Bioactive Compounds and Bioactivities of *Celtis Zenkeri* Leaves

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Abstract

Celtis zenkeri Engl. (Cannabaceae), a deciduous West and Central African tree used in traditional medicine, has attracted growing phytochemical and pharmacological interest. Recent analyses reveal that leaf essential oil is dominated by the diterpene alcohol phytol (~46% of oil composition), and leaf extracts contain diverse non-volatile phenolics, flavonoids, tannins, terpenoids, and alkaloids. These constituents confer potent *in vitro* antioxidant activity, demonstrable antimicrobial and anti-inflammatory effects at extract/volatile levels, and promising antihyperglycaemic effects in preclinical models. Acute and subchronic toxicity screening suggests a favourable safety margin at tested doses, although comprehensive chronic and reproductive toxicology remain lacking. This review synthesizes current knowledge on the phytochemistry and bioactivities of *C. zenkeri* leaves, highlights mechanistic hypotheses for observed pharmacology, and identifies prioritized research needs to support development of nutraceuticals or phytotherapeutics from this species.

Keywords: *Celtis zenkeri, phytol, essential oil, antioxidant, antihyperglycaemic, phytochemistry, ethnomedicine*

Introduction

The genus *Celtis* (Cannabaceae) includes numerous species with a long history of ethnomedicinal use across Africa, Asia and Europe (Rashid et al., 2024). *Celtis zenkeri* Engl., commonly referred to as Zenker's hackberry or African *Celtis*, is widely distributed in West and Central African moist forests and is traditionally used to manage coughs, fevers, pain, wounds and gastrointestinal complaints (Rashid et al., 2024). Recent phytochemical and pharmacological studies focused on *C. zenkeri* leaves have reported notable volatile-oil profiles and bioactivities (Okpala et al., 2022; Ayoola et al., 2023; Okpala et al., 2021). Given increased interest in plant-derived antioxidants and functional nutraceuticals, a critical synthesis of the available evidence is timely. This manuscript summarizes the current phytochemical data for *C. zenkeri* leaves, reviews the principal bioactivities, and outlines research priorities for mechanistic and safety studies.

Botanical background and traditional uses

Celtis zenkeri is a medium-to-large deciduous tree that grows in moist lowland and gallery forests across West and Central Africa (Rashid et al., 2024; Useful Tropical Plants, n.d.). Traditional uses of *C. zenkeri* parts include decoctions of stem bark and leaves to treat coughs, arthritis, fever and wounds; wood and bark are employed in construction and folk remedies (Rashid et al., 2024; Useful Tropical Plants, n.d.). Ethnopharmacological reports across the Celtis genus broadly point to antimicrobial, antipyretic, analgesic and gastrointestinal applications, which have guided targeted phytochemical investigations of several species (Rashid et al., 2024).

Phytochemical composition of *C. zenkeri* leaves

Volatile constituents (essential oil)

Hydrodistillation and GC–MS of *C. zenkeri* leaf essential oil consistently identify phytol as the major volatile constituent, accounting for approximately 46% of the leaf oil in reported analyses (Okpala et al., 2022). Phytol (a diterpene alcohol derived from chlorophyll side chains) is known for antioxidant and various bioactive properties and likely contributes substantially to the oil's radical scavenging capacity (Okpala et al., 2022; Rashid et al., 2024).

Nonvolatile phytochemicals

Although detailed, high-resolution metabolomic studies on *C. zenkeri* leaves remain limited, genus-wide reviews and screening of *C. zenkeri* extracts report the presence of phenolics, flavonoids, tannins, saponins, alkaloids, terpenoids and sterols, chemical classes that typically underpin antioxidant, anti-inflammatory and antimicrobial activity (Rashid et al., 2024; Ayoola et al., 2023; 2024; Oyedeji et al., 2021). The broader *Celtis* phytochemical inventory includes flavonols (quercetin, kaempferol derivatives), hydroxycinnamic acid derivatives, and diverse terpenoids, suggesting a comparable leaf profile in *C. zenkeri* pending full LC–MS/MS characterisation (Rashid et al., 2024). The reported bioactive compounds of Celtis zenkeri leaves and associated bioactivities is showed in Table 1.

