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Phytochemicals and pharmacological importance of Clitoria (*Clitoria ternatea* L.): A review

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Abstract

In traditional folk medicine, *Clitoria ternatea* L. plant is regarded as a significant herb, known for its medicinal properties. This plant contains a variety of metabolites including flavonoids, alkaloids, tannins, resins, starch, saponins, taraxerone, proteins, taraxerol, anthocyanins, carbohydrate and phenolic compounds as well as other active chemical components, which contribute to its therapeutic properties. *C. ternatea* is traditionally used to treat many ailments including fever, earaches, migraines, indigestion, headaches, throat infections, urinary tract infections, mouth infections, eye infections, skin infections, leprosy and constipation. The reported activities of this plant suggest that it has potential as a source of therapeutic molecules for treating a variety of illnesses. The objective of this review is to providing the detailed description of studies related to the phytochemistry, pharmacognosy and traditional uses of *C. ternatea* with a primary focus on its pharmacological actions.

1. Introduction

Flowers are one of the most admired creations of nature consistently enhancing the beauty and fragrance of the environment. Flowers are widely used for decoration purpose around the globe and also commonly found in gardens along roadsides, parks, cultivated fields, grasslands and forests. Flowers crops have a variety of therapeutic qualities that are used modern medicine to treat a range of various diseases. The world has seen a surge in interest in plant studies with a substantial amount of data accumulating to demonstrate the enormous scope of medicinal plants applied in various traditional methods. There are hundreds of important therapeutics and biologically beneficial compounds have been developed from traditional flower crops. *C. ternatea* is a plant species also known as Asian pigeonwings or butterfly pea. It belongs to the family Fabaceae with 1-2 inch long, bright blue blooms that have a white centre and a wavy rim standard flower. It is an elliptical shape and herbaceous perennial plant that thrives well in moist and neutral soil conditions. It typically grows as a creeper or vine are shown in Figure 1 (Chakraborty *et al.*, 2013). It is a twining herb found in regions such as India, Philippines, Madagascar and China. In traditional Ayurvedic medicine in India, it used to treat a various diseases and symptoms are shown in Figure 2 (Ramaswamy *et al.*, 2011). The roots of *C. ternatea* have laxative, diuretic, anthelmintic and anti-inflammatory properties which aid in the treatment of fever, asthma and acute bronchitis (Mukherjee *et al.*, 2008). The efficacy of various extracts against the tested microorganisms. These variations may be

attributed to the concentration, nature and mode of action of the antimicrobial properties in the extracts on different tested microorganisms (Barbour *et al.*, 2004). The flower juice of *C. ternatea* is used for treating insect bites and various skin conditions. Currently, it has garnered significant attention due to its diverse agricultural and medicinal applications, which used as fodder and for nitrogen fixation to its role in culinary colouring, cosmetics and traditional medicine. Additionally, it serves as a source of eco-friendly insecticides, further highlighting its versatility and potential in sustainable agriculture and natural health solutions. Phytoconstituent studies have identified the several metabolites isolated from the plant including anthocyanin glycosides, phytosterols, flavonoids and pentacyclic triterpenoids (Mukherjee *et al.*, 2002). It has also showed the broad spectrum of pharmacological properties including antioxidant, antibacterial, anticancer and anti-inflammatory, *etc.* Due to a lack of detailed information, it has not been studied as extensively as other plants regarding its potential as a source of antioxidants or medicinal uses. The plant bioactive compounds including antioxidants and other beneficial phytochemicals position it for developing new therapeutic agents and pharmaceutical applications. The comprehensive information on the morphological and chemical constituents of this plant will be valuable for new medical interventions.

Figure 1: *C. ternatea* flower images.

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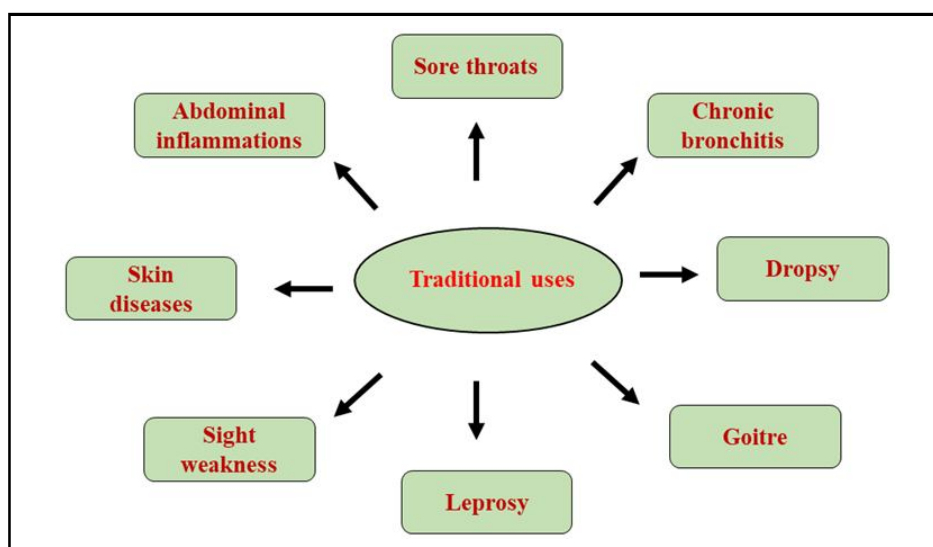


Figure 2: Traditional uses of *C. ternatea*.

2. Phytochemical constituents

Phytochemical constituents are essential for ensuring the quality of herbal medicines starting from the harvesting process and extending through to their use. Furthermore, methodical studies using phytochemical constituent analysis can contribute to the development of new drugs and the compounds have applications in various research areas including optimizing extraction and purification methods, assessing purity and verifying authenticity (Sapna *et al.*, 2022). According to reports indicate that seeds, leaves, roots and flowers of the *C. ternatea* plant have been used since ancient times. The different phytochemicals are identified in various parts of *C. ternatea* using different extraction methods and solvents are summarized in the

Table 1. The plant contains the variety of metabolites including pentacyclic triterpenoids such as ternatins, taraxerol, taraxerone, tannins, flavonoids, alkaloids, anthocyanins and saponins (Kosai *et al.*, 2015). Pentacyclic triterpenoids, specifically taraxerol and taraxerone are the main phytoconstituents of *C. ternatea*. A high-performance thin layer chromatography (HPTLC) method has been developed for quantify the amount of taraxerol in *C. ternatea* and this approach is simple, sensitive, selective and accurate. The analysis was performed on an aluminium thin layer chromatography plate (Gupta *et al.*, 2010). Numerous studies have shown that individual plant analyses reveal the presence of various types of metabolites. The chemical structures present in *C. ternatea* are outlined in Table 2.

