antibiotic resistance [54, 55, 56, 57, 58, 59]. Therefore, compounds/drugs are urgently needed which has antibacterial activity as well as prevents the emergence of antibiotics resistance. Several investigational studies were performed for the evaluation of antimicrobial activities (antibacterial, antifungal) of the *Clitoria ternatea* flowers. Antibacterial activity of aqueous flower extract of *Clitoria ternatea* was discovered by using agar well diffusion method and founded effective against cavities-causing bacteria [60]. In order to test the antimicrobial screening, isolates of *Salmonella enteritidis*, *Salmonella typhimurium*, *Klebsiella pneumonia*, *Pseudomonas aureginosa*, Enteropathogenic *E. coli*, and Uro-pathogenic *E. coli* from patients with acute gastroenteritis and urinary tract infections were used.

The Disc Diffusion Method was employed to evaluate the activity of the afore mentioned extracts. Extracts of *Clitoria ternatea* flowers in water, methanol, and chloroform showed efficacy against *Salmonella typhimurium*, *Pseudomonas aureginosa*, *Klebsiella pneumoniae*, enteropathogenic *E. coli*, and enterotoxigenic *E. coli*. Comparatively high activity is shown by the *Clitoria ternatea* methanol extract when compared to the chloroform and water extracts. While petroleum ether and hexane extracts showed no activity, water, chloroform, and methanol, extracts formed an inhibitory zone that measured 12 mm, 14 to 18mm, and 16 to 26 mm respectively, at a concentration of 4 mg/disc [61, 62, 63].

The protein with molecular mass of 14.3 kDa was isolated from the *Clitoria ternatea* plant seeds having antifungal property and was designated as Ct protein. The protein was purified by using different techniques such as ion exchange chromatography, gel filtration and ammonium sulphate precipitation. The lytic activity was showed against *Micrococcus luteus* and broad-spectrum fungi by antifungal protein. Fungicidal property was particularly showed against the most clinically relevant yeasts, including *Cryptococcus albidus*, *Cryptococcus neoformans*, *Cryptococcus laurentii*, *Candida parapsilosis* and *candida albicans*. This protein also showed an inhibition effect on mycelial growth in many mould species such as *Alternaria* sp., *Curvularia* sp., *Aspergillus flavus*, *Cladosporium* sp., *Aspergillus niger*, *Aspergillus fumigatus*, *Sclerotium* sp., and *Rhizopus* sp [64]. A highly basic small protein termed as finotin was purified from the seeds of *Clitoria ternatea* plant by using ultrafiltration. The protein has potent inhibition effect on the growth of several fungal pathogens of the plants, such as *Fusarium solani*, *Rhizoctonia solani*, *Colletotrichum lindemuthianum*, *Pyricularia grisea*, *Lasiodiplodia theobromae*, *Colletotrichum gloesporioides* and *Bipolarisoryzae* [65].

Antidiabetic Activity: Diabetes is speedily growing health challenge and potential epidemic in many countries like India. Recent studies showed efficacy of different extracts of *Clitoria ternatea* plant. One of the studies showed that chronic administration of different plant extracts for almost 14 days reduces the level of blood glucose of the diabetes induced animals such as Wistar Albino rats as compared to diabetic control group [66]. In streptozotocin-treated rats, aqueous extracts of the *Clitoria ternatea* plant demonstrated antihyperglycemic activity. This effect is due to an increase in glucose absorption and glycogen deposition in isolated rat hemi diaphragm. Rats with alloxan-induced diabetes mellitus respond favourably to the antihyperglycemic effects of *Clitoria ternatea* leaf and flower extracts. The aqueous extracts of *Clitoria ternatea*'s leaves and flowers dramatically decreased blood sugar, glycosylated haemoglobin, and glucose-6-phosphatase activity, but they also increased serum insulin and liver and skeletal muscle glycogen and the activity of glucokinase and glycolytic enzyme [67, 68]. In juvenile diabetic rat experimental models, the alcoholic root extract of *Clitoria ternatea* has demonstrated a considerable gross influence in reducing the potentially harmful effects on brain CA3 and pancreatic tissue [69]. On Streptozotocin-induced diabetic rats, Clitoriaternatea leaf extract has a synergistic effect with *Trichosanthes dioica* leaf extract [70].

