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Review Article

Coptis teeta Wall.: A Comprehensive Overview of its Traditional Uses, Pharmacological Uses, Phytochemicals and Conservation

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Abstract

Coptis teeta Wall. (*C. teeta*) is a herb that goes by the name "Mishmi Tita", and holds significant value as a medicinal plant for treating various health conditions. This endangered plant, listed in the Red Data Book, is commonly found in India, Nepal, Bhutan and China. The present review aims to comprehensively summarize the traditional, pharmaceutical, and phytochemical aspects of *C. teeta*, providing a foundation for researchers to explore this endangered plant, and take bold steps to conserve, cultivate, and promote awareness among local people. A thorough literature search was conducted on PubMed, Google Scholar, Research Gate, SciFinder, and the ISI Web of Knowledge, using the following terms: "*Coptis teeta*", "*Coptis teeta* Wall.", "Mishmi tita", "*Rhizoma coptidis*", "Chinese medicine from *Coptis teeta*", and "Traditional uses of *Coptis teeta*". A comprehensive examination of 69 articles published between 1982 and 2023 was conducted to explore the properties and traditional applications of *C. teeta*. It was found that this plant and its active compounds exhibit a range of effects, such as fighting against microbes, alleviating diarrhoea, lowering blood pressure, regulating heart rhythm, reducing inflammation, improving mood, treating trachoma, managing diabetes, providing pain relief, and countering reactions. A total of 27 compounds were identified in different parts of this plant, according to the surveyed literature. These have been traditionally utilized to address ailments, including conditions, eye disorders, skin issues, gastrointestinal troubles like constipation and jaundice, and urinary disorders. Furthermore, these have shown potential in cancer treatment and mitigating inflammation. *C. teeta* boasts diverse traditional uses and promising pharmacological activities due to its rich chemical composition. Berberine is the main constituent, and various communities utilize it for various ailments. While endangered, *C. teeta* offers exciting medicinal potential, warranting further research and sustainable conservation efforts. Cultivating the plant and raising public awareness are crucial steps towards its preservation.

Introduction

Coptis genus is a group of flowering plants in the family Ranunculaceae. There are 15 species in the genus, and all of these are native to Asia. These plants are known for their bitter taste and medicinal properties. The earliest record of Coptis plants dates back to the Eastern Han dynasty (25-220 AD), when these were mentioned in the earliest monograph in Chinese material medica. Coptis plants have been used in traditional Chinese medicine for over two millennia to treat a variety of ailments, including fever, diarrhoea, dysentery, jaundice, and malaria. Modern pharmacological studies have revealed that Coptis plants contain several alkaloids, including berberine, palmatine, jatrorrhizine, coptisine, columbamine, and epiberberine. These alkaloids exhibit a diverse range of pharmacological effects, including anti-inflammatory, antimicrobial, and antioxidant properties.[1]

Coptis teeta Wall. (*C. teeta*), also known as Mishmi Tita, is a small perennial herb, and is an important medicinal plant used to treat a variety of disorders. This plant is often found in India, Nepal, Bhutan, and the Himalayan areas of China. The particular

Keywords: *Coptis teeta* Wall.; Traditional uses; Pharmaceutical uses; Phytochemistry; Pharmacological activities; Conservation.

Abbreviations: C. *chinensis*, *Coptis chinensis* Franch; *C. deltoidea*, *Coptis deltoidea* C.Y. Cheng et Hsiao; *C. omeiensis*, *Coptis omeiensis*; *C. teeta*, *Coptis teeta* Wall.; IC_{50}, half maximal inhibitory concentration; IL, interleukin; LDL, low density lipoprotein; MECT, methanolic extract of *Coptis teeta*; S. aureus, *Staphylococcus aureus*; SHRs, spontaneously hypertensive rats.

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Fig. 1. *Coptis teeta* Wall. plant. (a) Whole plant, (b) Stems and Rhizomes with hairy Roots, (c) Leaf.

name "Tita" was derived from its bitter flavour. Due to its multiple health advantages, its thin brownish-yellow rhizome has long been utilized as a medicine in Ayurveda, traditional Chinese medicine, and other indigenous medicinal systems. Furthermore, the people of Arunachal Pradesh have the traditional knowledge of Mishmi tita, and its uses. Despite its multiple medicinal uses, *C. teeta* is only known to survive in this region as a traditional medicinal plant, without written documentation. Thus, preserving its record is essential to prevent its extinction. The pungent, bitter, and cooling root of Mishmi tita suppresses bacterial and viral infections, relieves spasms, lowers fever, and stimulates circulation. The root contains numerous compounds that inhibit various bacteria, and this can provide a safe and efficient treatment for various disorders caused by bacteria, such as several forms of dysentery. Mishmi tita is endemic to a relatively small area in the eastern Himalayas, where its habitat is rapidly disappearing due to deforestation, over collection, and habitat destruction. Since this species has a low reproductive success rate, this must be conserved. The Red Data Book lists this plant as an endangered species.[2–4] This ranges from East Asia, mainly North China, to the Himalayan temperate zones. Few species are indigenous to India, and are found exclusively in the Himalayan regions of Arunachal Pradesh, Darjeeling, West Bengal, and Sikkim, at elevations that range within 2,500–3,000 mts. This has been reported in Arunachal Pradesh's Lohit, Dibang Valley, Siang, and upper Subansiri districts.[4,5] A few local farmers are cultivating this important plant in a few areas around Arunachal Pradesh. They are familiar with the process of growing these plants. Cultivation is a time-consuming and arduous operation. Since India harbours approximately 90% of the global *C. teeta* population, India has become a representative of the global population. *C. teeta* is presently priced at approximately Rs. 2,000/kg.[2–4] Mishmi tita grows best in a variety of soils, including light sandy, medium loamy, and heavy clay soils. This plant prefers acidic soil, and can thrive in both semi-shade and full sunlight. Furthermore, this plant requires moist soil. Increased demand has put commercial harvesting pressure on wild populations, which are already declining due to deforestation. As a result, wild populations are presently on the verge of extinction. Dried root and rhizome are in high demand in the market. In recent years, locals in Arunachal Pradesh and Nagaland have begun cultivating Mishmi tita, albeit on a smaller scale in Nagaland. The Arunachal Pradesh Forest Department has also begun cultivating this plant. Seedlings raised from seeds or wildings can be used to cultivate this plant.[5] The Lisu people in Yunnan, China cultivate Mishmi tita on a modest scale using traditional agroforestry methods that have little negative impact on the ecosystem. This provides them with a significant portion of their income.[6]

The present review focuses on the natural products of *C. teeta*, including its chemistry, biological activity, and conservation concerns. The majority of the data was gathered through databases (for example, Sci-finder, ISI Web of Knowledge, Google Scholar, Research Gate, PubMed, and so on).