Table 1: Different phytochemicals reported in plant parts of *C. ternatea* (Ashraf *et al.*, 2024)

Plant parts	Extraction method	Extraction solvent	Phytochemicals
Leaves	Maceration	Acetone	Terpenoids, tannin, carbohydrate, saponin, alkaloids and phenols
	Maceration	Water	Flavonoid, carbohydrate, phenols, alkaloids, saponin and tannin
	Soxhlet	Ethanol and water	Glycosides, alkaloids, steroids, flavonoids, tannins and phenol
Flowers	Maceration	Methanol	Kaempferol and anthocyanins (Ternatin and delphinidin derivatives)
	Maceration	Water	Flavonoids, phenolics and anthocyanins
	Ultrasonic	Ethanol: water	Phenolics
Roots	Maceration	Chloroform: Methanol (15:1)	Alkaloids
	Maceration	Hexane: Ethyl acetate (80:20)	Taraxerol
	Soxhlet	Ethanol	Alkaloids, phenolic, glycosides flavonoids and tannins

2.1 Leaves

The leaves contain various secondary metabolites such as flavonoids, mucilage, coumarins, terpenoids, alkaloids, phenols, glycosides, quinines, catechol, gum and protein. The leaves have laxative, emetic, diuretic and antiperiodic properties. When combined with salt to make a paste they are highly effective in treating mastoid lymph node irritation. The extract from the leaves can aid in detoxifying the

body. Fresh leaves when combined with ginger juice can help treat hepatic fever, excessive perspiration and inflammation of the surrounding glands and the area around the ear (Patil and Patil, 2011a).

2.2 Flower

The flowers are traditionally believed to be effective in treating snake bites and scorpion stings. In Cuban folk medicine, decoctions made

from the roots and flowers of the plant are used as emmenagogues to stimulate or regulate menstruation (Patil and Patil, 2011a). The flowers are utilized to treat chlorosis and digestive problems. In mice with experimentally induced diabetes, the ethanolic extract of the flowers has been shown to significantly reduce serum glucose levels (Mukherjee *et al.*, 2008). Flavonoids have been identified in the flower with different petal colours including delphinidin 3-O-(6''-O-malonyl)- α -glucoside, delphinidin 3-O-glucoside, delphinidin 3-neohesperidoside and delphinidin 3-O-(2''-O- α -rhamnosyl-6'-O-malonyl)- β -glucoside and additionally they found three other anthocyanins (Kazuma *et al.*, 2003).

2.3 Seeds

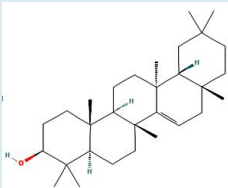
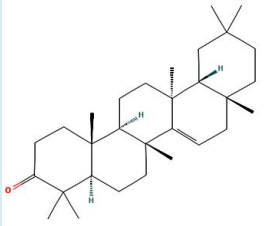
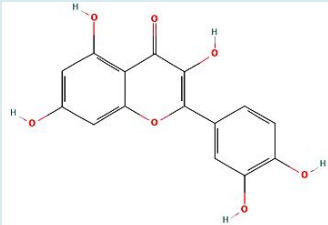
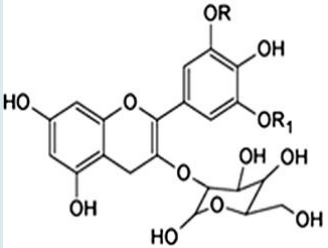
The seeds contain a diverse range of metabolites including water soluble mucilage, p-hydroxycinnamic acid, ethyl- α -D-galactopyranoside, adenosine, a polypeptide, hexacosanol, oligosaccharides, flavanol-3-glycoside, anthoxanthin glucoside, delphinidin 3,3,5-triglucoside (a potential food colour), 3-rhamnoglucoside, anthoxanthin, γ -sitosterol, 3,5,7,4'- tetrahydroxyflavone and β -sitosterol are reported (Mukherjee *et al.*, 2008). The lectin contains present in the seeds to agglutinate human B erythrocytes that had been treated with trypsin. They began an initiative to develop a

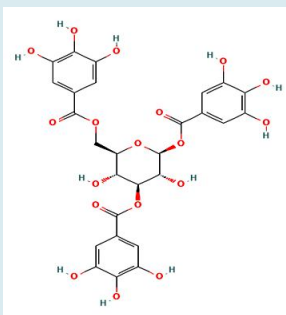
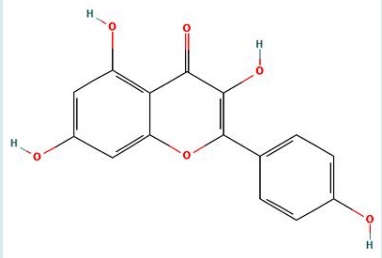
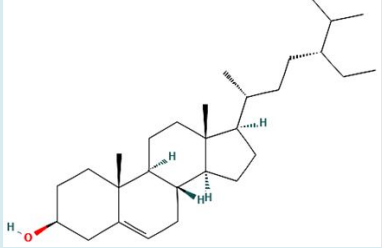
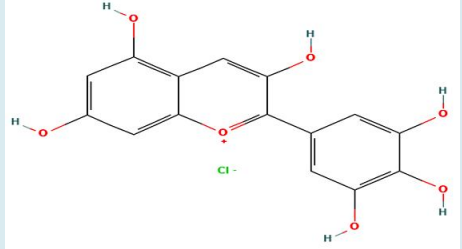
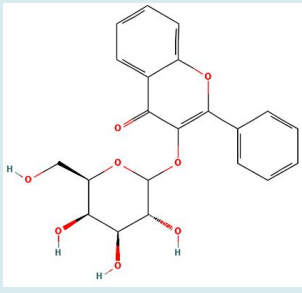
more efficient method for purifying *C. ternatea*, a protein found in the seeds of this Leguminosae family recognizing its potential utility in cancer research (Naeem *et al.*, 2007). The seeds when combined with ginger powder offer a useful remedy for digestive issues due to their cathartic, laxative and purgative properties. Additionally, they are prescribed for rheumatic infections, spleen problems, coughs and hepatic illnesses. The seeds are also regarded as safe for treating conditions like arthritis, colic, dropsy and visceral abdominal pain (Atul *et al.*, 2017).

2.4 Roots

The roots are known to possess laxative, anthelmintic, diuretic, anti-inflammatory and cooling properties. They are characterized by a harsh, bitter or caustic taste (Atul *et al.*, 2017). Studies have shown that root contains tannins, taraxerol, proteins, taraxerone, flavonoids, ternatins, carbohydrates, alkaloids, starch, saponins and resins (Lijon *et al.*, 2017). Root nodules have been found to contains a variety of amino acids including aspartic acid, alanine, histidine, leucine, arginine, glutamic acid, gamma-aminobutyric acid (GABA), glycine, valine, aminobutyric acid and ornithine. Additionally, a study found that the root bark contains starch, resin, flavanol glycosides and tannin.

