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Zingiber neesanum vs. the Genus Zingiber: Phenylbutanoid-Dominant Chemistry, Chemotaxonomic Distinction, and Emerging Therapeutic Promise: A Comprehensive Review

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Abstract: *Zingiber neesanum (Graham) Ramamoorthy, an understudied rhizomatous herb endemic to the Western Ghats of India, holds ethnomedicinal value for treating inflammation, gastrointestinal disorders, colds, fever, and respiratory ailments, yet it remains less explored than commercial relatives like Zingiber officinale. This comprehensive review synthesizes available phytochemical data, primarily from rhizome essential oil analyses, revealing a distinctive phenylbutanoid-dominated profile. Major constituents include (E)-1-(3',4'-dimethoxyphenyl)butadiene (DMPBD, ~31.1%), (E)-1-(3',4'-dimethoxyphenyl)but-1-ene (~23.1%), (E)-β-ocimene (~12.7%), β-pinene (~7.4%), and, in Konkan-region samples, elevated (E)-3,4-dimethoxy cinnamic acid methyl ester ([E]-3,4-DCME) contributing to ~62% phenylpropanoids. This composition positions Z. neesanum within the phenylpropanoid/terpenoid-rich chemotype of the genus Zingiber, contrasting with gingerol-dominant or zerumbone-centric taxa. Non-volatile phenolics and flavonoids are inferred from related studies but require confirmation via targeted metabolomics. Emerging in vitro, in silico, evaluations demonstrate promising antimicrobial (e.g., against Staphylococcus aureus and Candida albicans), antioxidant (DPPH/ABTS/FRAP), and anti-inflammatory (albumin denaturation inhibition) activities, linked to phenylpropanoids, and favourable pharmacokinetics. These findings support traditional uses and highlight therapeutic promise. However, significant gaps remain in non-volatile profiling (LC-MS/HRMS/NMR), bioassay-guided isolation, population-level chemotype variability, and comprehensive preclinical validation. As a narrow endemic in a biodiversity hotspot, Z. neesanum warrants priority for advanced metabolomics, pharmacological advancement, and conservation-integrated research to harness its potential in natural product discovery and sustainable utilization.*

Keywords: *Zingiber neesanum*, Zingiberaceae, Essential oil, Phenylbutanoids, Antioxidant properties, Anti-inflammatory effects, Western Ghats endemics

1. Introduction

Medicinal plants remain cornerstone sources of bioactive compounds, fuelling drug discovery, traditional healthcare systems, and nutraceutical development. Over 80% of the world's population relies on plant-based remedies, and many modern therapeutics trace their origins to natural products. The Zingiberaceae family stands out for its aromatic rhizomatous species, rich in secondary metabolites with applications in food, cosmetics, and medicine. These plants exhibit a broad spectrum of bioactivities, including antioxidant, anti-inflammatory, antimicrobial, hepatoprotective, and anticancer effects, owing to constituents like terpenoids, gingerols, phenolics, and flavonoids [1].

The genus Zingiber encompasses over 150 species, predominantly distributed across tropical and subtropical Asia, with India serving as a major centre of diversity. Well-documented species such as ginger (*Z. officinale*), zerumbet (*Z.*

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zerumbet), and cassumunar (*Z. cassumunar*) are prized for their essential oils abundant in sesquiterpenes, gingerols, diarylheptanoids, and phenolics. Phytochemical diversity in Zingiber arises from conserved biosynthetic pathways influenced by ecological, genetic, and environmental factors, aiding in bioactive compound identification and evolutionary studies [2].

While commercial Zingiber species receive extensive research attention, endemic taxa like *Z. neesanum* are overlooked. This perennial herb, endemic to India's Western Ghats, a global biodiversity hotspot, exhibits a faint aroma and has ethnobotanical documentation for alleviating inflammation, digestive ailments, colds, fever, and respiratory issues. Limited investigations focus on its rhizome essential oil, revealing phenylbutanoid dominance. This comprehensive review compiles chemical data on *Z. neesanum*, analyzes its metabolites, compares them with other Zingiber taxa to discern chemotaxonomic patterns, and identifies research gaps. It aims to establish a robust foundation for advanced metabolomics, bioactivity-guided isolation, and pharmacological evaluation, potentially elevating Z. neesanum's role in natural product innovation [3,4].

