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

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Abstract

Background and Objective: *Coptis teeta* Wall 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. This 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.

Methods: A thorough literature search was conducted using PubMed, Google Scholar, Research Gate, SciFinder, and the ISI Web of Knowledge and by using the terms "*Coptis teeta*", "*Coptis teeta* Wall.", "Mishmi tita", "*Rhizoma coptidis*", "Chinese medicine from *Coptis teeta*", "Traditional uses of *Coptis teeta*".

Results: A comprehensive examination of 70 articles published between 1982 and 2023 was conducted to explore the properties and traditional applications of *Coptis teeta*. 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 found in different parts of this plant, according to the literature surveyed. Furthermore, it has been traditionally utilized for addressing ailments including conditions, eye disorders, skin issues, gastrointestinal troubles like constipation and jaundice as well as urinary disorders. Notably, it has also shown potential, in cancer treatment and mitigating inflammation.

Conclusion: *C. teeta* has both pharmacological and traditional potential. It is important for future studies to emphasize conducting *in vitro*, *in silico*, *in vivo*, and clinical studies to validate the traditional uses and establish strategies, for sustainable conservation.

Keywords: *Coptis teeta* Wall., medicinal plant, traditional uses, pharmaceutical uses, phytochemistry, pharmacological activities, conservation

Introduction

The Coptis genus is a group of flowering plants in the family Ranunculaceae. There are 15 species in the genus, all of which are native to Asia. These plants are known for their bitter taste and their medicinal properties. The earliest record of Coptis plants dates back to the Eastern Han dynasty (25–220 AD) when they were mentioned in the earliest monograph on 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 shown 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, also known as Mishmi Tita, is a small perennial herb that is an important medicinal plant used to treat a variety of disorders. This plant is often found in India, Nepal, Bhutan, and China's Himalayan areas. The particular name 'Tita' is derived from its bitter flavour. For 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. The people of Arunachal Pradesh have also had traditional knowledge of Mishmi tita and its uses. Despite its multiple medicinal uses, *Coptis teeta* is only known to survive in this region as a traditional medicinal plant without written documentation. Preserving its record is now essential to prevent its extinction. The pungent, bitter, and cooling root of Mishmi tita suppresses bacterial and viral infections, relieves spasms, lowers fevers, and stimulates circulation. The root contains numerous compounds that inhibit various bacteria and are a safe and efficient treatment for many 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, overcollection, and habitat destruction. It also has a low reproductive success rate and therefore 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 ranging from 2500 to 3000 mts. It 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 them. Cultivation is a time-consuming and arduous operation. As India harbours about 90% of the global *C. teeta* population, it is a representative of the global population. *C. teeta* is currently priced at around Rs. 2000/kg.[2-4] Mishmi tita grows best in a variety of soils, including light sandy, medium loamy, and heavy clay soils. It prefers acidic soils and can thrive in both semi-shade and full sunlight. It requires moist soil. Increased demand has put commercial harvesting pressure on wild populations, which were already declining due to deforestation. As a result, wild populations are now 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 it. Seedlings raised from seed or wildings can be used to cultivate it.[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 focus of this review is on natural products in *C. teeta*, including the chemistry, biological activity, and conservation concerns. The majority of the data was gathered through databases (for example, Scifinder, ISI Web of Knowledge, Google Scholar, ResearchGate, PubMed, and so on).

Morphological Description

Coptis teeta is a small, stemless, perennial, flowering, evergreen, and herbaceous medicinal plant that is native to the eastern Himalayas. It grows to a height of 30-50 cm and has a rhizome that is horizontal to oblique and 5-15 cm long. The 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. The fruits are capsules that are up to 6 mm long and contain several black seeds.[4,7]