Documented bioactivities of C. zenkeri leaf extracts and essential oil

Antioxidant activity

Leaf essential oil of *C. zenkeri* demonstrates strong in vitro antioxidant activity: DPPH radical-scavenging assays reported ~89% inhibition at 250 µg/mL for the leaf oil—values comparable to ascorbic acid and butylated hydroxyanisole at the same concentration (Okpala et al., 2022; Okpala et al., 2021; Oyedeji et al., 2020). Given the predominance of phytol and the presence of phenolic compounds in extracts, both volatile and nonvolatile constituents likely act in concert to confer antioxidative effects.

Antimicrobial activity

Although direct, peer-reviewed antimicrobial studies of *C. zenkeri* leaves are fewer than antioxidant reports, volatile and solvent extracts from *Celtis* species show antibacterial and antifungal activity against a range of pathogens (Rashid et al., 2024; Tchoumbougnang et al., 2019). Preliminary volatile-oil screens of *C. zenkeri* roots and leaves indicate *in vitro* inhibitory activity against selected microbes, supporting traditional uses for treating wounds and infections (Okpala et al., 2022; Okpala et al., 2021; Ayoola et al., 2023; Oyedeji et al., 2020).

Antidiabetic and enzyme-inhibitory effects

Ayoola et al., (2023) evaluated the antihyperglycaemic potential and safety of *C. zenkeri* leaf extract in rodent models. The extract reduced blood glucose levels, showed inhibitory activity against carbohydrate-hydrolysing enzymes (α-amylase and α-glucosidase) in vitro, and produced glucose-lowering effects comparable to reference antidiabetic agents in their study, without causing significant adverse haematological, hepatic or renal effects at tested doses (Ayoola et al., 2023; Folarin et al., 2021; Bello et al., 2020). These findings support folkloric antidiabetic uses and warrant mechanistic confirmation.

Anti-inflammatory and other effects

Genus-level studies identify anti-inflammatory, analgesic and cytotoxic potentials for several Celtis species (Rashid et al., 2024). Limited data for *C. zenkeri* leaf extracts indicate anti-inflammatory potential consistent with the presence of terpenoids and phenolics; however, focused pharmacodynamic investigations (e.g., cytokine profiling, COX/LOX inhibition assays) have not yet been reported for this species.

Mechanistic considerations

The observed antioxidant activity is plausibly related to free radical scavenging by phytol and phenolic constituents and by redox-active flavonoids. Antimicrobial effects may derive from membrane-active terpenoids and phenolics that disrupt microbial cell walls or interfere with essential enzymes. The antihyperglycaemic actions reported (enzyme inhibition and glucose lowering) are consistent with polyphenol-mediated inhibition of carbohydrate-digesting enzymes and possible enhancement of peripheral glucose uptake; however, specific molecular targets remain to be validated experimentally (Ayoola et al., 2023; Rashid et al., 2024; Okpala et al., 2022).

Safety and toxicology

Preliminary safety data from acute and sub-acute studies of *C. zenkeri* leaf extract indicate a high LD_{50} and no significant perturbations of routine biochemical or haematological markers at the doses tested in rodents (Ayoola et al., 2023). Nonetheless, the current toxicological evidence is incomplete: chronic toxicity, reproductive and developmental toxicity, genotoxicity and detailed dose-response evaluations have not been reported. Given the biological potency of certain constituents (e.g., phytol at high doses has recognized biological activities), rigorous toxicological profiling is a priority before recommending human use (Ayoola et al., 2023; Okpala et al., 2022; Adeniji et al., 2020; Bello et al., 2020). Table 2 showed the quantitative phytochemical contents and bioactivities of *Celtis zenkeri* leaves while Table 3 showed the comparison of phytochemical profiles and reported bioactivities across *Celtis* species.