Morphological description

C. teeta is a small, stemless, perennial, flowering, evergreen, and herbaceous medicinal plant that is native to the eastern Himalayas. This plant grows to a height of 30–50 cm, and has a 5–15 cm long, horizontal to oblique rhizome. Its leaves are 5–20 cm long, pinnatifid, lamina 3-lobed, and glabrous. The inflorescence is panicled, and contains few flowers that are white or yellowish. Its fruits are capsules that grow up to 6 mm long, and contain several black seeds (Fig. 1).[4,7]

Traditional uses

In India

Arunachal Pradesh is home to approximately 15 major tribes. These tribes have their own method of treating ailments, and employing different medicinal plants. The Adi, Galo, Memba, Nyishi, and Tagin groups of Arunachal Pradesh use the entire *C. teeta* plant (mostly the leaves and rhizome). This is used to treat malaria, stomach ache, diarrhoea, loose motions, dandruff, and insect bites, among other things. Furthermore, *C. teeta* is used to treat a variety of inflammatory conditions, eye problems, skin problems, stomach problems, constipation, jaundice, and urine disorders. Moreover, this is used to treat the following: cancer, inflammation, heat, dampness, fire and toxicity; cough and colds; gastric problems; fever; eye infections; loss of appetite; backache; headache; skin allergies. In addition, *C. teeta* is commonly used to treat bacterial dysentery, typhoid, tuberculosis, meningitis, empyema, pertussis,

and other infectious diseases.[4,8–15] The Nyishi people use *C. teeta* rhizomes to treat various eye disorders, and as appetisers to help with digestion. Rhizomes are consumed with water as a tonic, and are used to treat fever, headaches, and gastrointestinal problems. Furthermore, rhizomes have anti-inflammatory properties, and can help with skin conditions.[13,16] The Adi community uses decoctions of the leaves and roots of *C. teeta* to treat blood clotting, gastrointestinal problems, and malaria. The dry rhizome of *C. teeta* infusion is used as an anti-dysenteric, anti-diarrheic, antipyretic, and anti-malaria. The powder is made from shade-dried *C. teeta* roots. This powder is mixed with water, and boiled for a few minutes before being given to malaria patients. The preparation for abortion is created by blending the leaves with *Caraca papaya*, *Moringa oleifera* (bark), *Solanum spirale* (roots), and *Alstonia schlolaris* (bark).[17–19] In Arunachal Pradesh and other North-eastern states in India, *C. teeta* is used to treat a wide range of ailments, including fever, malaria, backache, headache, jaundice, stomach ache, gastric problems, jaundice, diabetes, dysentery, ulcer, insomnia, vomiting, heart disease, and bacterial and viral infections. Furthermore, this is used as an analgesic, anaesthetic, ophthalmic, and pectoral remedy, and as a root tonic to treat jaundice and diabetes.[20–25] The Minyong people of Arunachal Pradesh treat several ailments with the roots and leaves of *C. teeta*. After drying, the roots are crushed and pulverised. Then, the powder is boiled with water, and given to the malaria patient. Women use the extract of the leaves in combination with raw papaya as an abortifacient.[26]

In China

The Lhoba people of Tibet use *C. teeta* roots to stop bleeding, relieve pain, and reduce inflammation and toxicity in wound care, while Tibetans use these to treat intestinal diseases, anthrax, dysentery, and pyogenic infections.[27] *Rhizoma coptidis*, which is the dried rhizome of *Coptis chinensis* Franch. (*C. chinensis*), *Coptis deltoidea* C.Y. Cheng et Hsiao (*C. deltoidea*), and *C. teeta*, is a frequently used Chinese herbal medicine for clearing heat, dampness, and toxicity. Furthermore, this can be used to treat vomiting, diarrhoea, jaundice, high fever, fainting, heartburn, upset stomach, toothache, and other conditions.[28–31] Huang Lian Jie Du Tang (HLJDT), which is a traditional Chinese medicine decoction of four herbs (*Rhizoma coptidis*, *Scutellariae radix*, *Phellodendri cortex* and *Gardeniae fructus*), in a dry weight ratio of 3:2:2:3, is a widely used anti-inflammatory treatment.[32] *Rhizoma coptidis*, which is a primary traditional Chinese medicine, has been used in powder, pill, or decoction form, as properly sorted by Wang *et al*. in 2019.[33]

In Myanmar

In Myanmar, *C. teeta* is used to relieve constipation, regulate bowel movement, stimulate digestion, lower fever, treat malaria, and boost vitality. When soaked in liquor, the roots can be used to treat malaria. In combination with *Piper nigrum*, *C. teeta* can be used to treat cough and asthma.[34,35]

Pharmacological uses

C. teeta has a wide range of pharmacological activities, including antimicrobial, antibacterial, antidiarrheal, antihypertensive, antiarrhythmic, antihyperlipidemic, anti-inflammatory, antidepressant, antioxidant, antitrachomatous, antidiabetic, analgesic, phosphodiesterase-inhibiting, and antihistaminic activities.

Antimicrobial and antibacterial activity

C. teeta can significantly suppress the growth of *Staphylococcus aureus* (*S. aureus*, with an inhibition zone of 11 mm), according to the study conducted by Li *et al*.[36] Feng *et al*.[37] investigated the effect of *Rhizoma coptidis* (the dried rhizome of *C. chinensis* Franch., *C. deltoidea*, and *C. teeta*) on *S. aureus* growth using micro calorimetry, principal component analysis, and a paired *t*-test of multiple parameters obtained from the heat flow power-time curve parameters. This study revealed that low concentrations of *C. teeta* have no inhibitory effects, while high concentrations can significantly hinder the growth of this bacteria. The minimum inhibitory concentration value of *C. teeta* was determined as 93.3 ± 2.0 µg/mL using the cylinder-plate method.[36,37]