Figure 1: *Coptis teeta* Wall. plant

Traditional Uses

1. In India

Arunachal Pradesh is home to around 15 major tribes. They all 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 *Coptis teeta* plant (mostly the leaves and rhizome). It is used to treat malaria, stomach aches, diarrhoea, loose motions, dandruff, and insect bites, among other things. *Coptis teeta* is also used to treat a variety of inflammatory conditions, eye problems, skin problems, stomach problems, constipation, jaundice, and urine disorders. It is also used to treat cancer, inflammation, heat, dampness, fire, and toxicity; cough and cold; gastric problems; fever; eye infections; loss of appetite; backache; headache; and skin allergies. *Coptis 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 with water are consumed as a tonic and are also used to treat fever, headaches, and gastrointestinal problems. Rhizomes have anti-inflammatory properties and can help with skin conditions.[13, 16] The Adi community uses decoctions of *C. teeta*'s leaves and roots 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-malarial. The powder is made from shade-dried *C. teeta* roots. The powder is mixed with water and boiled for a few minutes before being given to malaria patients. 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 of 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, ulcers, insomnia, vomiting, heart disease, and bacterial and viral infections. It is also 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. The powder is then 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]

2. 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 it to treat intestinal diseases, anthrax, dysentery, and pyogenic infections.[27] *Rhizoma coptidis*, the dried rhizome of *Coptis* *chinensis* Franch., *Coptis deltoidea* C.Y. Cheng et Hsiao, and *Coptis teeta* Wall., is a frequently used Chinese herbal medicine for clearing heat, dampness, and toxicity. It can also treat vomiting, diarrhoea, jaundice, high fever, fainting, heartburn, upset stomach, toothache, and other conditions.[28-31] Huang Lian Jie Du Tang (HLJDT), a traditional Chinese medicine (TCM) 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*, a primary TCM, has been used in powder, pill, or decoction form, as properly sorted by Wang et al., 2019.[33]

3. In Myanmar

In Myanmar, *C. teeta* is used to relieve constipation, regulate bowel movements, stimulate digestion, lower fever, treat malaria, and boost vitality. The roots, when soaked in liquor, are also used to treat malaria. *C. teeta*, in combination with *Piper nigrum*, is used to treat cough and asthma.[34-35]

Pharmacological Uses

Coptis 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.

1. Antimicrobial and Antibacterial Activity

Coptis teeta significantly suppressed the growth of *Staphylococcus aureus* (with an inhibition zone of 11 mm), according to **Li et al., 2018**. **Feng et al., 2011** investigated the effect of *Rhizoma coptidis* (the dried rhizome of *Coptis chinensis* Franch., *Coptis deltoidea* C.Y. Cheng et Hsiao, and *Coptis teeta* Wall) on *S. aureus* growth using microcalorimetry, principal component analysis, and a paired t-test of multiple parameters obtained from the HFP-time curve parameters. Their study revealed that a low concentration of *C. teeta* had no inhibitory effect, whereas a high concentration significantly hindered the growth of this bacteria. The MIC value of *C. teeta* was determined using the cylinder-plate method to be 93.3±2 µg/mL.[36,37]

Shwe et al., 2019 used the agar well diffusion method to evaluate the antimicrobial activities of different crude extracts (petroleum ether, ethyl acetate, 95% ethanol, and water) from *Coptis teeta* rhizomes against six microorganisms: *Bacillus subtilis*, *Bacillus pumilus*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Candida albicans*, and *Escherichia coli*. The ethanolic and watery extracts were found to have substantial antibacterial activity against six stains. Furthermore, the petroleum ether and ethyl acetate extract showed considerable antibacterial efficacy against six strains, but not against *P. aeruginosa* by ethyl acetate extract.[38]

Bora et al., 2022 investigated the antibacterial activity of *Coptis 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 (ZOI) 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 (MIC) and minimum bactericidal concentration (MBC) values ranged from 0.625 µg/mL to 5 mg/mL and 1.25 mg/mL to 5 mg/mL, respectively.[39]

2. Anti-diarrheal activity

The rhizome of *Coptis teeta* is used by tribes in North East India to treat diarrhoea. Berberine has 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., 2004** reported that ethanol extracts of Qinpi, Kushen, and Huanglian all reduced short-circuit current across forskolin-activated rat ileal epithelia. Forskolin stimulates the formation of cellular cyclic AMP, which increases Cl- migration and short-circuit current across the epithelia. The findings suggest that extracts of the three plants may influence ion transport in the rat ileum epithelia, which could be important for their therapeutic benefits as anti-diarrheal medicines.[41]

