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Clitoria ternatea: A Flower of Medicinal, Industrial and Agricultural Importance

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ABSTRACT
Clitoria ternatea , a common flower of Asian origin is found to be of immense commercial significances. Although it was known for its medicinal importance for centuries, but various in vitro studies have confirmed its multifaceted attributes and the modes of action involved. The phytocompounds like flavonoids, polyphenols and pigments are responsible for its therapeutic significances. Careful extraction of its phytocompounds justify its medicinal utilities as antihypertensive, antidepressant, antidiabetic, antitumorigenic and immune stimulatory activities. The nontoxic pigment extracted from the petals can be safely used as natural colourant in food and cosmetic industries. The antimicrobial, antiparasitic activities can be applied for the preparation of biopesticides and insecticides. Hence by the judicious utilisation of different attributes of these petals, new drugs can be designed for herbal therapy, nontoxic natural colourant and eco-friendly antimicrobials can be developed for industrial and agricultural use.
Keywords: *Clitoria ternatea, floral extract, antihypertensive, antidiabetic, antitumorigenic, antimicrobial, phytocompounds.*

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INTRODUCTION

Flowers being the unique gift of nature attract people with their powerful fragrance and beauty. They have long been regarded as a symbol of grace and elegance, as well as a visual feast. Flowers are generally used at all religious festivals, often given as gifts and used as floral ornaments and indoor decors. Apart from these, some flowers are found to have immense therapeutic importance and from the ancient time are recommended for treating many diseases [1]. In India, for hundreds of years, medical practitioners have recognized the therapeutic abilities of specific flowers and Indian Ayurveda accepted the efficacies of medicinal blooms to treat different ailments ranging from hair loss to other systemic diseases. One of the greatest benefits is that flowers proffer fully innate medical attributes, often without the frightening side effects. In addition to this, remedial products made from flowers are more cost- effective as compared to the drugs sold by pharmaceutical industries. Physiological illnesses that are caused due to psychological problems including asthma, hypertension, eating disorders, insomnia, allergies and migraines can be addressed by the bioactive compounds of the flowers. Therapies induced by flowers are proved to be successful in treating cognitive diseases such as stuttering, loss of memory and dyslexia and can balance emotions like fear, stress and anger. Although not all flowers are safe to eat, but many of them can offer health benefits, when being added in dishes. Hence, many flowers are of industrial importance due to their medicinal, culinary importance, often for their fragrance and pigment. Many Indian flowers are recognised for their medicinal and commercial importance. One of them is *Clitoria ternatea*, locally known as Aparajita or Sankhapushpi, noted in ancient Indian Ayurveda for its well-known therapeutic activities. This plant species belongs to the family Fabaceae and is a persistent herb, with obtuse, elliptic leaves. It grows in moist soil with neutral pH. The most prominent feature of the plant is the vibrant blue (deep blue, cobalt blue or light blue) or white coloured butterfly shaped solitary or paired about 1-inch-longflowers, with light yellow markings with bract and bracteole. The five petals are differentiated into a large standard, two oblong wing petals and two partially fused petals forming a boat-shaped keel incurved with a yellow to white pattern. This flower is long been used as a conventional herbal remedy against numerous diseases and the

scientific investigations have validated those with contemporary significance [2]. The present review highlights the use of *Clitoria ternatea* flower for therapeutic, agricultural and industrial purposes.

Bioactive compounds present in *Clitorea ternatea* petals

The petals of *C. ternatea* are enriched with various bioactive phytocompounds, which include various polyphenols, flavonoids, pigments and other phytocompounds. Conventionally, pigments mainly anthocyanins *were extracted* from *C. ternatea* flower, [3], while other workers [4,5,6] concentrated on the extraction of flavonoid constituents. Since pigments are the most important feature of the petals, flowers of *C. ternatea* are categorised in three types, namely flower having blue petals with usual keel (BSPF), blue petals with distended keel petals (BMPF) and white petals with normal keel petals (WSPF), of which BMPF indicates the occurrence of notable quantities of biologically active compounds and nutritionally important elements [7]. Three flavonol glycosides including quercetin 3-O-(2"-O-α-rhamnosyl-6"-O-malonyl)-β-glucoside, myricetin 3-O-(2",6"-di-O-alpha-rhamnosyl)-β-glucoside, and kaempferol 3-O-(2"-O-alpha-rhamnosyl-6"-O-malonyl)-β-glucoside were extracted from *Clitoria ternatea* petals in combination with 11 identified flavonol glycosides. These were categorized as quercetin 3-(2(G)- rhamnosyl-rutinoside)s, kaempferol, quercetin, and 3-rutinosides, 3-glucosides and myricetin 3-neohesperidosides within the identical tissues. Furthermore, myricetin 3-O-(2"-O-α-rhamnosyl-6"-O-malonyl)-β-glucoside presence was anecdotal from the data obtained through LC/MS/MS for crude extracts of the petals [4]. Moreover, 8 anthocyanins (preternatins C4 and A3 and ternatins D3, C5, C4, C3, C2 and C1) were also extracted from the flowers, whereas 7.1% of cyclohexen, 1-methyl-4-(1-methylethylideme), 33.6% of mome inositol, 5.7% of hirsutene (5.7%) and 6.5% of acetic acid, cyano- were exracted from methanolic flower extract of *C. ternatea* Terahara [3].