1.1 Historical Context and Ethnobotanical Relevance

Z. neesanum's ethnobotanical use dates back to indigenous communities in the Western Ghats, where tribes like the Malaipandaram utilize Zingiberales plants, including *Z. neesanum*, for various ailments. Traditional applications include rhizome decoctions for gastrointestinal relief and poultices for inflammatory conditions. In Kerala and Tamil Nadu, it is known locally as "Kattukolinchi", meaning wild ginger, and used in folk remedies for fever and colds. These uses align with broader Zingiberaceae ethnopharmacology, where rhizomes are valued for their warming, digestive, and anti-inflammatory properties [5]. Nomenclatural history reveals complexities: Originally described as *Alpinia neesana*, it was later transferred to Zingiber. Recent studies clarify its identity, distinguishing it from similar taxa like *Z. anamalayanum*, with *Z. neesanum* predominant in the northern Western Ghats. This taxonomic resolution is crucial for accurate ethnobotanical and phytochemical studies [6].

1.2 Ecological and Conservation Significance

As an endemic species, *Z. neesanum's* restricted distribution underscores its vulnerability to habitat loss in the Western Ghats. Conservation efforts must integrate ethnobotanical knowledge to promote sustainable harvesting, potentially through cultivation programs [7].

2. Botanical Overview and Distribution

Zingiber neesanum is a perennial rhizomatous herb in the Zingiberaceae family, characterized by fleshy rhizomes, pseudostems formed from leaf sheaths, and broad lanceolate leaves. Inflorescences emerge directly from rhizomes, producing cadmium yellow flowers in spikes measuring 6–25 cm (up to 45 cm), enclosed by bracts. Unlike strongly aromatic gingers, its rhizomes emit a faint scent. The plant follows a seasonal cycle, thriving during monsoons and entering dormancy in dry periods [6].

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Fig. 1. Young plant

Mature plant

2.1 Morphological Details

Rhizomes are horizontal, branched, and pale yellow internally. Leaves are sessile or shortly petiolate, oblong-lanceolate, 15–35 cm long, with acuminate tips and entire margins. Flowers are tubular, with a yellow corolla and a labellum spotted purple. Fruits are capsules containing arillate seeds [8].

2.2 Habitat and Distribution

Endemic to peninsular India, *Z. neesanum* inhabits the Western Ghats, spanning Kerala (Wayanad), Tamil Nadu (Megamalai Wildlife Sanctuary, Theni), and Maharashtra's Konkan region. It thrives in well-drained, iron-rich soils within moist deciduous forests, open scrubs, and monsoon ecosystems at elevations of 500–1500 m. Populations are fragmented, reflecting ecological specificity and sensitivity to habitat disturbance. This distribution pattern is typical of Western Ghats endemics, suggesting adaptive metabolites for environmental stress [9].

2.3 Conservation Status

Listed as vulnerable due to habitat fragmentation, *Z. neesanum* benefits from protected areas like Bhimashankar Wildlife Sanctuary. Sustainable ethnobotanical practices are essential to prevent overexploitation [10].

3. Phytochemical Investigations of Zingiber neesanum

Phytochemical studies on *Zingiber neesanum* have primarily focused on its rhizome essential oil, reflecting the species' traditional ethnomedicinal applications and its characteristic faint aroma [3,4]. The oil is typically obtained by hydrodistillation, producing a pale-yellow volatile fraction with a mild scent [4]. Gas chromatography-mass spectrometry (GC-MS) has been the principal analytical technique, enabling identification of constituents via mass spectral comparison, retention indices, and co-injection with standards [4,8].

The essential oil displays a phenylbutanoid-rich profile, consistent with certain chemotypes within the genus *Zingiber*, where phenylpropanoids and terpenoids predominate over the gingerols or diarylheptanoids more typical of commercially important species [2]. More than 60 compounds have been detected, representing 97–99% of the total oil composition, with phenylbutanoids constituting the major fraction (~62%) [4]. Non-volatile constituents such as phenolics and flavonoids are expected based on patterns observed across the Zingiberaceae family, but direct evidence in *Z. neesanum* remains limited and requires confirmation through targeted LC-MS or HRMS-based metabolomic approaches [1,8].

Compositional variation has been observed across Western Ghats populations: southern collections tend to show greater terpenoid diversity, whereas northern (e.g., Konkan) samples exhibit elevated levels of certain phenylpropanoid derivatives [11]. These differences are likely influenced by environmental factors, including soil composition (e.g.,

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iron-rich lateritic soils), altitude, and seasonal monsoon conditions in fragmented habitats. Such variability underscores the ecological adaptability of the species and emphasizes the need for geographically representative sampling in future chemotaxonomic and bioactivity studies [11].