3. Anti-hypertensive activity

Liu et al., 2015 investigated the effects of berberine, an alkaloid isolated from *Rhizoma coptidis*, on endoplasmic reticulum (ER) stress and its underlying mechanisms in spontaneously hypertensive rats (SHRs). They found that berberine reduced endothelium-dependent contractions (EDCs) by activating AMPK, which decreased ER stress and subsequently scavenged reactive oxygen species (ROS), resulting in the down regulation of COX-2 in SHR carotid arteries.[42] **Guo et al., 2015** investigated the effects of berberine on the renin-angiotensin system (RAS), pro-inflammatory cytokines, blood pressure, and renal failure in spontaneously hypertensive rats (SHRs). They found that berberine delayed the onset attenuated the severity of hypertension, and ameliorated hypertension-induced kidney damage in SHRs. Berberine also inhibited the activities of RAS and the pro-inflammatory cytokines IL-6, IL-17, and IL-23, which are all involved in the pathophysiology of hypertension.[43]

4. Anti-arrhythmic activity

Lau et al., 2001 found that berberine and its derivatives, tetrahydroberberine and 8-oxo berberine, have cardiovascular effects. Berberine exhibits inotropic, chronotropic, anti-arrhythmic, and vasodilator effects, while both berberine derivatives exhibit anti-arrhythmic activity.[44]

5. Anti-hyper-lipidemic activity

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

6. Anti-inflammatory activity

Pretreatment with the methanolic extract of *C. teeta* (30, 100, and 300 mg/kg, p.o.) showed 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 3 hrs. In the cotton pellet-induced granuloma model, the methanolic extract of *C. teeta*-treated groups showed a significant ($P<0.05$) reduction in dry granuloma weight compared to the control group.[47]

7. Anti-depressant activity

Lee et al., 2012 investigated whether berberine treatment could reduce depression and anxiety-like behaviours and increase corticotrophin-releasing factor (CRF) and tyrosine hydroxylase (TH) expression in rats after chronic morphine withdrawal. Their findings supported the possibility that berberine has antidepressant and anxiolytic properties. They evaluated the dose-dependent activity of berberine (10, 20, or 50 mg/kg) in the forced swim test (FST) and elevated plus maze (EPM) tests and found that 50 mg/kg was most effective in preventing the negative effects of repeated morphine administration, such as depression- and anxiety-like behaviours. Berberine treatment significantly inhibited the increase in hypothalamic CRF and TH expression in the locus coeruleus (LC) and the decrease in brain-derived neurotrophic factor (BDNF) mRNA expression in the hippocampus.[48] **Kulkarni et al., 2009** 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.) significantly increased the levels of norepinephrine and serotonin in the mouse brain.[49]

8. Antioxidant activity

Berberine, a compound found in high concentrations in *C. teeta* rhizomes, was tested for antioxidant properties. Researchers used a variety of *in vitro* methods to evaluate antioxidant activity by measuring inhibitory concentration for free radical scavenging. Tan et al. (2007) reported that the ethanolic root extract of *C. teeta* has high antioxidant potential. Treatment with 1 mmol/L H_2O_2 significantly decreased cell viability, nitric oxide (NO) production, and superoxide dismutase (SOD) activity of corpus cavernosum smooth muscle cells (CCSMCs), and increased lactate dehydrogenase (LDH) release and malondialdehyde (MDA) content. Berberine administration (10 - 1000 mol/L) prevented the harmful effects of H_2O_2, increasing cell viability, NO generation, and SOD activity while decreasing LDH release and MDA content. These findings suggest that berberine has antioxidant activity in oxidative stress-induced cultured CCSMCs, which could be useful in preventing penile erectile dysfunction.[50]

A study conducted by **Bora et al., 2022** revealed that the acetone extract of *Coptis teeta* exhibited the highest DPPH radical scavenging activity, with an 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 assay, both the water extract and acetone extract exhibited superior antioxidant activity compared to ascorbic acid, with IC_{50} values of 1.41 µg/mL and 1.91 µg/mL, respectively, compared to ascorbic acid's IC_{50} value of 2.73 µg/mL. Furthermore, in the FRAP assay, the methanol extract displayed 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]