Extraction of Bioactive compound present in *Clitorea ternatea* petals

For screening of active compounds present in *Clitorea ternatea*, the dried petals are pulverized to reduce the size and are mixed with solvent where they are to be extracted. Amongst various extraction methods, the best technique is to be adopted which can guarantee the maximum release of phytochemicals in the extraction medium [8]. Most extraction methods [9,10,11] utilized fresh flowers, oven/ air-dried, or grounded/ powdered, dried flowers [12, 13, 14, 15, 16, 17] . Few studies used clean flowers, which were chopped into small pieces, cleaned and kept at −25 °C temperature and extracted within a month [18] or freeze dried and subsequently ground [19]. A majority of the studies engaged in extractions utilizing aqueous solvent mixtures of methanol or ethanol in comparison to using just water along with heating for studying the potential biological activities and the phytochemical constitution, whereas a several studies investigated about the optimum extraction and/or solvent parameters. Recently some non-conventional extraction methods are used which are found to be highly efficient, environment friendly and with more advantageous than conventional extraction methods. These include ultrasound mediated method of extraction, microwave aided extraction, extraction by enzymes, ion pressurized liquid extraction and supercritical fluid extract [8, 20]. In ultrasound assisted extraction, acoustic waves lead to the molecular solvent movement present in the sample that allows the discharge of inorganic and organic compounds [21]. Yield of phenolic content was found to be more when extracted in the ultrasound assisted extraction [9].

Analysis of bioactive compound present in *Clitorea ternatea* petals

Different workers analysed the bioactive phytocompounds present inside *C. ternatea* petals using different extraction solvents. Depending on the nature of solvent the relative amount of the compound varies [22] . Other important phytochemicals include anthocyanins (pigment), tannins (polyphenol), triterpenoids, saponins, phenols, anthraquinone, and cardiac glycoside [23]. Scientists quantified quercetin-3- rutinoside (0.0290 to 0.368 %); procyanidin A2 (0.331 to 0.738 mg%); (-)- epicatechin (0.009 to 0.026 %); and delphinidin-3-O-glucoside (0.0318 to 0.0405%) as the major flavonoids. Prolonged exposure to high temperature (100 °C), although increase the release of phytocompounds to extraction solvent, but have the risk of denaturation of most flavonoids. Few noteworthy compounds were quantified [24] from the lyophilized fresh aqueous floral extract from *C. ternatea*: (-)-epicatechin (0.0321 %); quercetin-3-rutinoside (0.0296 %); myricetin (0.01% g); quercetin (0.001 %); kaempferol (0.018 %) and delphinidin (0.074 %) of which quercetin-3-rutinoside (0.0038 %); myricetin (0.005 %); quercetin (0.00609 %) and kaempferol (0.004 %) remain present in the methanolic extract of the flowers of *C. ternatea* in tert-butylhydroquinone and HCl [25]. On the other hand, the extract contained syringic (9.3 to 11.1 mg/100 g); gallic (1.3 to 21.8 mg/100 g); 2,4 dihydroxybenzoic; 2-hydroxycinnamic; caffeic (21.4 to 23.3 mg/100 g); protocatechuic p-coumaric; ferulic (7.1 to 8.5 mg/100 g); and also, ellagic acid (40.0 to 70.8 mg/100 g) as the key phenolic acid. The yield of phytocompound depends on the nature of extraction medium used as it was found that protocatechuic acid (72 mg/100 g), chlorogenic acid (54 mg/100 g) and gallic acid (67 mg/100 g), and in lyophilized aqueous extract whereas protocatechuic acid (0.2 mg/100 g), gallic acid (3.3 mg/100 g), caffeic acid (1.0 mg/100 g), ferulic acid (3.5 mg/100 g) and p-coumaric acid (1.2 mg/100 g),

and in the methanolic extract of the flowers of *C. ternatea* comprising tert- butylhydroquinone and hydrochloric acid (HCl). The utilization of high-performance liquid chromatography (HPLC) for the isolation of bioactive phytocompounds on a huge scale is generally inconvenient and costly. Hence, the phytochemical selection of tannins, flavonoids, glycosides, alkaloids, steroids was performed by Thin Layer Chromatography (TLC) fingerprints using standard protocols. Total antioxidant capacity (TAC) and phenol content (TPC) were estimated by spectrophotometric analyses. The aqueous extract of the petals was found to contain compounds like quercetin and kaempferol glycosides, whereas the alcoholic extract was dominated by phytosterols, fatty acids, and tocopherols since the medium of extraction plays a pivotal role on the extracted compounds [19]. The strong blue colour of *C. ternatea* petals is imparted by the pigment, anthocyanins [26] , which is produced as a result of summation of optical densities found at various wavelengths (620, 520 and 420nm) corresponding to the colours of red violet-blue (anthocyanins) and yellow respectively. The extracted pigment content varies with the use of hydrophilic medium like methanol and hydrophobic medium, like the mixture of hexane and ethyl acetate [27]. The highest amount of anthocyanins were extracted in ethanol medium, whereas ethyl ether extract showed the least efficacy since higher the polarity of ethanol, higher will be the efficacy in extraction of the polar compounds including anthocyanins. Scientists found that acidic pH [27,28] enhances the yield of anthocyanins in the extraction medium since lowering of pH changes anthocyanins to flavium cation that in turn causes breakage of cell wall and enhancement of the solubility of the pigments. On the other hand, the optimum temperature for anthocyanin extraction was found to be 70 °C [27].