Table 2: Chemical structure of biomolecule present in *C. ternatea*

S.No.	Phytochemical constituents	Chemical structures
1.	Taraxerol	
2.	Taraxerone	
3.	Quercetin	
4.	Anthocyanin	

5.	Tannin	 <p>The image shows the chemical structure of a tannin, specifically a polyphenolic compound. It consists of a central glucose molecule (a six-membered ring with multiple hydroxyl groups) that is esterified to three gallic acid units. Each gallic acid unit is a benzene ring with three hydroxyl groups and a carboxyl group that has formed an ester bond with the glucose. The overall structure is highly polar and complex.</p>
6.	Kaempferol	 <p>The image shows the chemical structure of kaempferol, a flavonoid. It features a central chromone ring system (a benzene ring fused to a pyrone ring). The chromone core is substituted with two hydroxyl groups on the benzene ring and a 4-hydroxyphenyl group at the 3-position. The structure is shown in a skeletal representation with red highlighting on the oxygen atoms.</p>
7.	β -sitosterol	 <p>The image shows the chemical structure of β-sitosterol, a steroid. It has the characteristic four-ring steroid nucleus. The A-ring has a hydroxyl group at the 3-position. The B-ring has a double bond between C5 and C6. The D-ring has a side chain at C17 consisting of an ethyl group and an isopropyl group. The structure is shown in a skeletal representation with red highlighting on the hydroxyl group.</p>
8.	Delphinidin	 <p>The image shows the chemical structure of delphinidin, a flavonoid. It consists of a central chromone ring system. The chromone core is substituted with two hydroxyl groups on the benzene ring and a 3,4,5-trihydroxyphenyl group at the 3-position. A chloride ion (Cl⁻) is shown below the structure, indicating it is a salt. The structure is shown in a skeletal representation with red highlighting on the oxygen atoms.</p>
9.	Flavanol glycosides	 <p>The image shows the chemical structure of a flavanol glycoside. It features a flavan-3-ol core (a benzopyran ring system) that is glycosylated with a glucose molecule. The glucose is attached to the flavan-3-ol via an ether linkage at the 7-position. The structure is shown in a skeletal representation with red highlighting on the oxygen atoms.</p>

3. Pharmacological activities

C. ternatea is a significant plant in both traditional as well as modern medicine due to its diverse range of pharmacological properties. Its wide range of therapeutic effects enhances its usefulness across various health conditions and treatments. It contains a variety of phytoche-

micals that could indicate the multiple potential biological activities such as anti-inflammatory, antioxidant, anthelmintic, antimicrobial, anticancer, anticonvulsant, nephroprotective, anxiolytic, antidiabetic, hepatoprotective, antidepressant, larvicidal and proteolytic activity (Figure 3). Some important pharmacological activities are listed in Table 3 with various extracts.

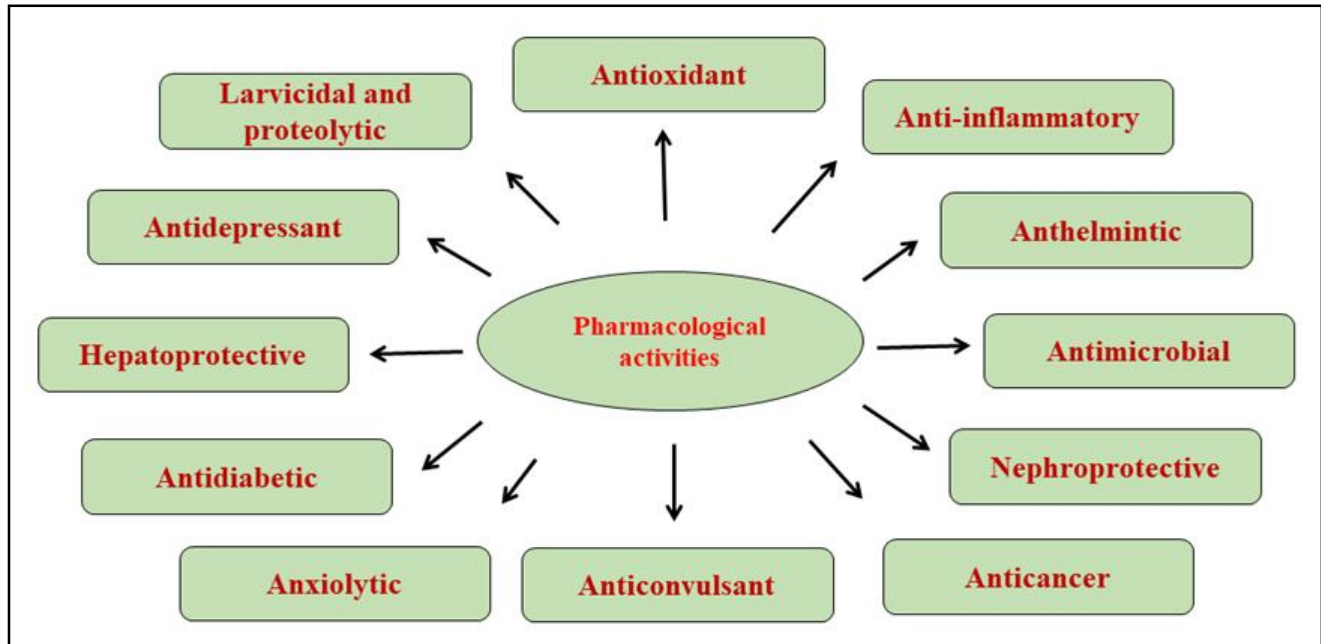


Figure 3: Pharmacological activities.

3.1 Antioxidant activity

Biologically, antioxidants are sourced from plants that have been evaluated and potentially safe. Bioactive compounds derived from microorganisms are the source of antioxidants for used in the agricultural, industrial and medical sectors (Sailaja and Sasikal, 2022). *C. ternatea* contains a variety of phytochemicals including anthocyanins, polyphenols, flavonoids and phenolic acids. The plants intrinsic antioxidant properties which help in combat reactive oxygen species (ROS) are attributed to these phytochemical compounds. Several degenerative and chronic diseases such as neurological disorders, cardiovascular disease, autoimmune disorders and cancer are significantly influenced by oxidative stress. Natural sources of antioxidants provide significant health benefits and numerous studies have explored their antioxidant activity through a variety of assays (Jayanthi *et al.*, 2021). Flowers are extracted and utilized as cosmetics in Thailand. The flower chemical composition suggests that it may have potential antioxidant effect. The antioxidant level of aqueous leaf extracts was assessed by measuring the levels of both enzymatic and non-enzymatic antioxidants. Research has indicated that the aqueous extracts of this plant exhibit greater antioxidant activity compared to its ethanolic extracts (Kamkaen and Wilkinson, 2009). Various procedure such as the ferric reducing antioxidant power (FRAP) assay, the 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay, the reducing activity test and the hydroxyl radical scavenging activity extracts of antioxidant assays were used to evaluate the *in vitro* antioxidant ability. The findings have demonstrated that the antioxidant levels in the extracts are comparable to those of well-known antioxidants like rutin, ascorbic acid and butylated