9. Anti trachoma activity

Berberine has long been used to treat eye issues in North East India and China. **Babbar et al., 1982** reported that berberine was more effective than sulfacetamide in eliminating Chlamydia trachomatis from the eye and preventing symptom recurrence in the treatment of trachoma.[51] **Khosla et al., 1992** investigated the clinical and serological response to topical treatment of trachoma with 0.2% berberine, an indigenous medicine, in 32 microbiologically verified cases. Berberine was more effective than 20% sulfacetamide in both the clinical course of trachoma and inducing a decrease in serum antibody titers ($P<0.05$) against Chlamydia trachomatis in treated patients.[52]

10. Anti-diabetic activities

The rhizomes of *C. teeta* generated 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 controls, insulin (0.1 μM) and berberine (10 μM).[28] **Ni et al., 1995** 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. Clinical symptoms virtually subsided, while serum insulin levels increased. The entire efficacy rate was up to 90%, with no major negative effects.[53] **Yin et al., 2008** 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, FBG, PBG, fasting insulin, and postprandial insulin. Berberine also significantly reduced HbA1c levels in diabetics.[54] **Shah et al., 2022** investigated the therapeutic potential of ethanolic extract derived from *C. teeta* Wall. roots in a rat model of diabetes induced by alloxan. Their findings revealed significant ameliorative effects, with 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. Additionally, the extract treatment led to a significant increase in insulin levels and serum protein compared to diabetic rats without treatment.[55]

11. Analgesic activity

Goswami et al., 2017 investigated the analgesic efficacy of a methanolic extract of *Coptis teeta* (MECT) in validated rodent models. The results of MECT in an acetic acid-induced abdominal constriction assay revealed a significant reduction of the writhing reflex. These findings strongly suggest that MECT has a peripheral analgesic effect and that their mechanisms of action may entail inhibition of local peritoneal receptors, which may involve COX inhibition potential. MECT's potent analgesic action could be attributed to the active principle(s) interfering with the release of pain mediators. The hot plate test, a thermal nociception model, was utilised to assess 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 min of dosing in the pain paradigms. This agreement in maximum analgesic points could be explained by the drugs' similar metabolism rates. However, tramadol was found to be more potent than MECT (300 mg/kg).[47]

12. Phosphodiesterase Inhibition Activity

Chit et al., 2001 investigated the phosphodiesterase inhibition activity of berberine (as a standard) isolated from *C. teeta* and discovered that it inhibited phosphodiesterase by 2.05±5.33%.[56]

13. Anti-histaminic activity

The Unani eye drop, containing *Berberis aristata* DC. (stem wood), *Cassia absus* Linn. (seed), *Coptis teeta* Wall. (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. It was found to counteract the effects of histamine on tissue. Increasing doses of the test medication resulted in gradual inhibition of histamine-induced contraction of isolated guinea pig ileum.[57]

14. Anti-malarial activity

Goswami et al., 2021 conducted an *in vitro* study to evaluate the anti-malarial activity of methanol extracts derived from *C. teeta*. Their findings demonstrated 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, including molecular docking, molecular dynamics simulation, and DFT analysis, provided compelling evidence that noroxyhydrastinine, a bioactive compound found in *C. teeta*, holds promise as a potent anti-malarial agent.[58]

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] 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. Elemental analysis using EDXRF 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., 2019** reported that *C. teeta* rhizome contains 0.8% w/w berberine, while **Latif et al., 2008** reported a higher concentration of 8-8.5%.[29,60] The root of *C. teeta* has a berberine content of 6-7%, while the stem and leaf have lower concentrations of 2-3% and 1-1.97%, respectively.[34] **Chen et al., 2017** 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 of 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]