Hepatoprotective Activity: Hepatic cells of liver participate in various metabolic activities. Therefore, the development of hepatoprotective agents is of supreme importance against the liver damage. Various studies showed the hepatoprotective activity of different extracts of plant. By lowering the levels of aspartate aminotransferase, alanine aminotransferase, and bilirubin and improving histopathology, the methanolic extract of *Clitoria ternatea* leaf in mice demonstrated the protective action against paracetamol-induced liver injury [71]. Different extracts like chloroform, methanol and petroleum ether extract of roots of white and blue flowered types of *Clitoria ternatea* were assessed for their hepatoprotective potential against carbon tetrachloride (CCl_4) instigated hepatotoxicity in rats. It was founded that white colour flowered variety of plant showed more hepatoprotective activity in comparison to blue colour flowered variety [72, 73].

Nootropic Activity: *Clitoria ternatea* seeds and leaves are frequently used as brain tonics and are considered to improve memory and intelligence. The effectiveness of *Clitoria ternatea* in treating Alzheimer's disease was examined, and the main bioactive component responsible for the action was determined. The results demonstrated that *Clitoria ternatea*'s aqueous extract was effective in treating Alzheimer's disease through a variety of mechanisms [74]. Acetylcholine (ACh) concentration in hippocampus significantly increased after treatment *Clitoria ternatea* aqueous root extract (CTR) for 30 days in neonatal and young adult age groups of rats compared to age-matched controls. Their enhanced learning and memory may have a neurochemical basis due to an increase in ACh content in their hippocampus [75].

Central Cholinergic Activity: Researchers have noted variations in acetylcholine (ACh) and

acetylcholinesterase (AChE) activity in the brain following electroshock or scopolamine-induced amnesia and how these changes affect spatial memory retention. The alcohol extract of *Clitoria ternatea* or regular Shankapushpi syrup was given to the preselected trained rats once daily for 10 days. The animals in the corresponding groups underwent scopolamine or electroshock therapy, and then performed a radial arm maze test one hour after the previous dose. ACh and AChE levels were then estimated after the brain was promptly isolated. In rats treated with root extract, a study demonstrates considerable memory preservation against scopolamine and electroshock-induced amnesia. In a model of amnesia caused by scopolamine, the extract was found to be more effective. This effect was discovered to be qualitatively related with a considerable decrease in AChE activity and an increase in overall ACh content in several regions of the brain when compared to respective controls [76, 77].

Antidepressant Activity: In a mouse tail suspension test, the methanolic extract of *Clitoria ternatea* at dosages of high and low concentrations, demonstrated an antidepressant effect [78, 79]. At both doses, the *Clitoria ternatea* extract dramatically reduced the amount of time that patients were immobile. Compared to fluoxetine, i.p., the duration of immobility was reduced for a longer period of time at a *Clitoria ternatea* dose of high concentration. Another study found that *Clitoria ternatea* root ethanolic extract at two different doses of high and low concentration had antidepressant effects. Two substances, (Z)-9,17-octadecadienal and n-hexadecanoic acid isolated from the root of CT, were found to have potential as lead molecules for the development of novel selective MAO-A inhibitors that could provide a herbal remedy for the treatment of psychiatric disorders, according to the findings of a prior study involving anxiety and depression [80, 81].

Anti-Anxiety Activity: In a recent study, *Clitoriaternatea* showed a mild anxiolytic action in the Elevated plus maze (EPM) and light/dark exploration tests, two animal models of anxiety. Anxiolytic activity of the *Clitoria ternatea* is shown by an increase in the occupancy of the animals in the open arm or a decrease in the time spent in the enclosed arm. The amount of time spent in the open arm increased dose-dependently with *Clitoriaternatea*. The light/dark exploration test gauges mice and rats' innate aversion to brightly lighted areas [82, 83, 84].