hydroxytoluene (BHT) (Bhaskar *et al.*, 2009). The roots of the blue and white flowered varieties of *C. ternatea* were extracted and their antioxidant potential was examined using chloroform, methanol and petroleum ether extracts. The DPPH free radicals were substantially inhibited by these extracts at concentrations between 50 and 600 $\mu\text{g/ml}$. The roots of the blue flowered variety showed the strongest inhibition with chloroform, methanol extracts and petroleum ether demonstrating 35.42%, 70.67% and 49.11% inhibition at 600 $\mu\text{g/ml}$, respectively (Patil and Patil, 2011b). An analysis of the antioxidant activity of blue and white flowers and leaves of *C. ternatea* indicate the significant antioxidant activity. When it came to scavenging activities the blue flower variety outperformed the white flower variety. Moreover, the antioxidant activity and protective properties of the flower petal extracts were also identified (Sivaprabha *et al.*, 2008). *In vitro* antioxidant tests of the methanolic leaf extract were conducted to assess its hepatoprotective properties against paracetamol-induced liver damage in mice. The hepatoprotective properties were evaluated by monitoring the amounts of alanine aminotransferase (ALT), bilirubin and aspartate aminotransferase (AST) in addition to conducting histopathological analysis. Mice treated with the methanolic leaf extract at a dose of 200 mg/kg showed a significant reduction in ALT, bilirubin, and AST levels compared to those given paracetamol. Furthermore, treatment with *C. ternatea* leaf extract provided protective effects against histopathological changes (Al-Snafi, 2016).

3.2 Anti-inflammatory activity

Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly to treat anti-inflammatory conditions, but often come with various

adverse side effects. As a result, researchers are increasingly turning their attention to plant based therapies for treating inflammatory diseases. This approach aims not only to provide effective pain management but also to reduce the risks associated with NSAIDs (Ashraf *et al.*, 2024). Two experimental methods, carrageenan-induced and histamine-induced paw edema were used to evaluate the anti-inflammatory properties of an ethanolic extract of root. According to the study, the extract of 200 and 400 mg/kg doses reduced the synthesis, release or effect of histamine by (41.66% and 54.16%) at 90 min and (69.76% and 81.39%) at 180 min in a histamine-induced paw edema model. This result can be attributed to the ethanolic extract of root, ability to effectively reduce edema there by inhibiting the production, release or activity of histamine that cause the inflammation. An experiment found that, a methanolic flower extract were effectively reduced ROS levels, cyclooxygenase-2 (COX-2) activity, inducible nitric oxide synthase (iNOS) protein expression, nuclear NF- κ B translocation and nitric oxide (NO) production (Swathi *et al.*, 2021). *C. ternatea* exhibited a strong antipyretic effect in the methanolic extract of root was orally administered and evaluated in rats. Based on the study, the extract reduced carrageenan-induced swelling in rat paws and decreased acetic acid-induced vascular permeability. The extract 200 and 400 mg/kg doses significantly reduced carrageenan-induced edema by 21.6% and 31.8%. It showed the effective antipyretic, analgesic and anti-inflammatory properties (Devi *et al.*, 2003). Several antinociception models were used to examine possible mechanism generating the action of methanolic extracts of leaves and roots. The antinociceptive effects of both leaf and root extracts were assessed using naloxone, a non-selective opioid antagonist along with various antinociception paradigms including the tail-flick, hot plate and formalin tests. The formalin test findings suggest that antinociceptive effect of extracts may be mediated at both the peripheral and central levels. The antinociceptive level of root extract observed both at the spinal levels and supraspinal, whereas the leaf extracts antinociceptive activity is seen only at the supraspinal level from the tail-flick and hot plate tests. The scientists conclude that antinociceptive properties of root extract likely mediate through opioid receptors (Kamilla *et al.*, 2014). According to Chauhan *et al.* (2012) research on the extract of petroleum ether, 60-80°C from *C. ternatea* flower demonstrated significant anti-inflammatory effects of 200 and 400 mg/kg dose of body weight with a significance level of ($p < 0.01$) and this extract exhibited analgesic properties. *C. ternatea* could be valuable in developing drugs or nutraceuticals aimed at preventing long term inflammatory conditions.

3.3 Anthelmintic activity

Anthelmintics are consists of medications properties designed to effectively remove worms from the gastrointestinal tract and eliminate adult worms, that can cause systemic damage to organs and tissues (Ashraf *et al.*, 2024). When exposed to an ethanolic extract of 100 mg/ml dose of Indian earthworm *Pheritima posthuma* becomes paralyzed within 15-20 min and dies within 28-30 min (Nirmal *et al.*, 2013). However, *P. posthuma* were also utilized to evaluate the anthelmintic activity in extracts of ethanolic from the flowers, stems, roots and leaves. The findings indicate that the root extract caused the earthworms to become paralyzed and die more quickly when compared extracts from the other plant parts. Subsequently, the anthelmintic activity of the roots was assessed following extraction with petroleum ether, methanol, ethyl acetate and chloroform, when compared to the other standard extracts the methanol extract of the

root was the most effective (Shekhawat and Vijayvergia, 2011). An aqueous and ethanolic extract of leaves, 100 mg/ml dose showed anthelmintic action. Ethanolic and aqueous extracts of *Eisenia foetida* at three different dosage of 100, 50 and 25 mg/ml were used in this experiment. To achieve this, the study measured both the total time for the worms to die (D) and the time required for them to become paralyzed (P). The paralysis and death times for the aqueous extract were recorded as 18 ± 1.57 min and 53.33 ± 0.33 min, while the ethanolic extract showed paralysis and death times of 12.33 ± 0.80 min and 32.33 ± 0.71 min (Salhan *et al.*, 2011). In another experimental study, *C. ternatea* leaves of methanolic extract showed anthelmintic efficacy at concentrations of 10 mg/ml and 25 mg/ml whereas the ethanolic extract did not exhibit any activity at the same dose (Sarojini *et al.*, 2012). The methanolic extract of root found to be the most efficacious among the extracts requiring the minimum amount of time to kill and paralyze the worms (Chauhan *et al.*, 2012).