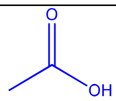
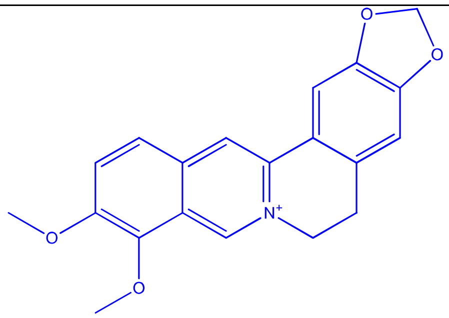
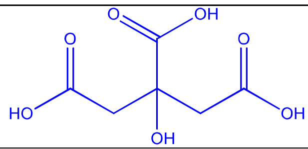
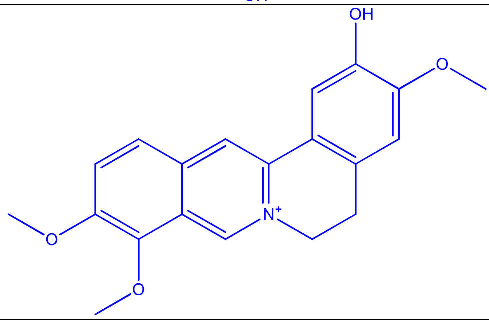
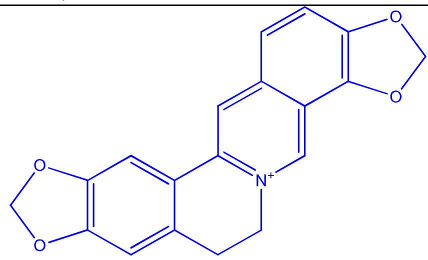
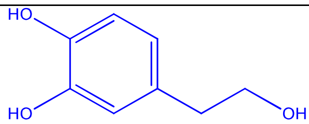
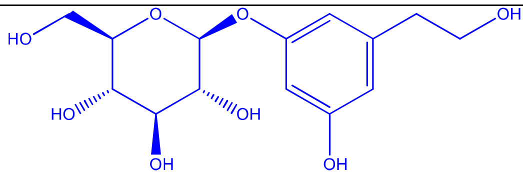
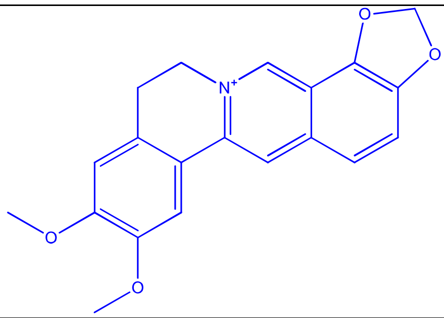
In a 2018 study, **Li et al.** conducted a quantitative analysis of the organic acid content of three Coptis species: *C. chinensis*, *C. teeta*, and *C. deltoidea*. They found that *C. teeta* had the highest total organic acid content (45 mg/g), which was approximately three times higher than that of *C. chinensis* and *C. deltoidea*. Specifically, *C. teeta* had the highest concentrations 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 that of *C. chinensis* and *C. deltoidea*. These findings suggest that *C. teeta* has a higher quality than *C. chinensis* and *C. deltoidea*, based on its higher content of organic acids.[36]