Anti-convulsant Activity: Seizures are caused by an imbalance of excitatory and inhibitory neurotransmitters. Numerous medications that boosted GABA levels in the brain have shown anticonvulsant properties against seizures brought on by MES (maximal electroshock seizure) and PTZ (Pentylenetetrazole-Induced seizures). The MES is most likely the most reliable tool for evaluating the effectiveness of antiepileptic medications in generalised tonic-clonic seizures. The symptoms of PTZ-induced seizures are identical to those of absence seizures, and PTZ-induced seizures are suppressed by the same medications that are used to treat absence seizures. Both the duration of tonic hindlimb extension and the onset of convulsions in PTZ- and MES-induced convulsions were considerably delayed by *Clitoria ternatea*. These findings point to the potential utility of *Clitoria ternatea* in the management of seizures [85, 86].

Anti-Inflammatory, Analgesic Activity: Since they are known to influence both COX-1 and COX-2, the currently available non-steroidal anti-inflammatory medicines (NSAIDs), such as acetaminophen and aspirin, are linked to adverse effects, mainly gastrointestinal and cardiovascular problems. To lessen the hazards associated with NSAIDs while still providing adequate pain management, new or alternative methods must be developed [87]. With healthy albino rats of either sex, the petroleum ether extract of *Clitoria ternatea* flowers was tested for anti-inflammatory efficacy using the carrageenan paw edema method. In Eddy's hot plate method, the treatment group had considerably longer reaction times than the control untreated group (measured as the time it took the animals to lick their fore or hind paws or jump in response, whichever occurred first). The extract significantly prevented paw edema compared to the control untreated group. According to the study, there is a chance that the extracts will operate as a barrier to the production of prostaglandins, kinnins, and other chemicals in carrageenan-induced edema [88]. Quercetin glycosides and ternatin anthocyanins from the blue flower petals of *Clitoria ternatea* also

reduced the lipopolysaccharide (LPS)-induced inflammation in macrophage cells by obstructing cyclooxygenase-2 (COX-2) activity, lowering reactive oxygen species (ROS) production, limiting nuclear NF-B translocation, reducing inducible nitric oxide synthase (iNOS) protein expression [89].

The analgesic activity of ethanolic extract of aerial parts of *Clitoria ternatea* was evaluated by using tail clip, radiant heat in rats and acetic acid instigated writhing in mice. Radiant heat testing revealed that *Clitoria ternatea* has considerable analgesic efficacy from 30 minutes to three hours after drug administration at two doses of high and low concentration, respectively. While acetic acid-induced writhing in mice did not exhibit any appreciable analgesic action, the tail clip test revealed that *Clitoria ternatea* had some analgesic activity. However, at two doses of high and low concentration, methanolic extract of *Clitoria ternatea* root demonstrated considerable analgesic efficacy in acetic-induced writhing [90, 91].

Antipyretic Activity: The ethanolic extract of aerial *Clitoriaternatea* sections at different doses, induced a noticeable drop in body temperature that was observed between 30 and 120 minutes, practically identical to chlorpromazine. Subcutaneous injections of a 20% suspension of dried Brewer's yeast in 2% gum acacia were used to cause pyrexia in rats. Rats received *Clitoria ternatea* dosages orally. The scientists discovered that rats exposed to *Clitoria ternatea* experienced a dose-dependent antipyretic effect [91]. Another study found that the *Clitoria ternatea* root's methanolic extract significantly reduced fever caused on by yeast [92]. At a high concentration dose, the ethanolic and acetone extracts of *Clitoria ternatea* leaves also had an antipyretic effect on rats [93].