3.4 Antimicrobial activity

The majority of studies have indicated that methanol and ethanol extracts are the most effective solvents for the antimicrobial bioactive components from *C. ternatea* flowers. According to Mahmud *et al.* (2018), ethanolic extract was potential in inhibiting the growth of various fungi and bacteria, whereas the extract of aqueous exhibited no antibacterial activity. The rich in anthocyanin from the blue flowers of ethanolic extracts exhibited the strongest antibacterial effect against *Bacillus subtilis* both *in vitro* and *in vivo*, with inhibition zones of 11 mm and 10 mm. The extract of ethanolic callus demonstrated significant antifungal effect *in vitro* with inhibition zones of 10 mm against *Fusarium* species and 12 mm against *Trichoderma* species. The pathogen *Proteus mirabilis* which is known to cause urinary tract infections was used to test the antibacterial efficacy of crude extracts. Their results also revealed that acetone extracts exhibited the strongest antibacterial effect against *P. mirabilis*, while antibacterial properties showed the minimum of both isopropyl alcohol and petroleum ether extract (Dhanasekaran *et al.*, 2019). Maximum zone of inhibition (ZOI) against *A. hydrophilia* (19 mm), *A. formicans* (18 mm), *P. aeruginosa* (21 mm) and *B. subtilis* (19 mm) was seen in *C. ternatea* extracts of ethyl acetate. The highest ZOI against *E. coli* (14 mm) and *A. formicans* (18 mm) was subsequently shown an ethanolic extract, whereas the highest ZOI against *K. pneumonia* (17 mm) and *S. agalactiae* (19 mm) was shown by an acetone extract (Ponnusamy *et al.*, 2010). The antibacterial properties of aqueous and alcoholic extracts from callus generated *in vitro* was assessed by using the technique of agar well diffusion. These extracts were tested against gram-negative bacteria specifically *Shigella dysenteriae* and *Salmonella* species which are known to cause intestinal fever. Both the extracts aqueous and alcoholic exhibit the antibacterial properties against these pathogens (Shahid *et al.*, 2009). The antibacterial activities of *C. ternatea* were studied using both agar disc and agar well diffusion techniques. The results have shown promising antibacterial action against the tested investigated microbiological pathogens. It was found that the methanolic extract exhibited a stronger inhibitory level compared to the other extracts (Anand *et al.*, 2011).

3.5 Nephroprotective activity

According to study, shown that administering an ethanol extract of *C. ternatea* possesses nephroprotective potential against acetaminophen nephrotoxicity (APAP) induced. Experimental

findings indicated that it increases the levels of myocardial antioxidant enzymes, preserves histoarchitecture and enhances heart function following APAP treatment. This was noted in the evaluation of its antioxidant activity, nephroprotective properties and phytoconstituents (Sarumathy *et al.*, 2011).

3.6 Anticancer activity

Chemotherapy is a cancer treatment method employed for various types of cancer. However, these drugs come with a wide range of toxicities and side effects and do not provide a definitive cure. Therefore, there is a high demand for new, safe and effective agents. Typically, there are four primary mechanisms through which an active substance can exhibit cancer antiproliferative properties (preventing or slowing the proliferation of cancer cells), inhibition of angiogenesis (process of preventing the formation of new blood vessels), initiation of apoptosis (programmed cell death) and preventing metastasis (spreading of cancer cells from the primary tumour to other areas of the body) (Ashraf *et al.*, 2024). Based on the latest studies, the most popular herbal medicines reduce tumour angiogenesis, interfere with cell cycle progression and enhance immunity. Extracts from *C. ternatea* exhibit anticarcinogenic or tumour suppressive properties that align with other research findings (Ramaswamy *et al.*, 2011). By using the trypan blue dye exclusion technique, the cytotoxic effects of ethanolic and petroleum ether in flower extract were evaluated *in vitro*. The plant extracts were used at concentrations of 10, 50, 100, 200 and 500 µg/ml in addition of control. The cytotoxic activity increased in a dependent upon dose manner at each concentration tested. The extract of petroleum ether resulted in an reduce 8% in cell viability at 10 µg/ml dose, while a concentration of 500 µg/ml led to a complete 100% reduction. The cell count showed a 1.33% decreased at 10 µg/ml and an (80%) decreased at 500 µg/ml (Kumar and Bhat, 2011). The antiproliferative effect of lipophilic and hydrophilic extracts from flowers were examined on laryngeal cancer cell lines. The hydrophilic fraction was more effective than the lipophilic fraction in inhibiting cancer cell proliferation. The formation of new blood vessels or angiogenesis is an important phase in the progression of a tumour from an inactive to a malignant state and also one key molecule in the angiogenesis process is vascular endothelial growth factor (VEGF) (Shen *et al.*, 2016). The Ehrlich ascites carcinoma (EAC) cell line has shown inhibition of angiogenesis by the methanol extract of blue flowers through the regulation of VEGF secretion. The methanolic extract of *C. ternatea* when tested on MCF-7 breast cancer cell line exhibited anticancer activity primarily by inducing the apoptosis (Shivaprakash *et al.*, 2015). The regulation of the cell cycle during the pre-G0, G1 and S phases has been shown by the ethanolic extract of flowers and this is linked to the activation of apoptosis (ALShamrani *et al.*, 2022). An *in vivo* mouse model was used to study the effects of blue flower petals an aqueous extract. It was found that the extract primarily composed of flavonoids identified by LC-MS reduced inflammatory mediators and improved oxidative stress (Wang *et al.*, 2022). According to another study, luteolin and other flavonoids may regulate the release of hypoxia-inducible factor 1 (HIF-1) and VEGF release (Samec *et al.*, 2021).

3.7 Anticonvulsant activity

An imbalance between inhibitory and excitatory neurotransmitters in the brain can lead to seizures. This disruption in the normal regulation of neural activity causes excessive neuronal firing which

can result in the onset of seizure occurrences. Drugs that increase GABA levels in the brain could exhibit anticonvulsant effect in experimental seizure models. The maximum electroshock (MES) model is a well-established procedure for evaluating antiepileptic treatments particularly for their potential to prevent generalized tonic-clonic seizures (Jiji and Muralidharan, 2020). Using the pentylenetetrazol (PTZ) test and the maximal electroshock seizure (MES) test, the aerial parts of an ethanolic extract from *C. ternatea* was resulted to exhibit anticonvulsant effects in rats. There were no discernible anticonvulsant effects of the ethanolic extract in either dosage group of 230 and 460 mg/kg (Verma *et al.*, 2024). When administered directly 100 mg/kg dose methanolic extract from aerial parts demonstrated anticonvulsant effects in mice used in seizure models induced by PTZ and MES. In the PTZ test the extract delayed the onset of convulsions while in the maximal electroshock seizure test it reduced the duration of tonic hind limb extension. These findings suggest that *C. ternatea* has potential as an antiepileptic medication (Jain *et al.*, 2003).

