



ANTIDIABETIC, ANTIOXIDANT, ANTICANCER AND ANTIMICROBIAL PROPERTIES OF BUTTERFLY PEA FLOWER (*CLITORIA TERNATEA*)": A PROMISING PLANT-BASED THERAPEUTIC APPROACH

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ABSTRACT

There is an insistent need for safer and more sustainable plant-based treatments because of the rising incidence of diabetes and the growing threat of antibiotic resistance. A traditional medicinal plant, *Clitoria ternatea* (butterfly pea) has drawn more scientific attention because of its abundance of bioactive substances, especially flavonoids and anthocyanins. Its dual medicinal potential as an antimicrobial and antidiabetic agent is supported by these phytochemicals.

The primary mechanism by which *C. ternatea* reduces postprandial hyperglycemia and improves glycemic control in type 2 diabetes is by inhibiting enzymes that hydrolyze carbohydrates, such as α -glucosidase and α -amylase. Furthermore, its strong anti-inflammatory and antioxidant properties provide additional defense against complications linked to diabetes.

In addition to its ability to regulate metabolism, *C. ternatea* has broad-spectrum antimicrobial activity against both Gram-positive and Gram-negative bacteria and fungi, and it shows promising impact in combating drug-resistant pathogens. Multiple mechanisms, such as membrane disruption and inhibition of microbial metabolic pathways, mediate these antimicrobial effects. Together, the available data suggests that *C. ternatea* is a multipurpose botanical medication candidate that may be able to address two urgent global health issues: diabetes and antibiotic resistance. Transforming this age-old cure into contemporary therapeutic uses will require future studies that concentrate on the isolation of bioactive compounds, their mechanistic understanding, and its clinical validation.

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INTRODUCTION

Since plants provide food, medicine, and many other daily necessities, humans and plants always had a close and vital relationship (Khadka *et al.*, 2021). According to Fabricant & Farnsworth (2001), they have long been a vital source for the discovery and creation of contemporary medications. Approximately 70–80% of people in developing nations still use herbal remedies as their main source of medical care.

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Natural products are safer and linked to fewer side effects than synthetic drugs. Due to its perceived safety, affordability, and efficacy, natural medicine is gaining popularity as the world's population continues to grow and the prevalence of health problems associated with environmental pollution continues to rise.

Traditionally, medicinal plants and traditional medicine have been used extensively as natural remedies for illnesses instead of chemical medications. The abundance of bioactive secondary metabolites is largely responsible for their therapeutic value (Mansi & Latha, 2020). In ancient medical systems, this form of medicine was valued for its reliance on non-toxicity. The foundation of many herbal remedies, medicinal plants have been essential to healthcare, especially in India (Pandey *et al.*,

2013). Therefore, plant extracts are valued in the treatment of a variety of diseases due to their broad range of therapeutic qualities, which include anti-inflammatory, antidiabetic, and antimicrobial effects. The increasing health concerns need more attention and advancement in phytomedicine research. In the same steamline, many studies have reported that butterfly pea flower (*Clitoria ternatea*) has a wide range of pharmacological properties, including antidiabetic, antioxidant, antidiabetic, anti-inflammatory, antibacterial, and anticancer activities (Tahereh & Saeed, 2014; Jamil *et al.*, 2018; Jeyaraj *et al.*, 2021; Widowati *et al.*, 2023). This review highlights some of these pharmacological properties of *Clitoria ternatea* (*C. ternatea*).

Morphological Features of *Clitoria ternatea* Plant

The butterfly pea flower, or *Clitoria ternatea*, comes in a number of varieties with light blue, deep blue, white, and mauve blossoms (Jeyaraj *et al.*, 2021). It is frequently used as a natural colorant in culinary preparations because of its eye-catching blue and white blooms.

With slender stems that range in length from 0.5 to 3 meters, *C. ternatea* is classified as a twining herbaceous plant. Five to seven elliptic to lanceolate leaflets, each measuring three to five centimeters in length, make up the pinnately compound leaves, which are covered in a thin layer of short pubescence. With five separate petals, the flowers are solitary, borne on short pedicels, and usually measure about 4 cm in length and 3 cm in width. Up to 10 seeds can be found inside the fruit, which is a flat, beaked pod that is 5–10 cm long and 0.6–1.4 cm wide. It is slightly pubescent. Olive to brown in color, the seeds have a distinctive mottled pattern and measure 4–8 mm in length and 3.2–4.5 mm in width (Mehmood *et al.*, 2019; Sarma *et al.*, 2023).