Shwe *et al*.[38] used the agar well diffusion method to evaluate the antimicrobial activities of different crude extracts (petroleum ether, ethyl acetate, 95% ethanol, and water) obtained from *C. teeta* rhizomes against six microorganisms: *Bacillus subtilis*, *Bacillus pumilus*, *S. aureus*, *Pseudomonas aeruginosa* (*P. aeruginosa*), *Candida albicans*, and *Escherichia coli*. The ethanolic and watery extracts were identified to exhibit substantial antibacterial activity against six stains. Furthermore, the petroleum ether and ethyl acetate extract exhibited considerable antibacterial efficacy against six strains, but not against *P. aeruginosa* by ethyl acetate extract.[38]

Bora *et al*.[39] investigated the antibacterial activity of *C. teeta* extracts against *Streptococcus mutans*, *Streptococcus pyogenes*, *Vibrio cholerae*, *Shigella flexneri*, and *Salmonella typhi* using disk diffusion and well diffusion methods. The results revealed that the zone of inhibition was highest at a concentration of 1.6 mg/mL, and lowest at 400 µg/mL for all three extracts: water, methanol, and chloroform. The minimum inhibitory concentration and minimum bactericidal concentration values ranged within 0.625–5.000 mg/mL and 1.25–5.00 mg/mL, respectively.[39]

Anti-diarrheal activity

The rhizome of *C. teeta* is used by tribes in North East India to treat diarrhoea. Berberine induces anti-diarrheal activities via limiting small intestinal transit, and its anti-diarrheal properties may be cured by delaying small intestinal transit.[40] Tsai *et al*.[41] reported that the ethanol extracts of Qinpi, Kushen, and Huanglian can reduce short-circuit current across forskolin-activated rat ileal epithelia. Forskolin stimulates the formation of cellular cyclic adenosine monophosphate, which increases Cl- migration and short-circuit current across the epithelia. These findings suggest that the extracts of these three plants may influence ion transport in the rat ileum epithelia, providing important therapeutic benefits as an anti-diarrheal medicine.[41]

Anti-hypertensive activity

Liu *et al*.[42] investigated the effects of berberine, which is an alkaloid isolated from *Rhizoma coptidis*, on endoplasmic reticulum stress, and its underlying mechanisms in spontaneously hypertensive rats (SHRs). They found that berberine can reduce endothelium-dependent contractions by activating denosine monophosphate-activated protein kinase, which in turn, decreases endoplasmic reticulum stress, and subsequently scavenges reactive oxygen species, resulting in the down regulation of COX-2 in SHR carotid arteries.[42] Guo *et al*.[43] investigated the effects of berberine on the renin-angiotensin system, pro-inflammatory cytokines, blood pressure, and renal failure in SHRs. They found that berberine can delay the onset and attenuate the severity of hypertension, and ameliorate hypertension-induced kidney damage in SHRs. In addition, berberine can inhibit the activities of renin-angiotensin system, and pro-inflammatory cytokines Interleukin 6 (IL6), IL17 and IL23, which are all involved in the pathophysiology of hypertension.[43]

Anti-arrhythmic activity

Lau *et al*.[44] reported that berberine and its derivatives, tetrahydroberberine and 8-oxo berberine, induce cardiovascular effects. Berberine exhibits inotropic, chronotropic, anti-arrhythmic and vasodilator effects, while both berberine derivatives exhibit anti-arrhythmic activity.[44]

Anti-hyper-lipidemic activity

Berberine, which is a key component of *Rhizoma coptidis*, has a preventive role in atherosclerosis due to its cholesterol-lowering activity. This has been shown to reduce blood cholesterol and lipids in animals and hyperlipidemic humans. In 32 hypercholesterolemic patients, the three-month oral treatment of berberine lowered the total blood cholesterol by 29%, triglycerides by 35%, and low density lipoprotein (LDL) cholesterol by 25%. In hyperlipidemic hamsters, the berberine treatment lowered the blood cholesterol by 40% and LDL cholesterol by 42%, with a 3.5-fold increase in hepatic LDLR (low density lipoprotein receptor) mRNA, and a 2.6-fold rise in hepatic LDLR protein. Berberine lowers total blood cholesterol and LDL cholesterol, and both cause heart attacks and stroke.[45] *Rhizoma coptidis* extract is useful in minimizing the pathological damage induced by hypercholesterolemia through lowering serum cholesterol levels. Furthermore, this can lower liver cholesterol, but not fecal cholesterol, suggesting that the cholesterol-lowering effect was due to the reduction in cholesterol synthesis, and not the increase in its excretion. In addition, after oral treatment of the *Rhizoma coptidis* extract, the blood thiobarbituric acid-reactive substance level decreased, showing that *Rhizoma coptidis* can prevent hypercholesterolemic illness by lowering lipid peroxidation.[46]

Anti-inflammatory activity

The pre-treatment with the methanolic extract of *C. teeta* (30, 100 and 300 mg/kg, p.o.) exhibited efficacy in the early phase of inflammation, which is predominantly attributable to the production of histamine and serotonin. The extract's anti-inflammatory effect lasted for up to three hours. In the cotton pellet-induced granuloma model, the methanolic extract exhibited a significant ($p < 0.05$) reduction in dry granuloma weight in the *C. teeta*-treated groups, when compared to the control group.[47]

Anti-depressant activity

Lee *et al*.[48] determined whether berberine treatment can reduce depression and anxiety-like behaviours, and increase corticotrophin-releasing factor and tyrosine hydroxylase expression in rats after chronic morphine withdrawal. Their findings support the possibility that berberine has antidepressant and anxiolytic properties. Furthermore, they evaluated the dose-dependent activity of berberine (10, 20, or 50 mg/kg) using the forced swim test and elevated plus maze test, and found that 50 mg/kg was the most effective in preventing the negative effects of repeated morphine administration, such as depression- and anxiety-like behaviours. Berberine treatment can significantly inhibit the increase in hypothalamic corticotrophin-releasing factor and tyrosine hydroxylase expression in the locus coeruleus, and the decrease in brain-derived neurotrophic factor mRNA expression in the hippocampus.[48] Kulkarni *et al*.[49] evaluated the antidepressant activity of berberine in mice using the forced swim test and tail suspension test. They found that berberine (5 mg/kg, i.p.) can significantly increase the level of norepinephrine and serotonin in the brain of mice.[49]