3.8 Anxiolytic activity

The aerial parts of alcoholic extract from *C. ternatea* on spatial discrimination in rats, oral administration of the extract at a concentration 460 mg/kg significantly time increased it took rats to complete the maze. This effect was comparable to that produced by chlorpromazine (Chauhan *et al.*, 2012). Oral administration of *C. ternatea* doses ranging from 100 to 400 mg/kg resulted in a dependent upon dose increase the time taken in open arm and lit box, while decreasing the time spent in the dark box. Oral administration of *C. ternatea* dose of 30 mg/kg did not show any significant effects in the animal models of anxiety. The nootropic effects were evidenced by significant improvements in the discrimination index and inflexion ratio in animals treated with a dose of 100 mg/kg (Gupta *et al.*, 2010).

3.9 Antidiabetic activity

Herbal based drugs are regarded as valuable for managing diabetes because they are perceived to be safer and have a lower risk of adverse effects. Biguanides, meglitinides, thiazolidinediones, sulfonylureas and dipeptidyl peptidase inhibitors which are commonly used as oral antidiabetic drugs have been associated with various side effects. Many studies have focus on evaluating the antidiabetic potential of *C. ternatea* extracts. Rats with streptozotocin-induced diabetes were used to investigate the hypoglycemic effects of leaf extract both subacute and acute of methanolic, petroleum ether, aqueous and chloroform. The hypoglycemic properties of the extract could be due to alkaloids and flavonoid compounds such as glycosides, flavanol and anthocyanins. *C. ternatea* extract at doses of 200 and 400 mg/kg led to a significant reduction in blood glucose levels in rats with streptozotocin-induced diabetes. The dose level of 200 mg/kg also reduced glucose levels though not as effectively as the 400 mg/kg dose, while the 400 mg/kg dose had a significant hypoglycemic impact. Subacute studies indicated that a 200 mg/kg dose of the extract administered over an extended period was more effective than a 100 mg/kg dose for managing blood glucose levels (Al-Snafi, 2016). Significant increases in serum insulin, protein levels, HDL cholesterol, the activity of the glycolytic enzyme glucokinase and liver and skeletal muscle glycogen content were observed with 400 mg/kg body weight of both aqueous extract of leaves and flowers (Gupta *et al.*, 2010). A study indicated

that short-term consumption of flower extract or beverage when combined with sugar, people with good health it lowered plasma glucose and postprandial insulin levels (Jeyaraj *et al.*, 2022; Chusak *et al.*, 2018). Another study showed that floral extract effectively suppresses the production of advanced glycation end products (AGEs) at doses ranging from 0.25 to 1.00 mg/ml. The extract reduces protein oxidation and fructosamine levels. This is achieved by preventing the depletion of free thiols and lowering the protein carbonyl content (Chayaratanasin *et al.*, 2015). The flower extract used as a substrate derived from starches such as corn, rice, potato, wheat, cassava and glutinous rice flour substantially decreased the activity of the pancreatic amylase enzyme at a dose of 1% and 2% w/v. An ethanolic extract was found to dramatically reduce the blood stream levels in artificially induced diabetic subjects by inhibiting the activities of the galactosidase and glucosidase enzymes (Dhanasekaran *et al.*, 2019). The flower with chloroform extract exhibited more effective hypoglycemic properties compared to methanol ethyl and acetate extracts. This superior activity was attributed to non-polar bioactive components in the chloroform extract which contributed to the hypoglycemic effect by enhancing insulin secretion (Rajamanickam *et al.*, 2015).

3.10 Hepatoprotective activity

Paracetamol also known as N-acetyl-p-aminophenol or acetaminophen is widely used antipyretics and analgesics. Due to its non-steroidal anti-inflammatory properties and greater safety profile compared to aspirin paracetamol is used by millions of people globally as an over-the-counter medication to reduce the risk of gastrointestinal bleeding (Naveen *et al.*, 2023). Research on paracetamol-induced liver toxicity revealed that mice treated with 200 mg/kg of the methanolic extract of leaves had notably lower levels of AST, bilirubin and ALT compared to the group receiving paracetamol-only group which exhibited significantly higher levels of these substances. Treatment with leaf extract also demonstrated protective effects against histopathological changes in the liver (Nithianantham *et al.*, 2011). The hepatoprotective activity of white and blue flowered leaf extracts were evaluated in rats with carbon tetrachloride-induced hepatotoxicity. The results indicated that the white flowered leaf extract exhibited a more potent hepatoprotective effect than the blue flowered variant. White flowered leaf extract had a more potent hepatoprotective effect than the blue flowered variety (Jayachitra *et al.*, 2012).

3.11 Antidepressant activity

The primary goal of most antidepressant treatments is to normalize neurotransmission by increasing the levels of neurotransmitters in neurons. Antidepressant properties work by raising the levels of these neurotransmitters in the central nervous system (CNS) (Naveen and Neelam, 2023). The antidepressant effect of aerial parts of methanolic extract was evaluated using the tail suspension test. The concentration of 100 and 400 mg/kg of extract demonstrated particularly with antidepressant activity. When extract was given directly, the length of immobility in the tail suspension test was dramatically reduced. Extract improved cognitive abilities reduced total immobility period and did not cause drowsiness or behavioural

toxicity (Jain *et al.*, 2003). The sedative effects of an alcoholic extract from the aerial parts were assessed in rats using conditioned avoidance response test. The conditioned avoidance response in rats was unaffected by the directly administration of the alcoholic extract at a concentration of 230 mg/kg. On the other hand, very high amount of dose 460 mg/kg suppressed in 66% conditioned avoidance response of rats without affecting their unconditioned response. It is still unclear if such high doses have any pharmacological significance. In comparison, the conventional medication chlorpromazine led to an 83% reduction in the conditioned avoidance response while leaving unconditioned avoidance response (Kulkarni *et al.*, 1988). The antidepressant properties of root ethanolic extract were documented in a different study at doses of 150 and 300 mg/kg. The study found that the extracts of 150 and 300 mg/kg, significantly reduced the immobility time of rats in a dose-dependent manner in both the tail Suspension and forced Swim tests. The ethanolic root extract exhibits significant antidepressant activity when compared to the standard imipramine and a mild sedative effect at 300 mg/kg. Thus, it could be a promising natural psychotherapeutic agent for treating depression and mood disorders (Parvathi and Ravishankar, 2013). Some research findings suggest that two compounds are namely n-hexadecanoic acid and (Z)-9,17-octadecadienal extracted from the root may have potential as lead molecules for the development of novel selective MAO-A inhibitors. These inhibitors could be utilized as an herbal remedy to treat mental health issues like depression and anxiety (Margret *et al.*, 2013).

3.12 Larvicidal activity

C. ternatea demonstrated the significant mosquito larvicidal activity. *Anopheles stephensi*, *Culex quinquefasciatus* and *Aedes aegypti* are the three main mosquito vectors used to test the mosquito larvicidal properties of *C. ternatea*. The methanol extract of seeds demonstrated efficacy against the larvae of *A. stephensi*, *C. quinquefasciatus* and *A. aegypti* with LC₅₀ values of 65.2 ppm, 54.4 ppm and 154.5 ppm, respectively. Among the three plant species tested, *C. ternatea* exhibited the most encouraging larvicidal effectiveness against mosquitoes (Mathew *et al.*, 2009).