Optimization of extraction parameters could be accomplished by Response Surface Methodology (RSM) adopting a multivariate system [29] , where the three factors evaluated were extraction temperature (30 to 60°C), blanching time (0 to 12 min), and extraction time (30 to 120 min) [30].

Medicinal activities of *Clitoria ternatea* petals

Clitoria ternatea petals are recommended for the treatment of many neurological and psychological problems as they act as antistress, anti-depressive, anxiolytic, anticonvulsant, nootropic tranquilizing and sedative agent and also as memory enhancer. Animals treated with floral extracts showed betterment in condition for their analgesic, antipyretic, anti-inflammatory, antioxidant properties. Moreover, their antiasthmatic, antidiabetic, anti-arthritic, antilipidemic, diuretic, cognitive enhancing and wound healing properties made them one of the most attractive sources of herbal medicine [31]. Ethanolic floral extracts of *Clitoria ternatea* can reduce the histamine-induced breathing trouble or dyspnoea in Guinea pigs, and muscular contraction of goat trachea and guinea pig ileum. It also causes the diminution in inflammation of the lungs, coughing, and reduction in white blood cell counts, immunoglobulin G1 and interleukin levels within mice, which are albinos [32]. Methanolic petal extract of *C. ternatea* can reduce the release or expression of receptors, enzymes, or molecules concerned with inflammatory responses. Aquas extract increases in plasma antioxidant capacity leading to the increase in postprandial antioxidant status and reduction in postprandial sucrose and insulin levels [33].In canines, erythrocytes are protected from haemolysis, if treated with aqueous floral extract of *C. ternatea*. It also causes decline in peroxidation of lipid, oxidation of protein and increase in glutathione levels [10]. The floral extract also brings about an inhibition of α-amylase activities, decrease in release of glucose, hydrolysis index and glycaemic index. [34].

Neuropharmacological activities:

C. ternatea is reported to be an effective therapeutic agent for mental illness, as administration of aqueous extract of *C. ternatea* plant in mice improved spatial learning performance and often acts as antidepressant through modulation of the activities of neurotransmitters [35]. It is reported that the intraperitoneal injection of floral alcoholic from *C. ternatea* on mice and rats, could bring about sedation and diminished alertness [36]. The alcoholic extract of the whole plant including the flowers could reduce memory loss, induced by electric shock through enhancement of the activity of acetylcholinesterase in various sections of the brain [36]. It is opined from various experimental results on mice that this plant has the ability of modulating obsessive compulsive disorder and thereby decreases psychiatric instability [37]. The aerial part of the plant shows the efficacy in restring the normal growth and functioning of neurons and associated cells and therefore scientists think it a potential candidate to fight neurological diseases like amnesia and Alzheimer's disease. The extract of *C. ternatea* flowers has exhibited good efficacy as an anti-neuroinflammatory substance [38] devoid of severe toxicity and considerable nephroprotective and hepatoprotective activities in vivo models of mice. Ethyl acetate extract of the flowers of *C. ternatea* showed remarkable reduction in NO (nitric oxide) in a dose-dependent way, having no toxic impacts on normal development of embryo, formation of blood vessels, and apoptosis in models of zebrafishes. Scientists expect that the anti-neuroinflammatory and neuroprotective potentials of *C. ternatea* flower extracts may be utilised for treating brain-associated disorders in the near future [39].

Antihypertensive activities:

Hypertension is a severe mortality and morbidity causing health condition that leads to the development of cardiovascular disease.Nω-Nitro-L-arginine Methyl Ester Hydrochloride(L-NAME) can experimentally induce hypertension in rats and it was found that *C. ternatea* flower extract at a dose of 300 and 100 mg/kg/day could counter such hypertensive effect in such rats. Such anti-hypertensive effect is probably accomplished by modulation of the activities of renin–angiotensin system (RAS). Oxidative stress that can aggravate the hypertensive conditions is alleviated by treatment of *C. ternatea* extract [40]. These antihypertensive activity of *C. ternatea* petal extract is actually exerted by the flavonoids and is precisely related to the arrangement and number of the OH^- groups [23].