Antioxidant activity

Berberine, which is a compound found in high concentrations in *C. teeta* rhizomes, was tested for antioxidant properties. The researchers used a variety of *in vitro* methods to evaluate the antioxidant activity through measuring the inhibitory concentration for free radical scavenging. Tan *et al*.[50] reported that the ethanolic root extract of *C. teeta* has high antioxidant potential. The treatment with 1 mmol/L H_2O_2 significantly decreased the cell viability, nitric oxide production, and superoxide dismutase activity of corpus cavernosum smooth muscle cells, and increased the lactate dehydrogenase release and malondialdehyde content. The administration of berberine (10–1,000 mol/L) prevented the harmful effects of H_2O_2, increasing cell viability, nitric oxide generation, and superoxide dismutase activity, while decreasing lactate dehydrogenase release and malondialdehyde content. These findings suggest that berberine has antioxidant activity in oxidative stress-induced cultured corpus cavernosum smooth muscle cells, which can be useful in preventing penile erectile dysfunction.[50]

A study conducted by Bora *et al*.[39] revealed that the acetone extract of *C. teeta* exhibited the highest DPPH (2,2′ diphenyl-1-picryl hydrazyl) radical scavenging activity, with an half maximal inhibitory concentration (IC_{50}) value of 7.37 µg/mL, while the n-hexane extract demonstrated the lowest activity, with an IC_{50} value of 76.11 µg/mL. Conversely, in the ABTS (2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)) assay, both the water extract and acetone extract exhibited superior antioxidant activity (IC_{50} value: 1.41 and 1.91 µg/mL, respectively), when compared to ascorbic acid (IC_{50} value: 2.73 µg/mL). Furthermore, in the ferric reducing antioxidant power assay, the methanol extract exhibited the highest antioxidant activity (with a value of 113.93 µM Fe[II]/g), followed by the acetone extract (with a value of 98.81 µM Fe[II]/g).[39]

Anti-trachoma activity

Berberine has long been used to treat eye issues in North-East India and China. Babbar *et al*.[51] reported that berberine is more effective than sulfacetamide in eliminating Chlamydia trachomatis from the eye, and preventing symptom recurrence in the treatment of trachoma. Khosla *et al*.[52] investigated the clinical and serological response to the topical treatment of trachoma with 0.2% berberine (an indigenous medicine) in 32 microbiologically verified cases. Berberine was more effective than 20% sulfacetamide, both in the clinical course of trachoma, and in inducing a decrease in serum antibody titers ($p < 0.05$) against Chlamydia trachomatis in treated patients.[52]

Anti-diabetic activity

The rhizomes of *C. teeta* generate the highest increase in glucose uptake in 3T3-L1 adipocytes, with glucose absorption (at a concentration of 40 µg/mL) being greater than that of the positive control (insulin of 0.1 µM and berberine of 10 µM).[28] Ni *et al*.[53] investigated the effects of berberine on blood glucose levels in 60 individuals with non-insulin-dependent diabetes mellitus, and in animal models of diabetes. Their findings revealed that berberine has a significant effect on blood glucose levels, in both humans and animals. The clinical symptoms virtually subsided, while the serum insulin levels increased. The entire efficacy rate reached up to 90%, with no major negative effects.[53] Yin *et al*.[54] evaluated the efficacy of berberine in patients with type-2 diabetes mellitus. They found that berberine was as effective as metformin in modulating glucose metabolism parameters, such as HbA1c (glycated haemoglobin), fasting blood glucose, post 2-h blood glucose, fasting insulin, and postprandial insulin. In addition, berberine can significantly reduce the HbA1c levels in diabetics.[54] Shah *et al*.[55] investigated the therapeutic potential of ethanolic extract derived from *C. teeta* roots in a rat model of diabetes induced by alloxan.

Their findings revealed significant ameliorative effects in rats treated with the extract, demonstrating a halt in body weight loss, and notable reductions in food and fluid intake, serum glucose, serum urea, and serum creatinine levels. In addition, the extract treatment led to a significant increase in insulin levels and serum protein, when compared to diabetic rats without treatment.[55]

Analgesic activity

Goswami *et al*.[47] investigated the analgesic efficacy of the methanolic extract of *Coptis teeta* (MECT) in validated rodent models. The MECT results in an acetic acid-induced abdominal constriction assay revealed a significant reduction in writhing reflex. These findings strongly suggest that MECT has a peripheral analgesic effect, and that its mechanism of action may entail the inhibition of local peritoneal receptors, which may involve COX (Cyclooxygenase) inhibition potential. The potent analgesic action of MECT can be attributed to the active principle(s) that interfere with the release of pain mediators. The hot plate test, which is a thermal nociception model, was utilized to assess the central analgesic action. In the hot plate test, MECT had a strong analgesic effect, indicating both spinal and supraspinal analgesic mechanisms. Tramadol, which acts similarly to opioid agonists (e.g. morphine), and MECT raised the pain threshold level within 30 minutes of dosing in the pain paradigms. This agreement in maximum analgesic points can be explained by the similar metabolism rates of the drugs. However, tramadol was identified to be more potent, when compared to MECT (300 mg/kg).[47]

Phosphodiesterase inhibition activity

Chit *et al*.[56] investigated the phosphodiesterase inhibition activity of berberine (as a standard) isolated from *C. teeta*, and revealed that this can inhibit phosphodiesterase by 2.05 ± 5.33%.

Anti-histaminic activity

The Unani eye drop, which contained *Berberis aristata* DC. (stem wood), *Cassia absus* Linn. (seed), *C. teeta* (rhizome), *Symplocos racemosa* Roxb. (bark), *Azadirachta indica* A. Juss (flower), alum, and *Rosa damascena* Mill, exhibited a strong antihistaminic effect on isolated guinea pig ileum. This was found to counteract the effects of histamine on tissues. Increasing doses of the test medication resulted in the gradual inhibition of the histamine-induced contraction of isolated guinea pig ileum.[57]

Anti-malarial activity

Goswami *et al*.[58] conducted an *in vitro* study to evaluate the anti-malarial activity of methanol extracts derived from *C. teeta*. Their findings revealed remarkable anti-malarial properties, with IC_{50} values of 0.08 µg/mL against the 3D7 strain, and 0.7 µg/mL against the Dd2 strain of *Plasmodium falciparum*. Further molecular investigations, which included molecular docking, molecular dynamics simulation, and density functional theorem analysis, provided compelling evidence that noroxyhydrastinine (a bioactive compound found in *C. teeta*) holds promise as a potent anti-malarial agent.[58]