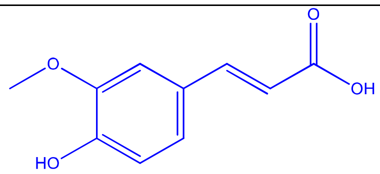
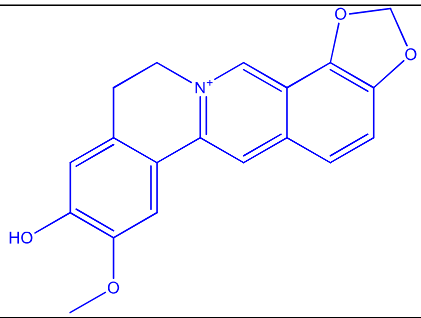
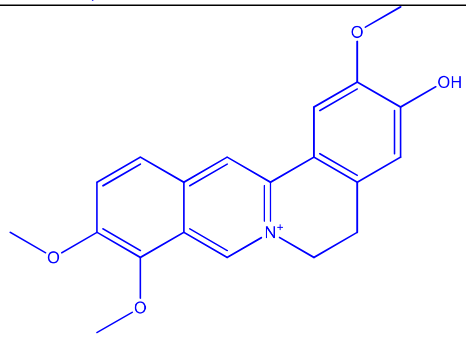
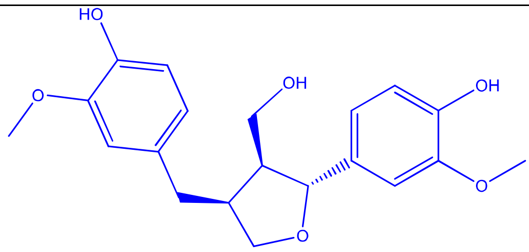
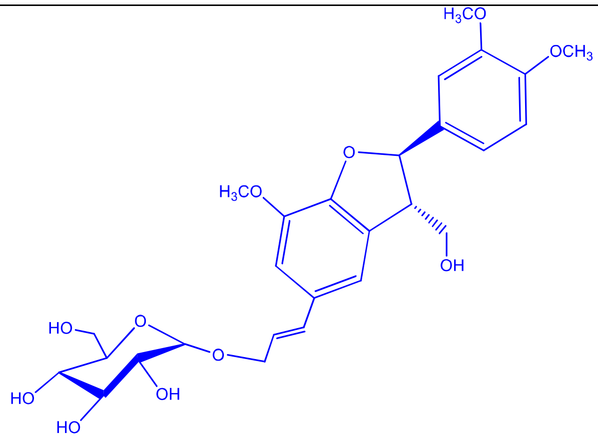
In 2013, **Meng et al.** used a variety of chromatographic methods to isolate and purify twelve compounds from the ethanol extract of *C. teeta*. The structures of these compounds were determined using spectral techniques and physicochemical properties. The twelve compounds identified were ferulic acid, 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]

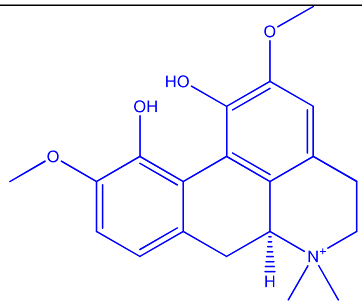
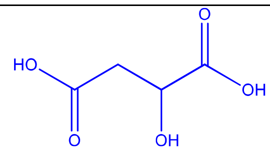
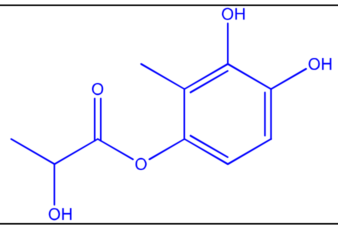
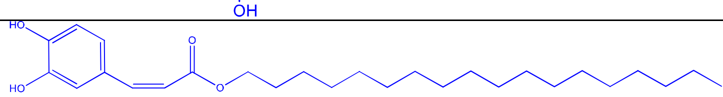
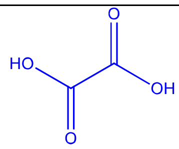
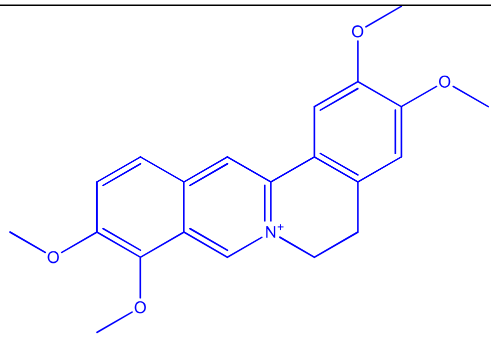
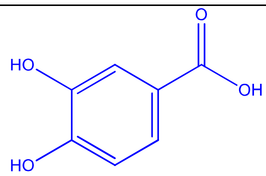
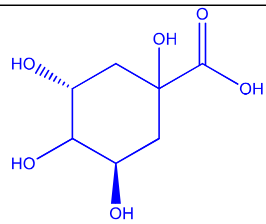
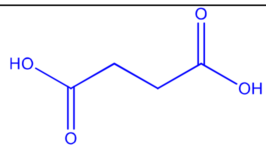
For the first time, **Chen et al., 2020** reported the presence of magnoflorine and groenlandicine in *C. teeta*.[63]