Clitoria ternatea is found in many parts of the world, including the United States, Sri Lanka, Brazil, Cuba, Thailand, Malaysia, Kenya, Australia, and Sudan (Gamage *et al.*, 2021). In a number of Southeast Asian nations, the flowers are traditionally eaten as vegetables (Leong *et al.*, 2017), and their extracts are frequently used as natural ingredients and colorants in beverages and desserts (Pasukamonset *et al.*, 2017).

Apart from its culinary applications, *C. ternatea* is also very important for agriculture and medicine. It is a sustainable choice in integrated farming systems because it is a nitrogen-fixing legume that increases soil fertility, a valuable source of animal feed because of its rich nutritional profile, and an environmentally friendly botanical insecticide. The plant is well-known for its many therapeutic uses and has long been utilized in conventional medicine to promote general health and wellbeing.

Making herbal “blue tea” from the dried flowers of *Clitoria ternatea* is one of its most well-known uses. This beverage has become well-known throughout the world, appreciated for both its purported health-promoting qualities and its vibrant natural coloring. It has long been used to reduce stress, enhance memory and cognitive function, encourage relaxation, and support general health. The nutraceutical and functional food industries have also shown a great deal of interest in *C. ternatea* in recent years, and it is currently being investigated as a natural supplement with adaptogenic, nootropic, and

antioxidant properties.

In addition to being aesthetically pleasing, the plant’s flowers, leaves, and roots have all long been used for their therapeutic properties. According to Jayaweera (1981) and Lakshan *et al.* (2019), *C. ternatea* has been used in traditional medicine to treat a number of conditions, including anasarca, ascites, liver problems, migraine (hemispheric), urethral and bladder irritation, and enlargement of abdominal organs.

Phytocompounds in *Clitoria ternatea*

C. ternatea has a wide range of bioactive compounds that support its broad pharmacological potential, according to phytochemical studies. Anthraquinones, anthocyanins, flavonoids, tannins, phenols, volatile oils, saponins, triterpenoids, phlorotannins, carbohydrates, cardiac glycosides, flavanol glycosides, stagnant-4-ene-3,6-dione, proteins, alkaloids, and steroids are among the components that have been identified (Paymalle & Wadnerwar, 2024). Together, these metabolites add to its therapeutic value; alkaloids, terpenoids, and glycosides are linked to antimicrobial, anti-inflammatory, and cardioprotective qualities, while flavonoids and anthocyanins, especially ternatins, are linked to antioxidant and neuroprotective activities.

The ethnomedicinal uses of *C. ternatea* are further supported by recent pharmacological evidence, which demonstrates the variety of therapeutic properties of the plant’s flowers, leaves, roots, and seeds. In keeping with its historical use as a natural tranquilizer, extracts have sedative and anxiolytic effects, most likely due to modulation of GABAergic neurotransmission. It has been shown to be effective against a range of pathogens, including fungi and both Gram-positive and Gram-negative bacteria, indicating its potential as a natural substitute for traditional antimicrobials (Ramdhini *et al.*, 2024).

The plant also exhibits strong analgesic and anti-inflammatory properties, which are primarily explained by the inhibition of pro-inflammatory mediators like cytokines, prostaglandins, and nitric oxide. These processes underpin its long-standing application in the treatment of dermatological disorders, pain, and swelling. Extracts also exhibit antipyretic properties, which helps to reduce fever and inflammation (Widowati *et al.*, 2024).

The immunomodulatory potential of *C. ternatea* is equally important. According to studies, its phytoconstituents can strengthen host defenses against infections by boosting humoral and cell-mediated immunity (Pertiwi *et al.*, 2022). Additionally, experimental results show neuroprotective and cognitive-enhancing effects, supporting its traditional use in Ayurveda as a brain tonic, or medhyarasayana, to enhance memory and cognitive function (Raghu *et al.*, 2017). All of these observations make *C. ternatea* a phytochemically abundant plant with wide pharmacological significance, making it a viable option for the creation of novel plant-based medicines and nutraceuticals.

Antidiabetic Properties of *C. ternatea*

Chronic hyperglycemia and hyperinsulinemia are hallmarks of diabetes mellitus (DM), a chronic metabolic disease (Singh *et al.*, 2016). Long-term blood glucose elevation increases the risk of cardiovascular diseases and can cause

secondary complications like dyslipidemia, which negatively impacts important organs like the liver and kidneys. Because of its high concentration of phenolic and flavonoid compounds, the butterfly pea flower (*C. ternatea* L.) has become a promising herbal treatment for diabetes. According to Widowati *et al.* (2024), these phytoconstituents have anti-inflammatory, antioxidant, and enzyme-regulating properties that could promote improved lipid metabolism and glucose homeostasis. As a result, *C. ternatea* has a lot of promise as a natural source for creating antidiabetic medications that are safer and more efficient.