Anti-ulcer Activity: Study examined into the stomach protective effects of *Clitoria ternatea* extracts (chloroform and methanol) in pylorus ligation- and ethanol-induced ulcer models. When compared to the standard medication Omeprazole, the extracts produced a protective effect on ulcer-induced models for a number of biochemical parameters, including gastric volume, pH of gastric content, ulcer index, free acidity and total acidity, dissolved mucous substances like total protein, and mucin [94]. Another study's findings showed that in a rat model of stomach ulceration caused by Pylorus ligation and Indomethacin, an alcoholic extract of the entire *Clitoria ternatea* plant has antiulcer efficacy. The extract containing flavonoids exhibits antiulcer action, demonstrating that the flavonoids in the extract are what give the extracts their effectiveness [95].

Wound Healing Activity: The study was undertaken to look into the ability of *Clitoria ternatea* seed and root extracts to treat wounds. Rat models of rat dead-space, rat incision, and rat excision were used to examine the impact on wound healing. By using the HPTLC method, the extracts were standardised. When given orally by gavage and used topically as an ointment, *Clitoria ternatea* seed and root extracts dramatically enhanced wound healing in excision, incision, and dead-space models. These results are similar to what cotrimoxazole ointment produces. According to the study's findings, *Clitoria ternatea* may have an impact on all three stages of wound healing-inflammation, proliferation, and remodelling. It was discovered that phenolic chemicals were present in plant extracts, while flavonol glycosides were present in seed extract [96].

Anticancer and Cytotoxic Activity: Among the methods used to treat and control cancer include chemotherapy, radiation therapy, and targeted therapy, however these treatments do not offer a permanent cure and have been linked to a number of toxicities and side effects [97]. Therefore, there is an urgent need for new agents that are secure, accessible, and efficient. The anticancer potential of *Clitoria ternatea* flowers extracted using various solvents was examined in several research.

In the *in-vitro* cytotoxic assay against Dalton's lymphoma ascites (DLA) cells, the 100% petroleum ether extract was found to be more effective than the 100% ethanol extract, which may be related to the distinct phytochemical makeup of the two extracts. While only flavonols were present in the ethanol extract, it was discovered that the petroleum ether extract comprised tannins, steroids, triterpenoids, and saponins as well [98]. In a study conducted, the water extract had much lower IC_{50} values than the methanol extract and was more active against the human ovary cancer cell line (Caov-3), the human liver cancer cell line (HepG2),

the hormone dependent breast cancer cell line (MCF-7), and the non-hormone dependent breast cancer cell line (MDA-MB-231) [99]. In a brine shrimp lethality bioassay test, the crude methanol extract of *Clitoria ternatea*'s leaves, seeds, and stem-bark showed a substantial amount of cytotoxic activity [100]. In mice with Dalton's lymphoma (DLA), *Clitoria ternatea*'s anticancer efficacy was examined. DLA cells were injected intraperitoneally into mice to cause tumours. Methanol extract of *Clitoria ternatea* (MECT) was given for 14 days in two different doses after the tumour was inoculated for 24 hours. In vitro cytotoxicity, survival time, peritoneal cell count, haematological investigations, and antioxidant parameters were used to evaluate the impact of MECT. MECT therapy reduced viable count, packed cell volume, and tumour volume. Additionally, it enhanced the mean survival time and non-viable cell count, lengthening the mice's lives who carried the Ehrlich-Lettre ascites carcinoma (EAC) [101].