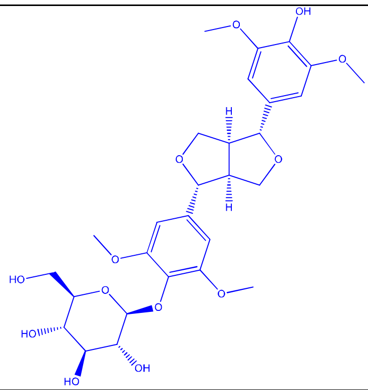
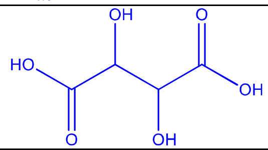
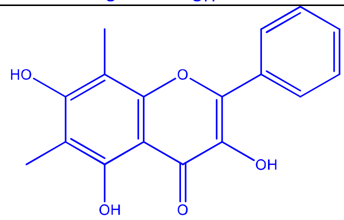
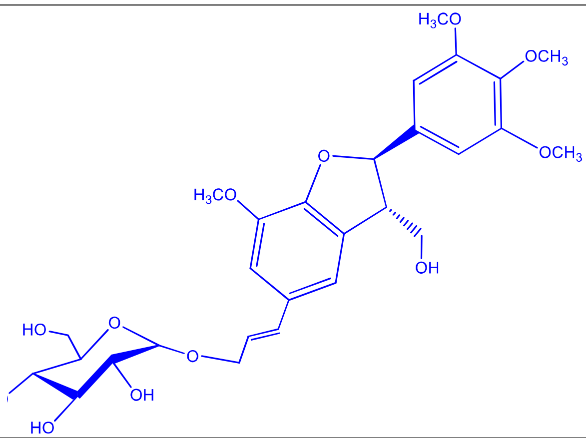
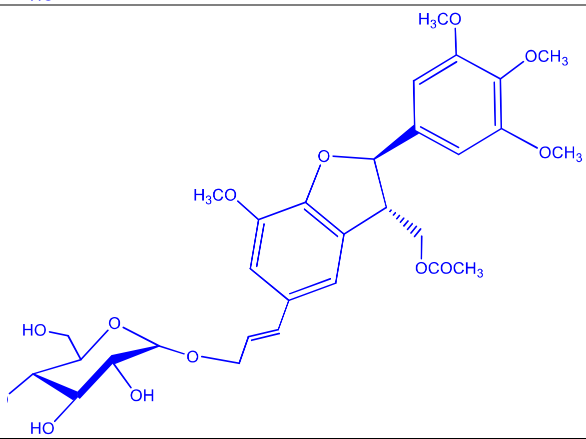
Table 1: Compounds with their structures

SL No	Compounds	Structures

1	Acetic acid	
2	Berberine	
3	Citric acid	
4	Columbamine	
5	Coptisine	
6	3,4-Dihydroxyphenethyl alcohol	
7	3,5-Dihydroxyphenethyl alcohol-3-O-β-D-glucopyranoside	
8	Epiberberine	

9	Ferulic acid	
10	Groenlandicine	
11	Jatrorrhizine	
12	(+)-Lariciresinol	
13	Longifolroside A	

14	Magnoflorine	
15	Malic acid	
16	Methyl-3,4-dihydroxyphenyl lactate	
17	*Z*-Octadecyl caffeate	
18	Oxalic acid	
19	Palmatine	
20	Protocatechuic acid	
21	Quinic acid	
22	Succinic acid	

23	(+)-Syringaresinol-4-O-β-D-glucopyranoside	
24	Tartaric acid	
25	3,5,7-Trihydroxy-6,8-dimethylflavone	
26	Woorenoside I	
27	Woorenoside II	

Liu et al., 2019 delved into the intricate relationship between endophytic bacteria and berberine content in both wild-type and cultivated *C. teeta* Wall. 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 their potential to enhance berberine yield and promote food and medicine safety.[64]