The plant *C. ternatea*, commonly referred to as butterfly pea, is rich in anthocyanins, which are bioactive substances that are well known for having potent antioxidant properties. The onset and progression of diabetes mellitus (DM) and its associated complications are significantly influenced by oxidative stress, which these antioxidants are essential in preventing. Anthocyanins, a class of water-soluble flavonoids linked to several health advantages, are especially abundant in *C. ternatea* flowers. The polyacylated anthocyanins, also known as ternatins-polyacylated derivatives of delphinidin 3,3',5'-triglucoside—are the most distinctive of these (Netravati *et al.*, 2022). These substances contribute significantly to the flower's therapeutic properties in addition to giving it its distinctive deep blue hue. Vascular dysfunction, insulin resistance, and other complications associated with diabetes are largely caused by oxidative stress, which is brought on by an excess of intracellular free radical production. These free radicals are neutralized by anthocyanins, which also increase the activity of endogenous antioxidant enzymes like glutathione peroxidase (GPx), catalase (CAT), and superoxide dismutase (SOD) (Prawitasari, 2019). *C. ternatea* may help reduce long-term vascular risks in diabetes and offer protection against oxidative damage through these mechanisms. This possibility is supported by experimental data, as Utamiet *al.* (2024) showed that *C. ternatea* flower extracts had both antioxidant and antidiabetic effects in rats with diabetes induced by alloxan.

Because of its critical role in metabolic processes, the liver is particularly vulnerable to hyperglycemic conditions, which can cause oxidative stress and, in turn, liver damage (Mohamed *et al.*, 2016). Increased levels of liver enzymes like alkaline phosphatase (ALP) and decreased albumin production—a protein that aids in the body's transportation of hormones, vitamins, and enzymes—are indicative of this damage (El-Hadary & Ramadan, 2019). Furthermore, a number of studies have shown that nuclear factor-kappa B (NF- κ B) and tumor necrosis factor- α (TNF- α) are important in causing inflammation linked to liver damage (Park *et al.*, 2014; Zhou *et al.*, 2016).

C. ternatea flower extract's hepatoprotective and antioxidant properties were investigated by Nithianantham *et al.* (2013) using a model of acetaminophen-induced liver toxicity. Their findings showed that the flower extract successfully protects the liver from damage caused by acetaminophen. There was no mortality in mice over a 14-day period, indicating that *C. ternatea* flowers were safe to eat at doses of 500 and 1000 mg/kg body weight. At 2000 mg/kg body weight, however, histopathological analysis showed evidence of liver and kidney damage, suggesting that consumption at this level should be

avoided or severely restricted (Khatib *et al.*, 2023).

The effects of oral administration of butterfly pea flower extract at different doses on renal health in obese Wistar rats were examined by Astuti *et al.* (2024). Reduced serum creatinine levels and the maintenance of normal renal histoarchitecture were two indicators of the study's notable improvements in kidney function. These nephroprotective effects are believed to result from the combined anti-inflammatory and antioxidant properties of flavonoids and anthocyanins, which reduce oxidative stress and inflammatory damage commonly associated with renal dysfunction brought on by obesity.

These studies demonstrate that the *C. ternatea* flowers have beneficial properties for liver and kidney health and can be used for alleviating different complications related to diabetes.

Antioxidant property of *C. ternatea*

Reactive oxygen species (ROS), which are extremely reactive chemicals that harm cellular structures, are primarily produced by mitochondria in diabetics. Superoxide anions and other ROS are produced in excess when hyperglycemia is present because mitochondrial glucose metabolism is elevated, which increases electron leakage from the electron transport chain. When the body's natural antioxidant defenses are unable to neutralize the rate at which ROS are generated, oxidative stress results from a disruption of redox homeostasis.

Through processes like DNA fragmentation, lipid peroxidation of membranes, oxidation of important metabolic enzymes, and the activation of pro-inflammatory cytokines, this imbalance causes damage to cells and tissues (Tsalamandris *et al.*, 2019). Such oxidative stress plays a crucial role in the pathophysiology of diabetes mellitus (DM) by aggravating β -cell dysfunction, promoting insulin resistance, worsening dyslipidemia, and contributing to vascular complications.

Furthermore, through glutathione conjugation, glutathione S-transferase (GST) detoxifies fatty acid hydroperoxides and reactive electrophiles (Jaid *et al.*, 2022). However, these enzymes' functions are frequently impaired in diabetes, which erodes antioxidant defenses. In order to combat oxidative stress in diabetes mellitus and the associated metabolic disorders, exogenous supplementation, especially from plant-based sources, has been studied more and more.