Phytochemicals/main elements

Botanical and pharmacological research has revealed that *Rhizoma coptidis* contains a number of alkaloids, including palmatine and berberine, which are known to have anti-inflammatory, antibacterial, and antioxidant properties.[28,29] The phytochemical analysis of *C. teeta* revealed the presence of alkaloids, carbohydrates, flavonoids, glycosides, organic acids, phenolic compounds, reducing sugars, saponins, starch, terpenoids and tannins, but not α-amino acids or steroids. The elemental analysis using energy dispersive X-ray fluorescence detected trace amounts of Li, B, Na, Mg, Al, Si, P, Ca, Fe, Mn, Zn, Ti, Cu, Ag, Ba and Sr, with S and K being the most abundant.[38,40,59] Goswami *et al*.[29] reported that *C. teeta* rhizome contains 0.8% w/w berberine, while Latif *et al*.[60] reported a higher concentration of 8.0–8.5%. The root of *C. teeta* has a berberine content of 6–7%, while the stem and leaf have lower concentrations of 2.00–3.00% and 1.00–1.97%, respectively.[34] Chen *et al*.[61] investigated the alkaloid content of *C. teeta* collected from three different habitats in Yunnan Province, China. The alkaloid content of *C. teeta* varied among habitats, with the highest levels for jatrorrhizine (6.07–7.76 mg/g), columbamine (1.58–1.73 mg/g), epiberberine (0.36–0.66 mg/g), coptisine (14.93–17.81 mg/g), palmatine (4.61–5.24 mg/g), and berberine (78.99–84.85 mg/g).[61]

In 2018, Li *et al*.[36] conducted a quantitative analysis of the organic acid content of three Coptis species: *C. chinensis*, *C. teeta*, and *C. deltoidea*. They found that *C. teeta* had the highest total organic acid content (45 mg/g), which was approximately three times higher than that of *C. chinensis* and *C. deltoidea*. Specifically, *C. teeta* had the highest concentration of quinic acid (27.83 mg/g), malic acid, and succinic acid (15.25 mg/g). These three acids accounted for more than 75% of the total organic acid content in *C. teeta*, and up to 94% in some samples. The content of quinic acid in *C. teeta* was approximately eight times of that of *C. chinensis* and *C. deltoidea*. These findings suggest that *C. teeta* has higher quality, when compared to *C. chinensis* and *C. deltoidea*, based on its higher content of organic acids.[36]

In 2013, Meng *et al*.[62] used a variety of chromatographic methods to isolate and purify 12 compounds from the ethanol extract of *C. teeta*. The structures of these compounds were determined using spectral techniques and physicochemical properties. The 12 compounds identified were, as follows: ferulic acid, Z-octadecyl caffeate, protocatechuic acid, methyl-3,4-dihydroxyphenyl lactate, woorenoside I, woorenoside II, longifolroside A, 3,4-dihydroxyphenethyl alcohol, 3,5-dihydroxyphenethyl alcohol 3-O-β-D-glucopyranoside, 3,5,7-trihydroxy-6,8-dimethylflavone, (+)-syringaresinol 4-O-β-D-glucopyranoside, and (+)-lariciresinol.[62]

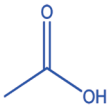
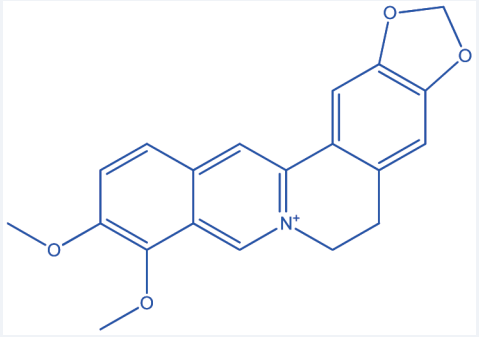
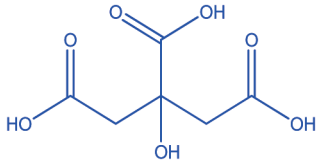
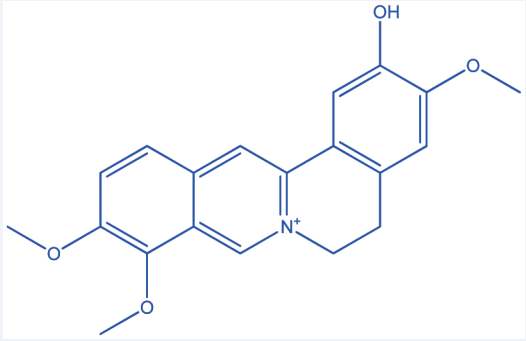
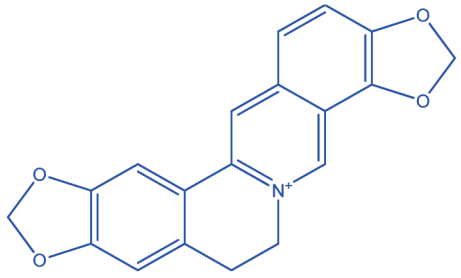
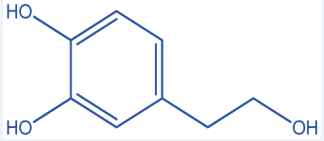
The study conducted by Chen *et al*.[63] as the first to report the presence of magnoflorine and groenlandicine in *C. teeta*. The data is shown in Table 1.

Liu *et al*.[30] delved into the intricate relationship between endophytic bacteria and berberine content, in both wild-type and cultivated *C. teeta*. By employing 16S rDNA sequencing and metabonomics techniques, they uncovered significant differences in the microbial composition of wild-type and cultivated plants, with distinct microbial communities inhabiting the root, stem and leaf tissues. Their findings underscore the crucial role of specific endophytic bacteria in berberine production, suggesting its potential to enhance berberine yield, and promote food and medicine safety.[30]