Anti-obesity activities:

Obesity is resulted when food intake exceeds energy expenditure. Today, obesity is a growing global health problem, responsible for the development of different diseases including increased blood sugar, cardiovascular diseases and atherosclerosis. Petal extract of *C. ternatea* inhibits adipogenesis and lipid accumulation and thereby prevents obesity. Such anti-adipogenic activity is found to be accomplished by and acetyl-CoA carboxylase and fatty acid synthase downregulation, through suppression of phospho-ERK1/2 and phospho-Akt signalling pathway expression and hindering the activities of adipogenic transcription factors such as C/EBPα and PPARγ. The extract also increased catecholamine-induced lipid breakdown in adipose tissues [40]. Consumption of *C. ternatea* petal extractdecreases fat enriched diet induced postprandial serum triglyceride level and reduces the amount of serum free fatty acids to check weight gain in obese individuals [41].

Antioxidant activities:

The antioxidant effects of floral extract of *C. ternatea* is well established. The plasma antioxidant status is found to be improved following ingestion of floral extract of *C. ternatea* through increase in the activity of glutathione peroxidase, an enzyme that protects the cell from oxidative damage [41]. On the other hand, this extract was found to protect blood cells from the oxidising activity of oxidative damage and haemolysis of erythrocytes in the canines induced due to 2, 2'-azobis-2-methyl-propanimidamide dihydrochloride (AAPH) [10]. The detailed biochemical screening shows that among the three varieties, the flowers of BMPF, i.e., flower with enlarged keel petals (BMPF) contains relatively highest amount of total flavonoid content (TFC), total phenolic content (TPC), and free radical scavenging activities, which in turn gives higher antioxidant efficiency [7]. Scientists [42] estimated the antioxidant effect of the floral extract from *C. ternatea* and its shielding action on bisphenol A (BPA)-induced oxidative damage in murine reproductive system among females. They have also found that the extracts from *C. ternatea* exhibited considerable protective and high antioxidant activities against *Bisphenol* A (***BPA***)-induced adverse reproductive effects in mice (*Mus musculus*).Similarly, the protective action of the floral extract of *C. ternatea* on damage of the testicles caused by ketoconazole among rats was observed [43]. The floral extract of *C. ternatea* immobilized in alginate beads showed improved antioxidant capacity with enhanced thermal stability [44].

Anti-inflammatory and anticancer activities:

The petroleum ether floral extract from *C. ternatea* was appraised for anti-inflammatory effect by the use of carrageenan paw oedema procedure with albino but healthy rats of both sexes. Such protective effect was accomplished by opposing kinnins, prostaglandins, and other substance release in oedema induced by carrageenan [45]. The flavonol and anthocyanin content of the floral extract **of** *C. ternatea* showed its inhibitory action against lipo polysaccharide induced inflammation. The anthocyanins were being also observed to highly inhibit production of NO in comparison with the flavonols [46]. Molecules of ternatin anthocyanins (9 molecules) and glycosylated quercetins (3 molecules), isolated from floral extracts of ***C. ternatea*** by HPLC displayed anti-inflammatory characteristics in inflammation induced by lipopolysaccharide (LPS) in RAW 264.7 murine macrophage cells thereby suppressing the TNFα production via Nrf-2 and AP-1 signalling pathway inhibition [46]. The anti-inflammatory and analgesic efficacy of the floral extract from *C ternatea* was determined in mice with the carrageenan-induced paw edema and rats suffering from thermal analgesia [47]. Although the methanol extract from *C. ternatea* seed could increase the life span of EAC tumour bearing mice and thereby exhibited potential antitumor and antioxidant activities [48], the aqueous extract from *C. ternatea* was reported to possess anti-proliferative effects that can inhibit the cancer cell lines [49]. Scientists (Shen et al, 2016) working on petal extract found both hydrophilic and lipophilic extracts of petals could decrease the HEp-2 carcinoma cell viability. Treatment with methanolic extract of *C ternatea* flowers brought about a reduction in the titres of HIF-1α in the nucleus of Ehrlich ascites carcinoma (EAC), which is a spontaneous murine mammary adenocarcinoma cells (Balaji et al, 2016). This is probably due to the suppression in the process of angiogenesis in murine carcinoma model in-vivo through the effective translocation of HIF-1α from cytosol to nucleus. After biomolecular analysis it is inferred that the flavonoids, especially scutellarin may be

responsible for such anticancer activities. The cyclotides of ***C. ternatea***, specifically known as cliotides, extracted and refined from the flowers showed significant anticancer and chemo-sensitizing abilities [19]. Moreover, these extracts can minimize the damages of target site cells by increasing the efficiency of chemo radiation drugs. The floral extract of butterfly pea flower (*C ternatae*) is found to have anti-breast cancer activity as it can check particularly metastasis via nuclear factor kappa B (NF-κB) inhibition and it was confirmed by that the floral extract had an antimetastatic action to MCF-7 HER2-positive cell line of breast cancer *in-vitro* [50].