3.1 Essential Oil Composition

The rhizome essential oil of *Z. neesanum* is characterized by a high proportion of phenylbutanoids, which account for approximately 62% of the total composition [4]. The dominant constituents are (E)-1-(3',4'-dimethoxyphenyl) butadiene (DMPBD, ~31.1%) and (E)-1-(3',4'-dimethoxyphenyl) but-1-ene (~23.1%), both identified and quantified through detailed spectral analysis (IR, UV, ^{1}H-NMR, MS) in the foundational study [4]. Monoterpenoids contribute additional diversity, including (E)-β-ocimene (~12.7%), β-pinene (~7.4%), and linalool (~4.0%) [4]. In certain northern Western Ghats samples, (E)-3,4-dimethoxy cinnamic acid methyl ester ([E]-3,4-DCME) is a notable phenylpropanoid component [11].

Table 1. Major Constituents of Zingiber neesanum Rhizome Essential Oil

(Based primarily on southern Western Ghats data [4]; regional notes from [11])

Compound	Approximate Percentage	Key Notes / Bioactivity Links	Reference
(E)-1-(3',4'-dimethoxyphenyl) butadiene (DMPBD)	~31%	Major phenylbutanoid; linked to anti-inflammatory potential	[4]
(E)-1-(3',4'-dimethoxyphenyl) but-1-ene	~23%	Significant phenylbutanoid; supports antimicrobial activity	[4]
(E)-β-ocimene	~13%	Major terpenoid; associated with antioxidant and antifungal effects	[4]
β-Pinene	~7%	Terpenoid; known antibacterial and anti-inflammatory properties	[4]
Linalool	~4%	Oxygenated monoterpene; contributes to antimicrobial activity	[4]
Other phenylpropanoids (incl. [E]-3,4-DCME in some northern samples)	~62%	Synergistic bioeffects; regional variation observed	[11]

Phenylbutanoids such as DMPBD are associated with anti-inflammatory and antimicrobial properties, likely through mechanisms involving membrane disruption in pathogens and modulation of inflammatory mediators [4,8]. Terpenoids (e.g., β-pinene and ocimene) provide synergistic support for these activities, consistent with broader Zingiberaceae bioactivity patterns [2]. The observed differences in phenylpropanoid proportions across populations (e.g., higher [E]-3,4-DCME in northern samples) may be attributed to habitat-specific factors such as iron-rich soils and habitat fragmentation [8,11]. These phytochemical findings highlight the therapeutic potential of the essential oil, while also indicating the need for more comprehensive non-volatile profiling to fully elucidate the species' medicinal value [1].

3.2 Terpenoid and Sesquiterpenoid Chemistry

Terpenoids constitute the principal class of volatile constituents in *Zingiber* species and are biosynthetically derived from the universal C5 precursors isopentenyl diphosphate (IPP) and dimethylallyl diphosphate (DMAPP) via the mevalonate (MVA) and methylerythritol phosphate (MEP) pathways. In rhizomatous taxa, these pathways give rise predominantly to monoterpenes (C10) and sesquiterpenes (C15), which define the characteristic aroma, ecological interactions, and pharmacological potential of the genus [12].

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In the present context, compounds such as β-pinene, ocimene, and linalool represent common monoterpenoid constituents, while sesquiterpene hydrocarbons and their oxygenated derivatives dominate the essential oil fraction. These molecules are synthesised through terpene synthase–mediated cyclisation of geranyl diphosphate (GPP) and farnesyl diphosphate (FPP), followed by oxidation, rearrangement, or modification of functional groups. The presence of such terpenoids indicates conserved biosynthetic machinery across medicinally important *Zingiber* species and supports chemotaxonomic relationships within the genus [13].

Sesquiterpenes often contribute more significantly to biological activity than monoterpenes due to their structural complexity and higher molecular weight. A well-documented example is zerumbone, a monocyclic sesquiterpene isolated from *Zingiber zerumbet*. Zerumbone has demonstrated notable anti-inflammatory, antioxidant, and cytotoxic activities, largely attributed to modulation of NF-κB, MAPK signaling pathways, and induction of apoptosis in various cancer cell lines. The pharmacological prominence of zerumbone underscores the therapeutic relevance of sesquiterpenoid-rich chemotypes in *Zingiber* [14].