3.13 Proteolytic activity

Extracts from the cotyledons of both resting and germinating seeds were used to measure the activities of various enzymes, including endopeptidases with haemoglobin at pH 3.5 and azocasein at pH 6.0, arylamidases with lysophosphatidic acid at pH 7.0 and α -N-benzoyl-L-arginine p-nitroanilide at pH 7.6 and carboxypeptidase using benzyloxy carbonyl Phe-Ala at pH 5.2. Notably, endopeptidase activity at pH 3.5 and arylamidase activity at pH 7.0 were particularly maximum in the cotyledons. The activity of arylamidase and carboxypeptidase activities in the cotyledons increased and peaked on day 9 (Chauhan *et al.*, 2012). While arylamidase activity remained minimum, carboxypeptidase and endopeptidase activities in the axial tissue increased until day 9 before declining. The increased activity of acidic carboxypeptidases and endopeptidases in germinating cotyledons suggests that these enzymes play an important role in the degradation of storage proteins (Verma *et al.*, 2024).

Table 3: Some important pharmacological activities of *C. ternatea*

Pharmacological activities	Plant parts	Extraction solvents	Results	Reference
Anti-inflammatory	Flowers	Ethanol	At a dose of 400 mg/kg, <i>C. ternatea</i> inhibited inflammation by 84% compared to 75% inhibition achieved by the medication diclofenac sodium.	Subrahmanyam <i>et al.</i> , 2018
	Flowers	Ethanol	The ethanolic extract of the flower demonstrated the maximum inhibition percentage of anti-inflammatory activity, showing (80 ± 5.60%) compared to aspirin which showed (73.3±5.13%).	Suganya <i>et al.</i> , 2014
	Leaves	Ethanol	The ethanolic extract from leaves showed the maximum percentage of inhibition in anti-inflammatory activity with (89.3 ± 6.25%) when compared to aspirin (73.3 ± 5.13%).	Suganya <i>et al.</i> , 2014
Antimicrobial	Leaves	Ethanol	Maximum zone of inhibition against <i>A. formicans</i> (18 mm) and <i>E. coli</i> (14 mm).	Ponnusamy <i>et al.</i> , 2010
	Leaves	Acetone	Maximum inhibition zone was observed with <i>Klebsiella pneumoniae</i> (17 mm) and <i>Streptococcus agalactiae</i> (19 mm).	Ponnusamy <i>et al.</i> , 2010
	Leaves	Methanol	ZOI against <i>Staphylococcus aureus</i> (8 mm), <i>E. coli</i> (6.5 mm), <i>Salmonella typhi</i> (9 mm), <i>B. subtilis</i> (7.5 mm), <i>Enterobacter aerogenes</i> (5.8 mm), <i>S. agalactiae</i> (7 mm).	Das <i>et al.</i> , 2020
Anthelmintic	Roots	Aqueous	The substance exhibited significant toxicity on the larvae of <i>Caenorhabditis elegans</i> .	Gilding <i>et al.</i> , 2016
Anticancer	Flower	Ethanol	The inhibition of MCF-7 HER2-positive breast cancer cells, as identified by the MTT assay was demonstrated with IC ₅₀ value 862 ig/ml.	Asyisyifa <i>et al.</i> , 2020
	Leaves	Methanol	The maximum cytotoxicity of 79.93% against human promyelocytic leukaemia cells (HL60) was observed in the MTT assay experiment at a dose of 250 µg/ml.	Das <i>et al.</i> , 2020
	Stems	Methanol	The compound clitorternalactone exhibited cytotoxic effects on the DLD-1, IMR-32 cell lines and CCRF-CEM with IC ₅₀ values of 2.54 ± 0.23 µM, 4.05 ± 0.43 iM and 3.68 ± 0.17 µM.	Wu <i>et al.</i> , 2020
Antidiabetic	Flowers	Ethanol	The flower extract of CT at 400 mg/kg dose, Wistar albino rats produced glucose level of 103.64 ± 3.14 mg/dl when compared to 102.34 ± 8.34 with glimepiride.	Subrahmanyam <i>et al.</i> , 2018
	Leaves	Ethanol	Insulin levels increased in streptozotocin-induced diabetic rats whereas blood glucose, creatinine and glycosylated haemoglobin levels are low.	Kavitha, 2015

4. Therapeutic and traditional uses

Traditional medicine system utilizes methods and practices based on the knowledge, experience, beliefs to treat a wide range of health conditions. The medicinal properties of plants are frequently linked to the presence of secondary metabolites or bioactive compounds like alkaloids, steroids, tannins, glycosides, phenols, volatile oils and flavonoids. These naturally occurring substances are stored in the plants and produce specific physiological effects on the human body when consumed (Sandip *et al.*, 2021). *C. ternatea* is renowned for its therapeutic properties and traditionally used across various cultures to treat a wide range of illnesses for many years. The roots, flowers and leaves of the plant are utilized for different therapeutic purposes as outlined in Table 4 such as infections, urogenital issues and physical discomfort. It acts as a tonic for the mind notably

enhancing mental abilities, physical strength and overall mental well-being especially in children. Rheumatism and ear problems are traditionally treated with the powdered or decocted roots. Additionally, laxatives made from powdered seeds of *C. ternatea* combined with ginger are effective though they may occasionally cause discomfort in the lower abdomen. The seeds are used to treat colic, joint edema, dropsy and the enlargement of abdominal organs (Mukherjee *et al.*, 2008). The key ingredient in “Medhya Rasayana” a traditional Ayurvedic formulation known for enhancing mental clarity and cognitive function, it has been utilized in the treatment of various neurological conditions. It is regarded by various groups as a medicinal plant effective in treating eye and throat infections, ulcers, skin diseases and urinary disorders. It is also known for its antidote properties making it useful in counteracting certain toxins (Atul *et al.*, 2017).

Table 4: Plant parts of *C. ternatea* and its functions

Plant parts	Functions
Flower	Natural food colouring used in value added products.
Root	A demulcent is given when the kidneys and urinary tract are irritated and protect the affected tissues anxiolytic, nootropic, anticonvulsant, antidepressant and antistress activity.
Whole plant	It is used to treat gonorrhoea.
Leaf	Preventing against neurodegeneration conditions and diabetes mellitus.
Seeds	They are utilized to enlarged abdominal viscera, swollen joints and dropsy.