Immunostimulatory activities:

Extracts of *C. ternatea* can increase immunity, reduce inflammation and angiogenesis. *C. ternatea* , being one of those plants enriched with cyclotide and display noteworthy immune-stimulating activity since at a lower concentration it can boost up the release of various cytokines and chemokines including macrophage inflammatory proteins (1β and 1α), interleukin 8, interferon γ-induced protein 10 and tumour necrosis factor α from human monocytes. Such data indicates clearly that cyclotides can be used as possible candidates for designing novel immunomodulating therapeutics [51].

Antidiabetic activities:

In rats, consumption of aqueous floral extract of *C. ternatea* (400 mg/kg rat body weight) for eighty four days notably decreased glucose in serum, glycosylated haemoglobin, and gluconeogenic enzyme glucose-6-phosphatase activity, whereas augmented insulin in serum, protein, glycogen content in skeletal and liver muscle and glycolytic enzyme glucokinase activity [52]. Such antihyperglycemic activities was evaluated in rats suffering from diabetes induced by streptozotocin and correlated with its ***in vitro and in vivo*** antioxidant action [53]. According to them the restoration of normal glycemic level after intake of ethanol extract of *C ternatae* was accomplished by formation of β-cells in the islets of Langerhans or by the replication of the existing residual islets leading to pancreatic regeneration and stimulation of insulin hormone. This caused the lowering of fasting blood glucose level and prevention of cellular atrophy by opposing to ubiquintin-proteasome pathway. The ultimate effect of which was reduction of all the diabetes associated disorders like elevated lipid levels and oxidative stress [53]. The antihyperglycemic and antioxidant effect of ethanolic floral extract from *C ternatae in vitro* ***was*** confirmed [54]. Rats suffering from diabetes induced due to alloxan, treated with ethanolic extracts of *C. ternatea* flowers (50-500mg/kg) for 21 days showed significant lowering of serum sugar level because of the inhibition of glucosidase and galactosidase actions but no fructosidase inhibiting action. The aqueous extracts of *C. ternatea* flowers (400 mg/kg) for a period of eighty-four days remarkably decreased glucose in serum, total cholesterol, glycosylated hemoglobin, urea, triglycerides, creatinine, and the action of gluconeogenic enzyme glucose-6-phosphatase, however rose insulin in serum, protein, HDL-cholesterol, skeletal and liver muscle glycogen content and the action of glycolytic enzyme glucokinase [55]. The floral extract of *C ternatae* was examined for antidiabetic effect and it was found to significantly reduce the glucose levels of the serum and augmented the body weight of the rats suffering from diabetes [56]. Possibly due to this reason it is widely used for treating diabetes by the rural people.

Other actions

Anti-arthritic activity was shown by both *C ternatae* petal extract and Quercetin which acts on synovial matrix-metalloprotease-2 in arthritic joints and TNFα-receptor 1. Hence a mixture of floral extract and Quercetin can be effectively used for the treatment of arthritis [16] . The methanolic floral extract was found to exert some protective effects against liver damage by antioxidant mechanism [57].

Industrial Applications of *C ternatae petals*

C. ternatae have numerous beneficial medical and agricultural applications, like crop for nitrogen-fixation, fodder, an environmentally-friendly insecticide [31], food colorant [15]and in conventional medicine for diseases like ascites and anasarca [12]. It is generally cultivated as a decorative plant and is even applied for revegetation of different mining sites [58].

In food industries: Food colorants and dyes play a key role in the food industries. A drift was observed at that time for utilizing natural dyes in place of artificial dyes. A natural dye can be isolated from *C. ternatae* flower because of its intense blue colour [59]. *C. ternatae may* be used as food colourant for its safety and effectiveness [38]. This flower is utilized for culinary uses and its isolated dye is utilized as a natural food colorant in the food industries for medicinal purposes and herbal drink preparations [60]. It has therapeutic benefits such as aiding in digestion, recovering eyesight, reducing blood pressure [61]. Juices of *C. ternatea* flowers are highly nutritious since it contains considerably higher amounts of dietary essential macro nutrients. As of the source bright blue colour, the petals of *C. ternatea* are very popular and widely used to prepare deserts and teas. Since, the colour changes with change of pH, by changing the pH different shades of hues from orange to red to blue can be generated which are used as a colourant for alcoholic beverage [62]. The main colouring molecules of the flowers of *C. ternatae* are a series of anthocyanin extracted from the fundamental types of delphinidin including ternatin B1–B4, A1–A3, D1–D3

and C1. Although till date, very less authenticated value-added commercial products from *C. ternatae* flower are globally available, a shelf stable *C. ternatae* enriched beverage was developed which was claimed to be a totally natural product without any preservative that could be used as an alternative for synthetic beverages [2].The major distress of food industries regarding the natural colour stability and extraction yield motivated many researchers to estimate proper pre-treatment and methods of extraction. This extract increases the antioxidant and polyphenolic contents of sponge cakes [63] , enhances the oxidative stability of cooked pork patties and diminished the measured glycemic index of flour [34].Moreover, i***t is found that the*** flowers of ***C. ternatea*** can be utilised as a pharmaceutical supplement or a potent drug along with food for amelioration of the effectivity of the drug [38].