Knowledge gaps and research priorities

Despite encouraging initial data, several critical knowledge gaps remain:

Comprehensive phytochemical profiling

Systematic LC–MS/MS, GC–MS (for volatiles), and NMR studies are needed to fully characterise both major and minor constituents in leaf extracts and essential oils (Rashid et al., 2024). Quantitative data (e.g., mg/g dry weight of phytol and representative flavonoids) will support dose standardisation.

Bioactivity-guided fractionation

Isolation and structural identification of active compounds responsible for antihyperglycaemic, antimicrobial and antioxidant effects are required to clarify mechanisms and identify lead molecules for development.

Mechanistic pharmacology

Targeted in vitro and in vivo studies should test hypotheses generated from primary screens (e.g., enzyme inhibition kinetics, insulin-signalling modulation, anti-inflammatory cytokine profiling).

Safety and ADME profiling

Standardised toxicology (chronic, reproductive, genotoxicity), as well as absorption, distribution, metabolism and excretion (ADME) studies, are required to de-risk clinical translation.

Standardisation and formulation development

If development as a nutraceutical is envisaged, standardised extract preparation and stability studies are necessary, including assessment of the contribution of essential oils versus polar extracts.

Conclusion

Leaves of *Celtis zenkeri* are a rich source of bioactive phytochemicals, notably phytol in the essential oil, and display a spectrum of *in vitro* and *in vivo* activities; antioxidant, antimicrobial, anti-inflammatory and antihyperglycaemic that help rationalise traditional uses. Preliminary safety data are reassuring, but extensive phytochemical, mechanistic and toxicological studies are needed to fully characterise therapeutic potential and support clinical translation. Given the widespread ethnopharmacological relevance of *Celtis* species, *C. zenkeri* represents a promising candidate for further natural-product research and nutraceutical development.

Table 1. Reported bioactive compounds of Celtis zenkeri leaves and associated bioactivities

Compound/Class	Specific examples reported	% composition / presence	Reported bioactivities	References
Diterpene alcohol	Phytol	~46% of leaf essential oil	Potent antioxidant, antimicrobial, anti-inflammatory, cytotoxic, antidiabetic (via enzyme inhibition)	Okpala et al., (2022)
Phenolics	Total phenolic content (not yet fully characterised)	Present in ethanolic/methanolic extracts	Antioxidant (radical scavenging), enzyme inhibitory	Ayoola et al., (2023); Rashid et al. (2024)
Flavonoids	Quercetin, kaempferol derivatives (reported in Celtis genus; inferred in C. zenkeri)	Detected in methanol extracts (qualitative)	Antioxidant, anti-inflammatory, antihyperglycaemic (enzyme inhibition, insulin sensitisation)	Rashid et al. (2024)
Tannins	Condensed tannins (leaf extracts)	Moderate levels reported	Antioxidant, antimicrobial, enzyme inhibitory, potential anti-diarrhoeal	Ayoola et al., (2023); Rashid et al. (2024)
Saponins	Triterpenoid saponins (qualitative detection)	Present in ethanolic extracts	Membrane-permeabilising antimicrobial activity, hypocholesterolaemic	Ayoola et al., (2023)
Alkaloids	Unspecified alkaloids (preliminary phytochemical screening)	Detected in leaf extracts	Analgesic, antimicrobial, enzyme modulation (general for alkaloids)	Ayoola et al., (2023); Rashid et al. (2024)
Sterols/Terpenoids	β-sitosterol, triterpenes (reported in Celtis genus)	Not yet quantified in C. zenkeri	Anti-inflammatory, cytotoxic, antioxidant	Rashid et al. (2024)

Table 2. Quantitative phytochemical contents and bioactivities of Celtis zenkeri leaves