Antiasthmatic and Antihistaminic Activity: In order to cure histamine-induced bronchospasm in experimental animals, the alcohol extract of *Clitoria ternatea* roots was evaluated in the study. The effects of the aqueous extract of *Clitoria ternatea* on Wistar rats which have histamine-induced bronchospasm were investigated. In wistar rats, treatment with an alcoholic extract of the *Clitoria ternatea* plant significantly reduced the incidence of bronchospasm brought on by histamine aerosols. These findings indicate that the aqueous extract of *Clitoria ternatea* not only has broncho dilating activity but also reduces bronchial hyperreactivity by preventing the infiltration of inflammatory cells into the airways and by stabilising the mast cell, which prevents the release of histamine-like mediators [102]. Histamine H1 receptor antagonists prevented the dose-dependent catalepsy that was brought on by the α2 adrenoreceptor agonist clonidine in mice. Histamine, which causes many asthmatic disorders, is released from mast cells by clonidine. The roots of *Clitoria ternatea* contain anti-inflammatory qualities and are helpful for severe asthma and bronchitis. In a study, mice with catalepsy brought on by the use of clonidine and haloperidol were used to test the antihistaminic activity of an ethanol extract of *Clitoria ternatea* root (ECTR) at various doses. The results of the study demonstrated that, when compared to the control group, chlorpheniramine maleate (CPM) and ECTR effectively inhibit clonidine-induced catalepsy, but not haloperidol-induced catalepsy. According to the study, ECTR has antihistaminic properties [103].

Antihelmintic Activity: Aqueous and ethanolic extracts of *Clitoria ternatea* leaves were used in the study employing *Eisenia fetida* at three different concentrations of each extract to compare the anthelmintic activity *in-vitro*. The timing of the worms' paralysis (P) and death (D) was determined for the study. Both the ethanolic and the aqueous extracts had extremely noteworthy activity when compared to the reference medication levamisole at the high concentration. Finally, it was discovered that the ethanolic extract of *Clitoria ternatea* had stronger anthelmintic activity than the aqueous extract [104].

Management of Urolithiasis: By using a titrimetric approach, it was examined whether different extracts of *Clitoria ternatea* might prevent the in-vitro development of calcium oxalate crystals, which is a common primary component of most urinary stones. It was discovered that the inhibitory power of the alcohol extract of *Clitoria ternatea* was equivalent to that of Cystone, a patented medication for the removal of kidney stones [105].

Platelet Aggregation Inhibition Activity: Blood platelet aggregation activity was assessed in relation to *Clitoria ternatea*. In a study using a rabbit model, platelet aggregation caused by collagen and adenosine diphosphate (ADP) were both significantly inhibited. This might be the outcome of Ternatin D1, one of the main anthocyanins that were extracted from the petals [106].

Antihyperlipidemic Activity: To research *Clitoria ternatea* 's ability to treat rats with hyperlipidaemia that has been artificially produced. For this experiment, the models of acute hyperlipidaemia brought on by poloxamer 407 and diet-induced hyperlipidaemia were both used. A significant decrease in the levels of blood total cholesterol, triglycerides, very low-density lipoprotein cholesterol, and low-density lipoprotein

cholesterol was observed after oral administration of the hydroalcoholic extract of the roots and seeds of *Clitoria ternatea*. The results were examined with reference standards gemfibrozil and atorvastatin. Increased biliary excretion and decreased dietary cholesterol absorption may be responsible for *Clitoria ternatea*'s ability to lower cholesterol [107].

CONCLUSION: The *Clitoria ternatea* is the promising medicinal plant with its traditional applications in ayurvedic medicine as memory enhancer and with neurogenic potential. Numerous useful studies on this plant over the years have revealed a wide range of health advantages, providing a deeper understanding of its prospective applications. *Clitoria ternatea*'s clinical effectiveness is still only limited. Future studies should concentrate on developing more precise models and delicate techniques that clarify the mechanism of action of this plant in various disease alleviation. In order to produce an efficient molecular marker with a precise dose for the treatment of various clinical illnesses, researchers should engage in a number of observational, case control studies.

ACKNOWLEDGEMENT: Nil

CONFLICTS OF INTEREST: Nil

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How to cite this article:
Diksha, Kaur H and Kaur J: A review article on antioxidant profile of blue tea polyphenols in the treatment of various diseases. Int J Pharm Sci & Res 2024; 15(8): 2198-09. doi: 10.13040/IJPSR.0975-8232.15(8).2198-09.