Comparison of main chemical constituents with a few related species

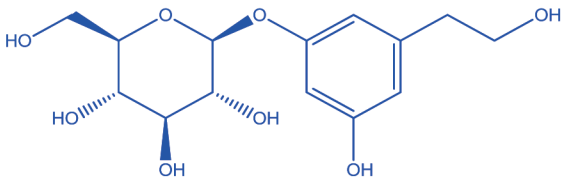
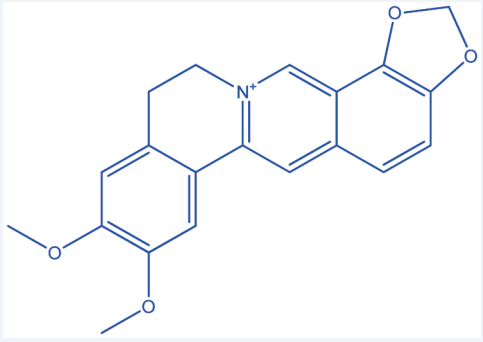
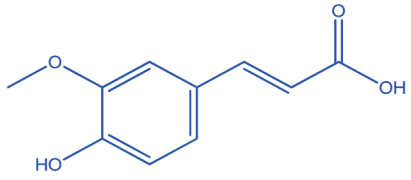
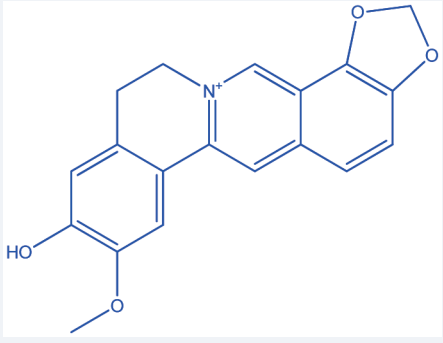
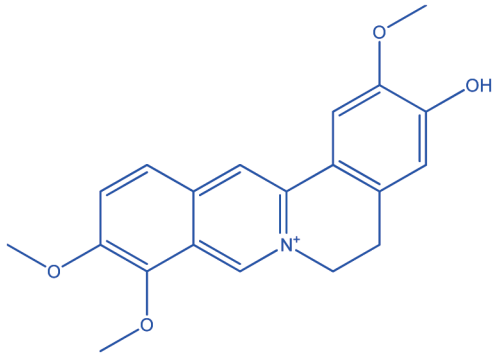
Chen *et al*.[61] investigated the alkaloid content of four Coptis species (*C. chinensis*, *C. teeta*, *C. deltoidea*, and *Coptis omeiensis* [*C. omeiensis*]) using high-performance liquid chromatography. The alkaloid content varied among the four species, and between the different habitats, with *C. chinensis* having the highest alkaloid content, followed by *C. deltoidea*, *C. teeta* and *C. omeiensis*. Table 2 summarizes the alkaloid content of the four Coptis species.[61]

Table 1. Compounds present in *C. teeta* with the corresponding structure

SL no.	Compounds	Structures
1	Acetic acid	
2	Berberine	
3	Citric acid	
4	Columbamine	
5	Coptisine	
6	3,4-Dihydroxyphenethyl alcohol	

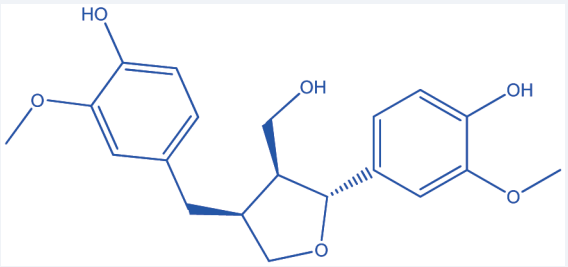
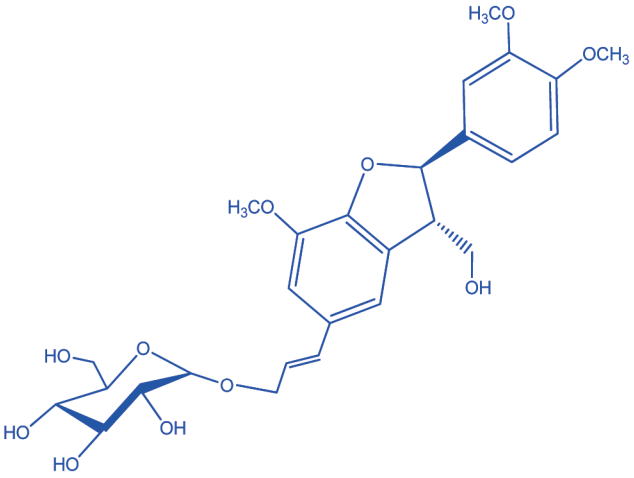
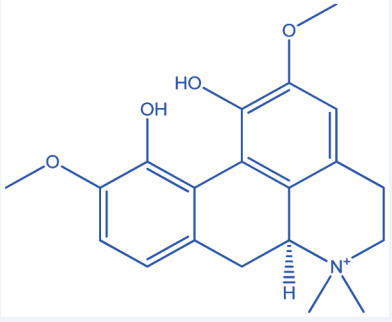
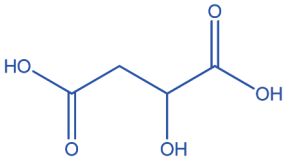
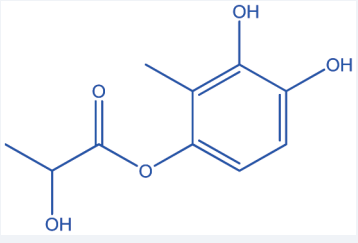
(continued)

Table 1. *- (continued)*

SL no.	Compounds	Structures
7	3,5-Dihydroxyphenethyl alcohol-3-O-β-D-glucopyranoside	
8	Epiberberine	
9	Ferulic acid	
10	Groenlandicine	
11	Jatrorrhizine	

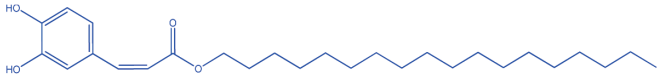
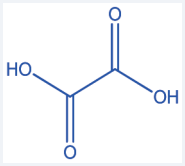
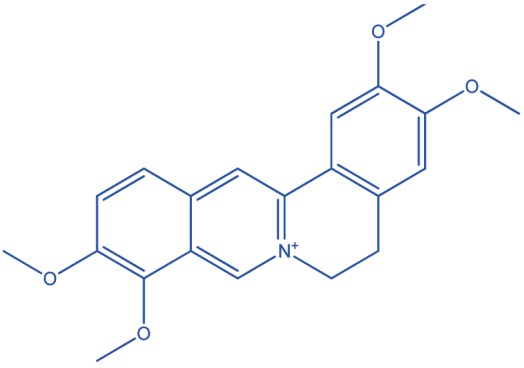
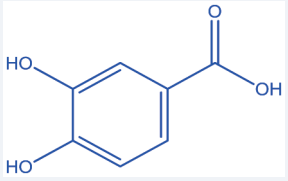
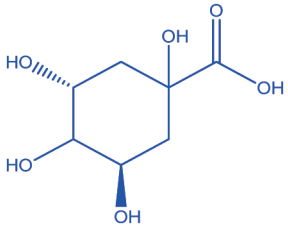
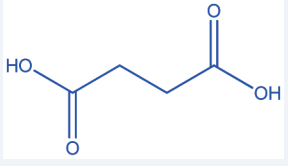
(continued)