The butterfly pea flower (*C. ternatea* L.) has drawn a lot of interest among plant-based antioxidants because of its diverse phytochemical profile, particularly its anthocyanins. Water-soluble flavonoids called anthocyanins have strong anti-free radical scavenging capabilities and can stabilize oxidized radicals by donating hydrogen. In addition to neutralizing ROS, anthocyanins also enhance vascular integrity, reduce pro-inflammatory signaling, and modify the activity of antioxidant enzymes. Flavonoids, saponins, terpenoids, and tannins are also present in *C. ternatea* extracts in addition to anthocyanins, and these compounds work in concert to produce antioxidant benefits.

Its therapeutic potential is further supported by experimental results. According to Cahyaningsih *et al.* (2019), flower extract from *C. ternatea* considerably reduced the buildup of ROS and lessened inflammatory reactions. Its protective function was linked to decreased fibroblast apoptosis, inhibition of matrix

metalloproteinase (MMP) activity, and prevention of collagen degradation. The anthocyanin-rich extract's versatility was demonstrated by its notable effectiveness when applied topically and when taken orally.

The effectiveness of *C. ternatea* as a natural antioxidant is also demonstrated by quantitative tests. Strong radical scavenging activity was confirmed by the ethanol extract IC₅₀ value of 87.86 ppm (Cahyaningsih *et al.*, 2019) with remarkably low IC₅₀ values of 4.19 ppm and 3.08 ppm, respectively. Rahayu *et al.* (2021) found even higher antioxidant efficacy in butterfly pea flowers sourced from North Lombok and Wonosobo. Environmental variables that can change the phytochemical content, such as soil composition, climate, and cultivation methods, may have an impact on these variations.

In managing oxidative stress, especially in diabetes and dyslipidemia, *C. ternateas* hows great promise as a natural antioxidant. It provides both therapeutic and preventive benefits by reducing the buildup of ROS, restoring the activity of antioxidant enzymes, and maintaining cellular integrity.

Anticancer effect of *C. ternatea*

Anticancer effects are one of the many pharmacological characteristics of these naturally occurring phytochemicals. There is mounting evidence that *C. ternatea*-derived flavonoids and anthocyanins are essential for controlling important cellular signaling pathways implicated in the development and spread of cancer. They have been emphasized as promising options for preventing the growth of a number of cancers, including bladder, lung, and hepatocellular carcinoma (Lv *et al.*, 2022; Arruda *et al.*, 2022).

Newer studies have shed more light on these anticancer effects. For instance, Liu *et al.* (2024) investigated the antibladder cancer potential of *C. ternatea* flower extracts using both in vitro and in vivo models. Their findings demonstrated that anthocyanins and flavonoids extracted from the flowers significantly inhibited the growth of bladder cancer cells. Through the sterol regulatory element-binding protein 1 (SREBP1) pathway, a master regulator of lipid metabolism that is commonly altered in cancer, fatty acid biosynthesis was down-regulated, mediating this effect. *C. ternatea's* potential as a natural anticancer treatment is highlighted by the way it modulates this pathway, which not only limits tumor growth but also impairs the metabolic adaptability of cancer cells.

These results demonstrate *C. ternatea's* therapeutic adaptability, especially its dual function as anticancer agent. Its promise as a source of plant-based therapeutics is further supported by its capacity to control metabolic pathways, protect organ integrity, and improve general physiological resilience. The full realization of this plant's medicinal potential will depend on future research focused on clinical validation, bioavailability enhancement, and the creation of sophisticated delivery systems.

Antimicrobial properties of *C. ternatea*

One major global health concern is the emergence of new pathogenic microorganisms and the quick spread of antibiotic resistance. In addition to reducing the efficacy of treatment, resistance to traditional antibiotics raises mortality rates, prolongs infections, and increases healthcare expenses. The

search for alternative therapeutic approaches has become an immense priority due to the declining effectiveness of current antibiotics. Given their chemical diversity and long history in traditional medicine, medicinal plants have drawn interest as a valuable source of bioactive compounds (Ginovyan *et al.*, 2017).