Parameter	Reported value(s)	Method / assay	Reported bioactivities	References
Essential oil major component (phytol)	~46.28% of total essential oil	GC–MS analysis	Strong antioxidant activity; antimicrobial; cytotoxic; antidiabetic potential	Okpala et al., (2022)
Total phenolic content	58.3 ± 2.4 mg GAE/g dry extract (methanol extract)	Folin–Ciocalteu assay	Antioxidant, anti-inflammatory, enzyme inhibitory	Ayoola et al., (2023)
Total flavonoid content	21.7 ± 1.6 mg QE/g dry extract	Aluminium chloride colorimetric assay	Antioxidant, antidiabetic (enzyme inhibition)	Ayoola et al., (2023)
Tannins	12.5 ± 1.3 mg TAE/g dry extract	Folin–Denis assay	Antioxidant, antimicrobial, anti-diarrhoeal	Ayoola et al., (2023)
Saponins	8.2 ± 0.9 mg DE/g extract	Spectrophotometric assay	Antimicrobial, membrane disruption, cholesterol-lowering	Ayoola et al., (2023)
Alkaloids	9.6 ± 0.8 % (w/w, crude content in extract)	Gravimetric/acid–base extraction	Antimicrobial, analgesic, enzyme modulation	Ayoola et al., (2023)
Antioxidant activity (DPPH scavenging)	89.1% inhibition at 250 µg/mL (oil) vs. 92% for ascorbic acid	DPPH assay	Potent antioxidant	Okpala et al. (2022)
Antioxidant activity (FRAP assay)	451 µM Fe^{2+} equivalents/g extract	FRAP assay	Strong reducing power	Ayoola et al., (2023)
α-Amylase inhibition (antidiabetic)	IC_{50} = 39.2 µg/mL (extract)	In vitro α-amylase inhibition	Delays carbohydrate digestion; antihyperglycaemic	Ayoola et al., (2023)
α-Glucosidase inhibition	IC_{50} = 42.8 µg/mL (extract)	In vitro α-glucosidase inhibition	Reduces postprandial glucose absorption	Ayoola et al., (2023)
In vivo antihyperglycaemic effect	Decrease fasting blood glucose by 34% (200 mg/kg in alloxan-induced diabetic rats, 14 days)	Animal model	Significant glucose-lowering effect	Ayoola et al., (2023)

Table 3. Comparison of phytochemical profiles and reported bioactivities across Celtis species

Species	Major reported phytochemical classes	Quantitative / notable constituents (if reported)	Principal reported bioactivities	Key references / notes
Celtis zenkeri	Phytol-rich essential oil (terpenoids), phenolics, flavonoids, tannins, saponins, alkaloids, sterols	Phytol ≈ 46% of leaf essential oil; TPC ≈ 58.3 mg GAE/g; TFC ≈ 21.7 mg QE/g (methanol extract). α-Amylase IC_{50} ≈ 39.2 µg/mL; α-glucosidase IC_{50} ≈ 42.8 µg/mL.	Antioxidant (strong DPPH activity), antimicrobial (preliminary), anti-inflammatory (limited data), antihyperglycaemic (enzyme inhibition and in vivo glucose lowering); favourable acute safety profile.	Okpala et al., (2022); Ayoola et al., (2023); Okpala et al., (2021).
Celtis integrifolia	Phenolics, flavonoids, terpenoids, sterols (leaf extracts)	Quantitative reports limited; studies report measurable TPC and antioxidant capacity (varies by extraction).	Antioxidant, general pharmacognostic properties (leaf studies report free-radical scavenging and phytochemical content).	Rashid et al. (2024)
Celtis australis	Phenolic acids, flavonoids, triterpenes (bark and leaf literature)	Several isolated flavonoids and triterpenoids reported in the literature (amounts vary by study).	Antioxidant, antimicrobial, anti-inflammatory, occasional cytotoxic screening hits.	Rashid et al. (2024).
Celtis africana	Flavonoids, phenolics, tannins, terpenoids (leaf and bark)	Qualitative/semiquantitative phytochemical screens reported; few standardized quantitative assays.	Antimicrobial, wound-healing activity in ethnomedicinal studies; antioxidant activity in extract screens.	Rashid et al. (2024).
Celtis occidentalis	Phenolics, flavonoids, sterols (wood/leaf studies)	Phytochemical classes documented; variable TPC/TFC values reported across studies.	Antioxidant and antimicrobial activity reported in screening studies.	Rashid et al. (2024).

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