Table 1. *- (continued)*

SL no.	Compounds	Structures
12	(+)-Lariciresinol	
13	Longifolroside A	
14	Magnoflorine	
15	Malic acid	
16	Methyl-3,4-dihydroxyphenyl lactate	

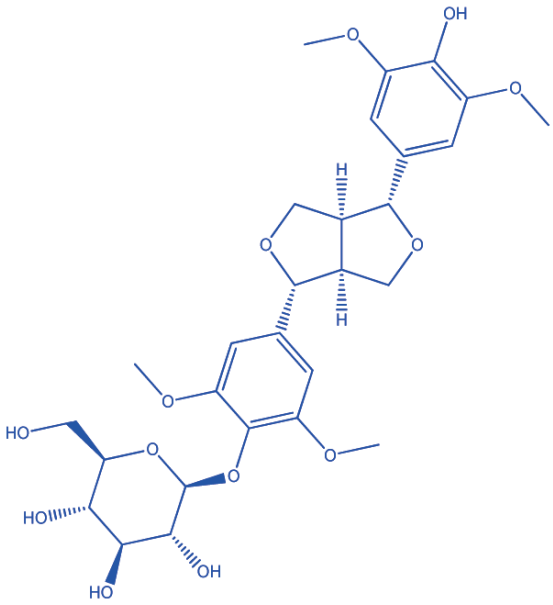
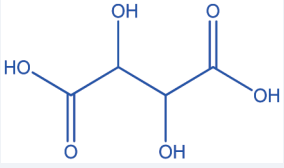
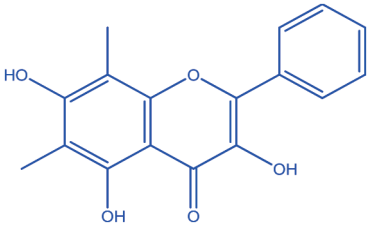
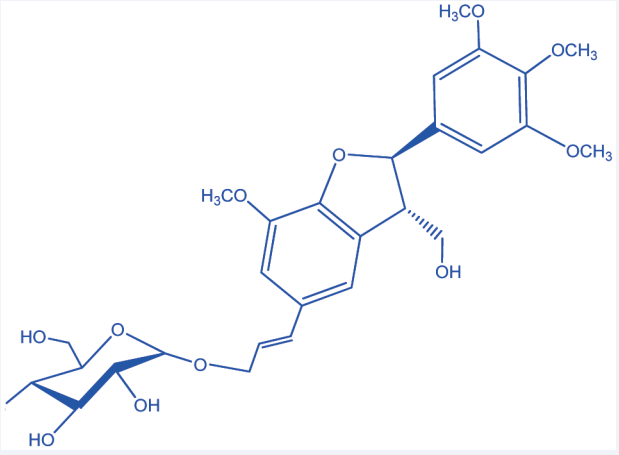
(continued)

Table 1. - *(continued)*

SL no.	Compounds	Structures
17	*Z*-Octadecyl caffeate	
18	Oxalic acid	
19	Palmatine	
20	Protocatechuic acid	
21	Quinic acid	
22	Succinic acid	

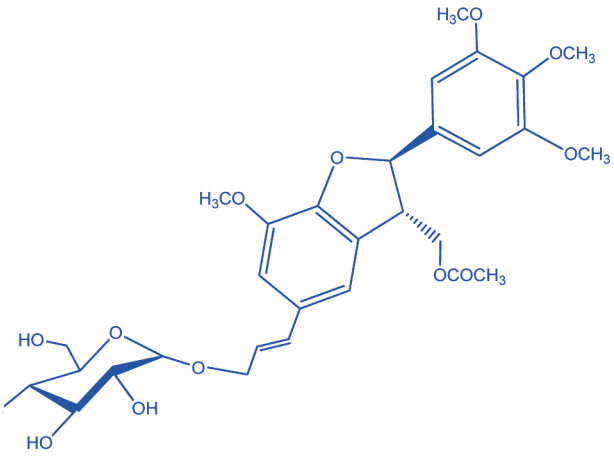
(continued)

Table 1. *- (continued)*

SL no.	Compounds	Structures
23	(+)-Syringaresinol-4-O-β-D-glucopyranoside	
24	Tartaric acid	
25	3,5,7-Trihydroxy-6,8-dimethylflavone	
26	Woorenoside I	

(continued)

Table 1. *- (continued)*

SL no.	Compounds	Structures
27	Woorenoside II	

By employing the high-performance liquid chromatography method, Li *et al*.[64] determined the contents (mg/g) of six alkaloids, and the total alkaloids in the rhizomes of three Coptis species: *C. chinensis*, *C. deltoidea*, and *C. teeta*. The concentrations of the six alkaloids varied across all three species, and these were influenced by the sample origin. Epiberberine, coptisine, and palmatine were found in significantly higher concentrations in *C. chinensis*, when compared to *C. deltoidea* and *C. teeta*. Conversely, the berberine levels were significantly higher in *C. chinensis* and *C. teeta*, when compared to *C. deltoidea*. Notably, *C. deltoidea* had the lowest total alkaloid concentration, while *C. chinensis* had an almost two-fold higher total alkaloid content (Table 3).[64]

In 2012, Fan *et al*.[65] used principal component analysis and analysis of variance to investigate the chemical composition of *C. chinensis*, *C. deltoidea*, and *C. teeta*. *C. chinensis* had significantly higher levels of palmatine, coptisine, epiberberine, columbamine, and fatty acids, when compared to the other two species, and had significantly lower levels of jatrorrhizine. *C. deltoidea* had the highest levels of sucrose, and *C. teeta* had the highest levels of chlorogenic acid. These authors concluded that the chemical composition of Coptis species is specific, and that the levels of the different compounds can be used to distinguish between the three species.[65] A study conducted by Singh *et al*.[66] revealed that the roots of *C. deltoidea* and *C. teeta* had the highest concentration of jatrorrhizine and berberine, respectively. Li *et al*.[67] undertook a study to investigate the free amino acid composition of three closely related Coptis species: *C. chinensis*, *C. teeta*, and *C. deltoidea*. By employing an automated amino acid analyzer, they determined the content of 20 free amino acids in each species to elucidate the differences. Their findings revealed that *C. chinensis* had significantly higher levels of the major amino acids (asparagine [Asn], arginine [Arg], and γ-aminobutyric acid [GABA]), when compared to the other two species. In addition, the aspartic acid (Asp) content was significantly higher in *C. deltoidea*. That study concluded that Asn can be used as a diagnostic marker to distinguish *C. deltoidea*, *C. chinensis*, and *C. teeta*, while glutamine (Gln) and