In cosmetic industries: Extracts of *C. ternatae* flowers are utilized in Thailand in the form of a constituent of cosmetics and the chemical constitution of *C. ternatea* flowers indicates that they might possess antioxidant effect. An eye cream from the aqueous extracts of *C. ternatae* having strong antioxidant activity was formulated [64]. Hence, according to them this extract can be used as cosmetic product at commercial scale. [11] . Due to its antioxidant properties, it protects tissue damage and makes the skin glowing [61]. At present, there is no large-scale anthocyanin production from ***C. ternatea***, since people think yielding of plant products at commercial-scale may not be reasonably viable. On the other hand, current advancements in engineering suspensions of plant cell cultures having genes of the regulatory pathway, which produce anthocyanin can be a substitute [65]. The shielding acrions of the flowers of *C. ternatea* which comprise flavonol glycosides and polyacylated anthocyanins as main ingredients, against UV and H_2O_2- induced oxidative damage of dermal cells, and might offer a little justification for the alleged conventional and cosmetic applications of the flower *C. ternatea* against aging of skin. [66].

Agricultural applications:

C. ternatea has been cultivated for a long time as a fodder and forage crop, and previous investigations evaluated the plant for such applications and it was found that the plant is adapted to heavy dry-season and heavy cracking clay soils [67] . The plant is evaluated for its efficacy of being used as a source of fodder, which showed that quite an appreciable amount of fodder has been generated from it in two consecutive cuts [68]. It is also known as the most important forage legumes, inter-cropped with rice. The major contribution of the plant in agricultural domain is its role in nitrogen fixation with the help of its root nodules. Numerous investigations have observed the beneficial impacts of *C. ternatea* on health of the soil [31].

As biopesticides: But the role of flower is in imparting defence to the plant through the production of some defence molecules called cyclotides, which are rich in disulphides, macrocyclic peptides (26–37 residue long) serving as self-protective metabolites [69]. It was found that the expression of cyclotide takes place in a tissue specific way. *C. ternatea* flowers are enriched with ultra-stable macrocyclic peptides that are potential insecticides and are drawn in as the biologically substances within a plant extract commercially used as an insecticide. Asparaginyl endopeptidase (AEP) is necessary to produce cyclic peptides, which provide with ultra-stability against chemical, enzymatic and thermal decomposition, which imparts defense against herbivore attack or environmental stresses. Cyclotides are peptides that disrupt the cell membrane and have been found to be active against nematodes, larvae of insects, fungi, bacteria, and both mammalian and plant cells and on the basis of their wide range of biological activities, it was indicated that cyclotides take part in host defence of the plant. *C. ternatea* are the only leguminous plant that is known to produce cyclotides. The flowers are m enriched with these ultra-stable macrocyclic peptides. They include cytotoxic, hemolytic, insecticidal, antimicrobial, molluscicidal, antifouling, and nematocidal effects. These circular molecules can even be utilized in the form of scaffolds for peptide-associated therapeutics but can be used commercially as a herbal insecticide. The broad-spectrum efficacy of these molecules has snatched the attraction of researchers on exploring the utilities of these molecules in the fields of biotechnology, agriculture, and medicine. In 2017, Sero-X®, which is a cyclotide- comprising environmentally-friendly pesticide, was commercially prepared from *C. ternatea* extracts and was recommended for availability in Australian market [70]. The cyclotide extracts from *C. ternatea* shoot-leaf-flower was found to permeabilize insect-like lipids of the membrane, causing the death of the target insect (74). Another investigation observed that the use of oil-based mixture of *C. ternatea* (1–2% v/v) affected oviposition, and larval feeding prevention and also direct toxicity to cotton bollworm, *Helicoverpa* spp. Adverse effects of the phytoextract against useful insects were not reported [71], demonstrating that extracts from *C. ternatea* can provide with the approach for environmentally-friendly natural insecticides. The anthelmintic characteristics of *C. ternatea* have been studied in numerous experiments. It has showed varying extent of resistivity against the root-knot parasitic nematode called *Meloidogyne incognita* [72] Methanolic *C. ternatea* extract was even observed to bring about 93% of inhibition among eggs of *M. incognita* from hatching [73]. In another experiment, which used *Caenorhabditis elegans* as a model organism, extracts from *C. ternatea* were observed to actively slay larvae of nematodes, with the extracts of roots displaying greater toxicity as

compared to the extracts from the leaves [74]. In addition to this, 2 studies found that *C. ternatea* also act against annelids [75, 76]. By the use of *Pheretima posthuma* as an experimental worm, a study demonstrated that the ethanolic extract of *C. ternatea* (50 mg/mL) remarkably increased rate of mortality and occurrence of paralysis of the worms in comparison with piperazine citrate, which is a normally applied drug to control parasitic worms [77]. Just like this, by the use of *Eisenia foetida* as an experimental worm, another experiment demonstrated that the aqueous and ethanolic extracts of *C. ternatea* led to paralysis of worms and mortality at a concentration of 100 mg/mL [73]. In contrast, with the frequently applied antiparasitic drug known as levamisole, the pace of paralysis of worms and death was remarkably slow with the extracts from *C. ternatea* [76]. *C. ternatea* are the only leguminous plant that is known to produce cyclotides. The flowers are enriched with these ultra-stable macrocyclic peptides. They include cytotoxic, hemolytic, insecticidal, antimicrobial, molluscicidal, antifouling, and nematocidal actions. These circular molecules can even be applied in the form of scaffolds for peptide-associated therapeutics but can be used commercially as herbal insecticides.