Comparison of main Chemical constituents with a few related species

Chen et al., 2017 investigated the alkaloid content of four Coptis species (*C. chinensis*, *C. teeta*, *C. deltoidea*, and *C. omeiensis*) using high-performance liquid chromatography (HPLC). The alkaloid content varied among the four species and between 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 2: Variation in alkaloid content

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. deltoidei	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

Employing the HPLC method, **Li et al., 2020** determined the contents (mg/g) of six alkaloids and 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 were influenced by the sample origin. Epiberberine, coptisine, and palmatine were found in significantly higher concentrations in *C. chinensis* compared to *C. deltoidea* and *C. teeta*. Conversely, berberine levels were significantly higher in *C. chinensis* and *C. teeta* compared to *C. deltoidea*. Notably, *C. deltoidea* exhibited the lowest total alkaloid concentration, while *C. chinensis* possessed an almost twofold higher total alkaloid content.[65] Data are shown in **Table 3**.

Table 3: Variation in alkaloid content

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. deltoidei	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

In 2012, **Fan et al.** used principal component analysis (PCA) and analysis of variance (ANOVA) 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 than the other two species, and significantly lower levels of jatrorrhizine. *C. deltoidea* had the highest levels of sucrose, and *C. teeta* had the highest levels of chlorogenic acid. The authors concluded that the chemical composition of *Coptis* species is specific and that the levels of different compounds can be used to distinguish between the three species.[66] A study by **Singh et al., 2020** revealed that the roots of *C. deltoidea* and *C. teeta* possess the highest concentrations of jatrorrhizine and berberine, respectively.[67] **Li et al., 2019** undertook a study to investigate the free amino acid composition of three closely related Coptis species: *C. chinensis* Franch., *C. teeta* Wall., and *C. deltoidea* C.Y. Cheng et Hsiao. Employing an automated amino acid analyzer, they determined the content of 20 free amino acids in each species to elucidate their differences. Their findings revealed that *C. chinensis* exhibited significantly higher levels of the major amino acids asparagine (Asn), arginine (Arg), and γ-aminobutyric acid (GABA) compared to the other two species. Additionally, aspartic acid (Asp) content was significantly higher in *C. deltoidea*. The study concluded that Asn can be used as a diagnostic marker to distinguish *C. deltoidea*, *C. chinensis*, and *C. teeta*, while glutamine (Gln) and Arg can be used to differentiate *C. teeta* from *C. chinensis* and *C. deltoidea*.[68]

Conservation and Cultivation Practice

In recent years, the cultivation of *C. teeta*, a valuable medicinal plant native to the Eastern Himalayas, has gained traction among locals in Arunachal Pradesh and Nagaland. While Nagaland's cultivation efforts are still relatively small-scale, Arunachal Pradesh's Forest Department has actively embarked on *C. teeta* cultivation. Propagation methods include raising seedlings from seeds collected from mature plants or transplanting wildings from natural habitats.[5] In the Yunnan province of China, the Lisu people have skillfully integrated *C. teeta* cultivation into their traditional agroforestry practices, demonstrating a harmonious balance between agriculture and environmental stewardship. Their cultivation methods, 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., 2019** 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 to 1.03%), available nitrogen (231.95 to 299.16 kg/ha), phosphorus pentoxide (17.11 to 22.11 kg/ha), and potassium oxide (186.19 to 273.11 kg/ha) at a pH of 4.5 to 5.6. Propagation was achieved through the use of rhizomes and seeds.[69] A study by **Mishra et al., 2023**, 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 is deemed more suitable for this species due to its restricted habitat distribution and challenging cultivation requirements.[70]

Conclusion

This review summarizes the traditional and pharmacological uses, and chemical constituents of *Coptis teeta*, and compares 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. This review reports the structures of 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 8-8.5% w/w. The Adi, Minyong (a sub-tribe of Adi), Galo, Memba, Nyishi, and Tagin groups of Arunachal Pradesh, Tibetans and Lhoba people of Tibet, and 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, it is now an endangered species due to habitat loss, overcollection, and low reproductive success. Further research is needed to fully understand the potential of *C. teeta* and to 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. Additionally, public awareness campaigns could 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.

Conflicts of interest

There are no conflicts to declare.

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