Table 2. Variations in alkaloid content reported by Chen *et al*., 2017[61]

Species	Habitat	Berberine (mg/g)	Columbamine (mg/g)	Coptisine (mg/g)	Epiberberine (mg/g)	Jatrorrhizine (mg/g)	Palmatine (mg/g)
C. chinensis	Wild	66.10–88.86	3.76–8.78	19.83–27.53	11.60–17.5	3.34–6.45	16.46–26.54
C. teeta	Wild	78.99–84.85	1.58–1.73	14.93–17.81	0.36–0.66	6.07–7.76	4.61–5.24
C. deltoidea	Wild	47.07–48.37	1.80–2.15	11.82–12.18	1.90–2.73	7.27–8.81	5.88–6.77
C. omeiensis	Wild	56.39–64.72	2.30–3.17	16.68–21.23	–	4.43–4.97	8.50–9.43

C. chinensis, *Coptis chinensis*; *C. teeta*, *Coptis teeta*; *C. deltoidea*, *Coptis deltoidea*; *C. omeiensis*, *Coptis omeiensis.*

Table 3. Variations in alkaloid content reported by Li *et al*., 2020[64]

Species	Habitat	Berberine (mg/g)	Columbamine (mg/g)	Coptisine (mg/g)	Epiberberine (mg/g)	Jatrorrhizine (mg/g)	Palmatine (mg/g)
C. chinensis	Wild	72.22–96.10	3.25–5.49	20.40–31.51	11.88–17.00	3.25–5.49	16.17–24.06
C. teeta	Wild	72.93–90.96	6.39–8.43	13.57–15.60	0.29–1.11	6.39–8.43	5.23–6.32
C. deltoidea	Wild	45.58–51.74	7.50–11.03	12.63–17.95	1.79–2.69	7.50–11.03	5.87–8.22

C. chinensis, *Coptis chinensis*; *C. teeta*, *Coptis teeta*; *C. deltoidea*, *Coptis deltoidea.*

Arg can be used to differentiate *C. teeta* from *C. chinensis* and *C. deltoidea*.[67]

Conservation and cultivation practice

In recent years, the cultivation of *C. teeta*, which is a valuable medicinal plant native to the Eastern Himalayas, has gained traction among locals in Arunachal Pradesh and Nagaland. Although the cultivation efforts of Nagaland remain relatively small-scale, the Forest Department of Arunachal Pradesh has actively embarked on *C. teeta* cultivation. The propagation methods include raising seedlings from seeds collected from mature plants, or transplanting wildings from natural habitats.[5] In Yunnan province, China, the Lisu people have skilfully integrated *C. teeta* cultivation into their traditional agroforestry practices, demonstrating a harmonious balance between agriculture and environmental stewardship. Their cultivation methods, which are characterized by a modest scale and low ecological footprint, provide a substantial portion of their income, while preserving the delicate balance of the ecosystem.[6] Mukherjee *et al*.[67] conducted a study on the cultivation and acclimatization of *C. teeta* in the Lava region of the Darjeeling Himalayas. Their findings revealed that this plant thrives in sandy loam soil, with high organic carbon content (0.73–1.03%), available nitrogen (231.95–299.16 kg/ha), phosphorus pentoxide (17.11–22.11 kg/ha), and potassium oxide (186.19–273.11 kg/ha), at a pH of 4.5–5.6. Propagation was achieved through the use of rhizomes and seeds.[68] A study conducted by Mishra *et al*.[69] highlighted the adoption of both *in situ* and *ex situ* conservation methods for preserving and sustainably utilizing elite plant generations of *C. teeta*. However, *ex situ* conservation was deemed more suitable for this species due to its restricted habitat distribution and challenging cultivation requirements.[69]

Conclusion

The present review summarized the traditional and pharmacological uses, and chemical constituents of *C. teeta*, and compared the main constituents of *C. chinensis*, *C. deltoidea*, and *C. omeiensis*. *C. teeta* contains alkaloids, carbohydrates, flavonoids, glycosides, organic acids, phenolic compounds, reducing sugars, saponins, starch, terpenoids, and tannins. Furthermore, the present review reports the structures of the 27 compounds identified or/and isolated from different parts of *C. teeta*. Berberine is the main constituent present in *C. teeta*, with a concentration of 8.0- 8.5% w/w. The Adi, Minyong (a sub-tribe of Adi), Galo, Memba, Nyishi, and Tagin groups of Arunachal Pradesh, the Tibetans and Lhoba people of Tibet, and the people of Myanmar and China traditionally use different parts of *C. teeta* for various ailments, including inflammation, eye problems, skin problems, stomach problems, constipation, jaundice and urinary disorders, eliminating dampness, inflammation, cancer, clearing heat, purging fire and detoxification, cough and cold, gastric, fever, eye infection, loss of appetite, backache, headache, and skin allergies. *C. teeta* is a promising medicinal plant species, with a wide range of potential pharmacological activities, including antimicrobial, antihypertensive, antiarrhythmic, antioxidant, antitrachoma, antidiabetic, antidiarrheal, antihyperlipidemic, anti-inflammatory, antidepressant, analgesic, phosphodiesterase inhibition, and antihistamine activities. However, this plant is presently an endangered species due to habitat loss, over collection, and low reproductive success. Further research is needed to fully understand the potential of *C. teeta*, and develop sustainable conservation strategies for this endangered species. One promising approach to conservation is to propagate and cultivate *C. teeta* in controlled environments. This would help to reduce the pressure on wild populations, and ensure a steady supply of this valuable plant. In addition, public awareness campaigns can help to reduce the demand for wild-harvested *C. teeta*, and promote the use of cultivated plants. With concerted efforts, it is possible to conserve *C. teeta*, and ensure that this important medicinal plant is available for future generations.

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Conflict of interest

There is no conflict of interest to declare.

Author contributions

Drafting of the manuscript (NC, HS, CT), collection of data (NC, HS, CT), compilation of data (NC, HS) and correction of manuscript (CT). All authors have made a significant contribution to this study and have approved the final manuscript.

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