5. Commercial products of *C. ternatea*

C. ternatea include a range of value added products derived from its flowers, leaves and roots. The dried flowers can also be ground into a fine powder used as a natural food colouring or as an ingredient in smoothies and desserts. This powder is also incorporated into cosmetic products such as face masks and hair treatments due to its potential skin and hair benefits. The flowers extracts are used in ointments and creams for their anti-inflammatory and soothing properties making them valuable in skincare formulations. *C. ternatea* tea is an indigo-colored herbal tea made from vibrant blue flowers and it's served as "Blue Tea" on Indigo and other airlines. It is widely recognized for its antioxidant properties and calming effects and health benefits. These products highlight the versatility of the plant extending its use beyond traditional applications. These commercial products contribute to the sustainability and economic viability of cultivation by minimizing waste and creating additional value streams. Some of the experimental commercial products are listed in Figure 4.

5.1 Ointment

The methanol extract of seeds and roots were extracted through reverse phase high performance liquid chromatography (RP-HPLC) was used to screening the hyaluronidase, elastase and matrix metalloproteinase-1 (MMP-1) compared to the regular oleanolic acid. This methanol extract was applied extracts topically as an ointment and orally as a gavage greatly enhanced wound healing in excision, incision and dead-space models. These outcomes were similar to the antibiotic cotrimoxazole. These findings showed that *C. ternatea* influenced the wound healing process in all three phases proliferative, inflammatory and remodelling (Solanki and Jain, 2012).

5.2 Food colourant

The aqueous and ethanol extract of flowers were employed for acute toxicity employing in Wistar albino rats which shows no abnormalities or symptoms of death and there was no discernible change in their haematological parameters (Srichaikul, 2018). The petals of *C. ternatea* could be used as a functional ingredient and incorporated into variety of food products like cakes, biscuits, breads, jelly and ice creams which enhances the food colour and also acts as antidiabetics, anti-inflammation and rich in natural phytonutrients (Jeyaraj *et al.*, 2021).

5.3 Food packaging material

Probe ultrasonication extraction proved highly effective achieving a 246.48% increase in anthocyanin yield from *C. ternatea* for food applications. Compared to other natural sources *C. ternatea* offers a significant advantage in food packaging due to their distinctive coloured spectrum across various pH levels. Numerous findings

have indicated that immobilizing *C. ternatea* within different polymeric film matrices may alter their physicochemical properties, yet they remain capable of effectively monitoring the quality of perishable food in real time. Developing intelligent films using anthocyanins represents a promising strategy for the future of food packaging systems (Hasanah *et al.*, 2023).

5.4 Fermented plant milk beverage

The chemical and physical properties of fermented beverages made from almond, soy, and a blend of almond-soy, infused with 10% *C. ternatea* flower extracts, were evaluated. These beverages demonstrated notable antioxidant activity, along with significant protein content, particularly in the fermented almond milk variants (Shirodkar *et al.*, 2023).

5.5 Beverage tea

The optimal ratio for a *C. ternatea* beverage with stevia as a natural sweetener and lime as a flavour was determined using response surface methodology and the Box-Behnken design. The antioxidant activity was evaluated using oxygen radical absorbance capacity (ORAC), DPPH and 2,22 -azino-bis-3-ethylbenzothiazoline-6-sulfonic acid (ABTS) assays, while the glycemic regulatory properties including antilucosidase and anti-amylase activities were also examined. The ideal extraction conditions of *C. ternatea* 3 g/l powder of water extracted for 37 min at 59.6°C yielding high antioxidant activity. The beverage exhibited a 28 days shelf life without the use of preservatives (Lakshan *et al.*, 2019).

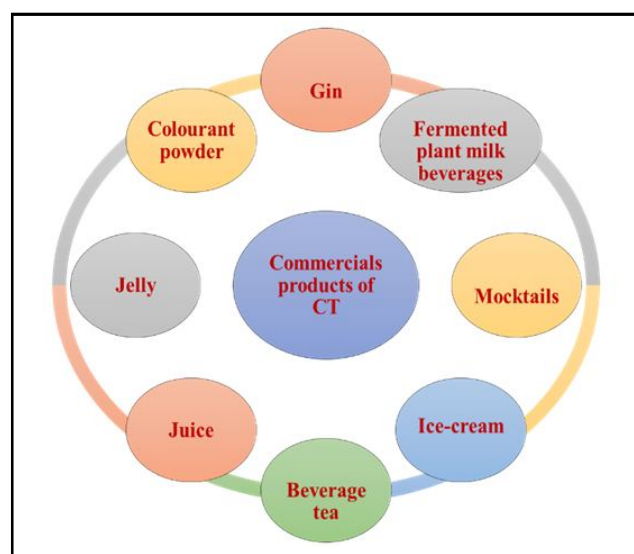


Figure 4: Commercial products.

6. Future thrust

The future potential of *C. ternatea* a traditional crop, lies in its abundant phytochemicals and wide ranging pharmacological properties. The pharmacological activities including anti-inflammatory, neuroprotective and antimicrobial activity, etc., make it a valuable resource for future pharmaceutical research. *C. ternatea* offers great potential for enhancing its role as both an antibacterial and anticancer agent. Its leads to novel solutions for tackling antibiotic resistance and advancing cancer therapies. Antidepressant activity through its bioactive compounds which may help modulate the mind and alleviate symptoms of depression. Moreover, antidiabetic agent as its bioactive compounds may help regulate blood glucose levels and enhance insulin sensitivity. As interest in natural and plant based medicines continues to grow it is poised to play a crucial role in advancing healthcare and providing new treatments for various diseases. The utilizing of *C. ternatea* for eco-friendly natural dyes and inks lies in expanding its applications across industries such as textiles, cosmetics, and printing. Research could focus on optimizing extraction methods to maximize yield and colour intensity while ensuring stability and longevity of the pigments. Additionally, exploring ways to scale up production in an economically viable manner can further enhance its commercial potential. Developing eco-friendly alternatives to synthetic dyes is crucial in reducing environmental pollution and it holds great promise in contributing to sustainable and green innovations.

7. Conclusion

C. ternatea is not just a wild herb but also a therapeutic plant with numerous medical applications beyond its traditional uses. It has so many traditional purposes as well as several medical applications. The pharmaceutical industry is heavily focused on designing and developing new drugs derived from plants by exploring ideas from conventional medical systems. For many years, *C. ternatea* used to traditionally as a memory booster and anxiety reliever. Extracts from its seeds, leaves, flowers and roots have been employed in traditional medicine for these purposes. Various metabolites from this plant including anthocyanins, flavonoids, quercetin and tannins have been identified. The development and commercialization of natural products often face challenges related to limited availability of source materials. However, *C. ternatea* does not suffer from this issue. This plants abundant supply of cyclotides present a significant advantage. This approach has proven successful with cyclotides from other plants and could similarly enhance the therapeutic applications of *C. ternatea*. While only a few of these cyclotides have been explored for their medicinal potential, there is substantial opportunity for further research. It is therefore strongly recommended that future studies focus on the therapeutic investigation, as it shows potential to be a valuable medicinal plant with a broad spectrum of pharmacological effects.

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Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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