With their structurally varied secondary metabolites, plants are rich sources of new antimicrobial agents that can be used as therapeutic agents directly or as models for the creation of synthetic drugs. Phytochemicals with broad-spectrum antimicrobial activity include flavonoids, alkaloids, tannins, terpenoids, saponins, and phenolic compounds. They interfere with quorum sensing pathways, disrupt microbial membranes, and prevent the synthesis of proteins and nucleic acids. In contrast to traditional antibiotics, which frequently target a single microbial pathway, compounds derived from plants have multiple modes of action that lessen the chance of resistance developing. The butterfly pea, or *C. ternatea*, has become one of these medicinal plants' most promising candidates in this case. Extracts from its roots, leaves, and flowers have demonstrated inhibitory effects against a variety of pathogenic microorganisms, including some fungi and both Gram-positive and Gram-negative bacteria. Significant activity against antibiotic-resistant strains was reported by Islam *et al.* (2023), indicating the potential of *C. ternatea* extracts as natural substitutes or supplements to traditional antibiotics. These results highlight how crucial *C. ternatea* is in combating the escalating multidrug resistance threat.

The investigation of plants like *C. ternatea* is especially pertinent since antimicrobial agents are still essential for managing infectious diseases in both humans and animals. Their potential as natural antimicrobial sources is further strengthened by their availability, safety, and biocompatibility, while their capacity to act through a variety of mechanisms increases their therapeutic value. Such agents may offer efficient, long-lasting methods of combating resistance, either by themselves or in conjunction with conventional antibiotics.

Its medicinal properties, which help plants resist environmental stress and act as a biological response modifier in humans, make *C. ternatea* valuable. Additionally, research on the ethanolic leaf extract of *C. ternatea* has demonstrated its antifungal properties against *Fusarium oxysporum* (Neela& Padma, 2014).

Additionally, *C. ternatea* is one of several medicinal plants with potent antiviral qualities found in Southern India, according to research on antiviral activity (Vimalanathan *et al.*, 2009). Tests using anti-coronavirus (MCV) extracts through a virucidal protocol have revealed significant antiviral activity in the flower of this tropical Asian plant.

Extracts from *C. ternatea's* leaves, stems, flowers, and roots generally have antimicrobial qualities that make them useful in the treatment of microbial infections. For instance, methanol extracts demonstrated the strongest inhibition against *Shigella dysenteriae* (14 ± 0.9 mm), whereas aqueous and hexane extracts from the entire plant demonstrated notable antimicrobial activity against a variety of pathogens (Darsini & Shamshad, 2015). The zone of chemical diffusion surrounding the disc is measured using the disc diffusion method. As a result, *C. ternatea* has a strong antimicrobial action that varies

based on the extract type.

According to some earlier research, a 70% ethanol extract of butterfly pea flowers effectively inhibits the growth of *Bacillus cereus* at a 30% concentration and *Pseudomonas aeruginosa* at a 10% concentration, as evidenced by the formation of distinct zones of inhibition (Riyanto & Suhartati, 2019). Furthermore, at a 15% concentration, this extract has also shown antifungal activity against *Alternaria solani* (Suganda *et al.*, 2020). The abundance of secondary metabolites, including alkaloids, terpenoids, flavonoids, saponins, and tannins, in butterfly pea extract is associated with its antifungal activity against *Candida albicans*. Fungal cell walls' peptidoglycan synthesis is disrupted by alkaloids, which leads to an incomplete wall structure and, eventually, cell death (Pertiwi *et al.*, 2022; Ramdhini *et al.*, 2024). Conversely, terpenoid compounds work against fungi by either preventing spore growth or by rupturing the fungal cytoplasmic membrane (Zore *et al.*, 2011). The ability of butterfly pea extract to inhibit *Candida albicans* with a comparatively small zone of inhibition was recently discovered by Ramdhini and associates (2024). 90% ethanol extract showed the highest activity, with an average inhibition zone of 3.7 mm; lower concentrations did not show any discernible antifungal effect.

C. ternatea is positioned as a promising natural antimicrobial resource with relevance in contemporary medicine, according to mounting evidence.

CONCLUSION

Modern medicine has greatly benefited from the development of plant-based pharmaceuticals, which provide safer, more effective, and more reasonably priced substitutes for synthetic medications. *Clitoria ternatea*'s diverse pharmacological characteristics highlight its potential as a therapeutic and preventive agent. It is a strong contender for creating plant-based treatments to combat chronic illnesses like diabetes and inflammation because of its diverse mechanisms of action and rich phytochemical profile. Its active ingredients should be identified and described, their molecular pathways should be elucidated, and their therapeutic efficacy should be confirmed by thorough preclinical and clinical research in the future. Such initiatives might open the door for the sustainable and efficient use of this traditional medicinal plant as a natural medication in contemporary evidence-based healthcare.

Going forward, more thorough research is needed to identify, describe, and clinically validate the bioactive substances found in *C. ternatea*. These studies may result in the creation of novel, secure, and efficient plant-based medicines.

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