As antimicrobials: Although the antimicrobial attributes of *C. ternatea* previously have been described by different scientists [77,78], they were isolated mainly from seed and shoot extract. Only a few reports are available on the antimicrobial activities of the *C. ternatea* extracts from the flowers [79] found the antimicrobial effect of the flower while using the aqueous, petroleum ether, methanol, chloroform and hexane extractions of the flower against various bacteria namely, *Escherichia coli, K. pneumoniae*, *Pseudomonas aeruginosa, Streptococcus mutans, Lactobacillus casei*, and *Staphylococcus aureus*. [80]. Another investigation observed that the ultrasound-mediated aqueous *C. ternatea* extract from the blue petals prevented *Staphylococcus aureus* growth. The antibacterial activity is presumed to be positively correlated with the anthocyanin content [81]. The methanolic floral extract of *C. ternatea* was found effective against several bacteria mainly *B. subtilis, Bacillus cereus, Staphylococcus aureus, , B. thuringiensis, Streptococcus faecalis, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Enterobacter aerogens, Salmonella typhi, Herbaspirillum* spp. and *Proteus mirabilis*, and Rhizopus, Candida, and Penicillium sp . The methanolic, aqueous, chloroform extracts of the flower were found to active against E.coli (Enterotoxigenic and Enteropathogenic), Klebsiella pneumoniae, and Pseudomonas aureginosa, of which methanolic extract was found to show the maximum antibacterial activities [82]. The antibacterial efficacy of ethanolic flower paste extract of *C. ternatea* against bacteria namely *B. subtilis*, *B. cereus*, **B.** *subtilis* subsp. *spizizenii*, *S. aureus, Proteus mirabilis, K. pneumoniae*, *E. coli*., and, *Yersinia enterocolitica* and fungi like *Aspergillus niger*, *Penicillium expansum* and *Rhizopus stolonifer* were determined [80](Anthika et al,2015) of which the growth of *Penicillium expansum* was completely suppressed. It was experimentally confirmed that the anthocyanin fraction is conferring the antimicrobial activity against *B. subtilis* and fungi like *A. niger, Fusarium* sp., and *Trichoderma* sp [83]. The anthocyanins are also used to make the collyrium or the eye drops with antimicrobial properties [84].

In recent year, biogenically synthesised ZnO nanoparticles by using of the extract from *C.ternatea* flowers, were found to be very effective in removing the biofilm caused by *Porphyromonsas gingivalis* and *Alcaligenes faecalis*, found to form oral plaque [85].

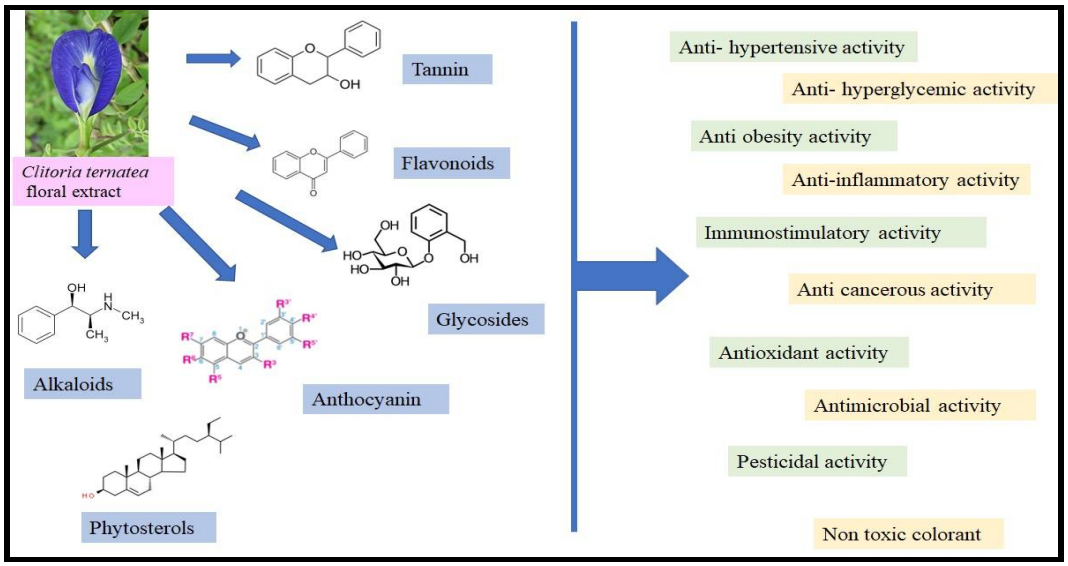

Figure 1. Therapeutic and commercial applications of the *C ternatea* extract.

Mechanism of action of bioactive compounds:

The major phytocompounds present within the extracts from *C. ternatea* flowers include the flavonoids, tannins, and few alkaloids, glycosides and phytosterols. The medicinal attributes of *C. ternatea* extract are imparted either by the individual or synergistic actions of these compounds (Figure 1). The antidiabetic and hypoglycaemic action of the flavonoids (Quercetin) is mediated by enhancement of insulin synthesis and activities, utilization of glucose inside the peripheral tissues and the prevention of absorption of glucose inside the intestines. The activation of 5'-AMP-activated protein kinase (AMPK) by flavonoids stimulates the expression and activation of glucose transporter proteins (GLUT 4). This in turn increases the uptake of the glucose by muscle cells lowering the serum glucose level [86]. Mammalian target of rapamycin (mTOR) participating in multiple signalling pathways and thereby regulating cell proliferation and immune cell differentiation, autophagy, apoptosis plays a key role in metabolism of tumour [87]. Flavonoids have the capacity of suppressing activity of mTOR and subsequently can induce T regulatory subset. Quercetin can control leukocyte biology along with a stimulus-specific activity and impacts Th1/Th2 balance within a murine model [88]. The anti-inflammatory activities of the flavonoids occupy the prevention of the biosynthesis and actions of various pro-inflammatory mediators like eicosanoids, cytokines, adhesion molecules and C-reactive protein. Molecular effects of flavonoids comprise prevention of transcription factors including NF-kappa B and activating protein-1 (AP-1), and also nuclear factor-erythroid 2-related factor2 (Nrf2) activation. Flavonoids exert a broad spectrum of anticancer efficacies via reactive oxygen species (ROS)-scavenging enzyme activity modification, participation in cell cycle arrest, apoptosis induction, suppression of cancer cell invasiveness and proliferation and autophagy [89]. Mechanistically, flavonoids carry out their antihypertensive activities by increasing the bioavailability of nitric oxide (NO), reducing oxidative stress in the endothelial cells or activity modulation of the vascular ion channels [90]. Antioxidant activity of flavonoids is accomplished by their capacity to decrease formation of free radical and for scavenging free radicals. Flavonoids and their respective metabolites usually exhibit an *in vivo* antioxidant effect [91]. The presently known anti-obesity activities of flavonoids emphasize numerous feasible means of weight loss, which involve reduction in absorption of fats in intestines, modulation differentiation of the adipocytes, adipogenesis, β-oxidation, enhancement of lipolysis, and apoptosis, stimulation of energy outflow by introduction of non- shivering thermogenesis on obesity-associated dysbiosis of the gut microbiota [92]. The tannins being natural polyphenols, possess an inhibitory action on the angiotensin converting enzyme (ACE), which bring about the relaxation of the blood vessels to lower blood pressure [93]. Tannins enhance glucose uptake and can improve the pathological oxidative state of a diabetic situation [94]. The alkaloids, apart from the increase in enhancement of uptake of glucose and secretion of insulin display antidiabetic action via inhibition of the activities of enzymes such as *α*-glucosidase, *α*-amylase, dipeptidyl peptidase-IV, aldose reductase and protein tyrosine phosphatase-1B; inhibition of the end products of advanced glycation thereby decreasing blood glucose level and increasing glucose tolerance [95]. The alkaloids act as antioxidant to protect against oxidative damage by scavenging radicals or by suppressing the production of radicals [96]. The phytosterols and glycosides generally use Na+/K+-ATPase in the form of a signal transducer for activating proliferation of tissues, contractility of the heart, hypertension within the arteries, and natriuresis through different intracellular signalling pathways [97]. It also exerts anti-cancerous activities. Antimicrobial activities of flavonoids, tannins, phytosterols are accomplished by the inhibition of bio synthesis of nucleic acid, hindering the function of the membrane of cytoplasm, prevention of metabolism of energy, disruption of the adherence and formation of biofilms, inactivation of the porins on cell membrane, modification of the permeability of membrane, and pathogenicity attenuation [98]

CONCLUSION

C. ternatea, a well-known flower of Asia is of immense commercial importance. Apart from its medicinal significances, it has got many agricultural, culinary and industrial applications. The phytocompounds including polyphenols and pigment Anthocyanin has conferred its antimicrobial properties, which can be used for preparing herbal antimicrobial agents. The colour changing anthocyanin for its enchanting colours developed at various pHs may be utilized as natural colourant both in food and herbal dye industries. Scientists have confirmed the medicinal attributes of the floral extracts, which were long being known, by in vitro and in vivo experiments. They have started designing various herbal drugs for human use. The synergistic actions of cyclotides and various peptide and non-peptide phytochemicals made the floral extract competent for being used as a potent bioinsecticide and antimicrobial agent. Due to its non-toxic nature, easy availability and convenience in handling the floral extract can be used for various commercial purposes and new biotechnological approaches are to be adopted to utilise it for developing various drugs for human use.

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CONFLICT OF INTEREST STATEMENT
The author declares no conflict of interest.

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