Furthermore, oxygenated terpenoids such as alcohols and epoxides enhance bioactivity through increased polarity and reactivity, often improving interactions with biological targets. Variation in terpenoid profiles among species may reflect ecological adaptation, genetic divergence, or environmental influence, thereby offering valuable markers for species authentication and chemotaxonomic classification. Overall, the dominance of mono- and sesquiterpenoids not only defines the organoleptic and ecological attributes of *Zingiber* taxa but also underpins their medicinal significance [15].

3.3 Phenolics, Curcuminoids, and Diarylheptanoids (Probable Constituents)

Although specific reports on phenolic constituents in *Z. neesanum* are currently lacking, members of the genus *Zingiber* are well known to accumulate diverse phenolics, flavonoids, gingerols, shogaols, and diarylheptanoids in addition to volatile terpenoids. Studies on related species such as Zingiber cassumunar and Zingiber officinale demonstrate the co-occurrence of volatile essential oils and non-volatile phenolic fractions contributing to antioxidant and anti-inflammatory activities. Diarylheptanoids and curcuminoid-type compounds are characteristic secondary metabolites within the family Zingiberaceae and often serve as chemotaxonomic markers. Therefore, advanced metabolomic approaches such as LC–MS/MS profiling and NMR-based structural elucidation are recommended to confirm the presence of these probable constituents in *Z. neesanum* [16].

3.4 Other Secondary Metabolites

Zingiber neesanum rhizomes contain diverse secondary metabolites, including high levels of flavonoids (up to 681.94 mg CE/100 g DW in ethyl acetate extract) and tannins, along with steroids and hydrocarbons, contributing to strong antioxidant activity via DPPH and FRAP assays. GC-MS analysis identifies key bioactives such as 2-Methyl-7-nonadecene (13.99%; antimicrobial, effective against gram-negative bacteria like Enterococcus faecalis) and Actinomycin C2 (8.57%; antineoplastic). These compounds, alongside others like Deoxyspergualin, support the plant's antimicrobial, antifungal, and potential therapeutic applications [8].

3.5 Extraction Methods and Yield Variations

Extraction methods for *Z. neesanum* rhizomes significantly influence yield, with ultrasound-assisted solvent extraction achieving an average of 0.6% (e.g., 0.9 mL from 150 g fresh rhizome), outperforming traditional hydrodistillation which typically yields lower amounts due to its thermal and time-intensive nature. This higher efficiency of ultrasound-assisted extraction (USAE) aligns with trends in Zingiber species, where advanced methods enhance recovery of volatile and non-volatile bioactives. Regional variations, such as those between Konkan (Maharashtra) and Wayanad (Kerala) in the Western Ghats, may affect yields and compositions owing to differences in soil, climate, and altitude, though specific comparative data remain limited and warrant further targeted studies [4,8,11].

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4. Comparative Phytochemistry Across the Genus Zingiber

Zingiber species display notable phytochemical variability: *Z. officinale* is characterized by high levels of gingerols (e.g., 6-gingerol) and related pungent compounds, while *Z. zerumbet* is dominated by the sesquiterpenoid zerumbone (often >60% in essential oil). In contrast, *Z. neesanum* aligns more closely with phenylbutanoid/terpenoid-rich taxa such as *Z. cassumunar* (syn. *Z. montanum*), featuring prominent phenylbutanoids like (E)-1-(3′,4′-dimethoxyphenyl) butadiene (31.1%) and (E)-1-(3′,4′-dimethoxyphenyl) but-1-ene (23.1%) alongside terpenoids (e.g., β-ocimene, β-pinene) in its rhizome essential oil. This chemotaxonomic similarity highlights shared biosynthetic pathways for phenylpropanoid-derived compounds in these taxa, distinct from the gingerol- or zerumbone-centric profiles of other Zingiber species [2,4,8,11].

Table 2. Major Phytochemical Classes in Selected Zingiber Species

Species	Major Phytochemicals	Key References
Zingiber officinale	Gingerols, shogaols, zingiberene, flavonoids	[17]
Zingiber zerumbet	Zerumbone, humulene epoxide, flavonoids	[18]
Zingiber cassumunar	Cassumunins, curcuminoids, terpenoids	[19]
Zingiber roseum	Terpenoids (linalool, pinene), phenolics	[20]
Zingiber montanum	Cassumunarins, essential oils	[21]
Zingiber neesanum	Phenylbutanoids, phenylpropanoids, ocimene, pinene	[4,8,11]

Table 3. Comparative Secondary Metabolite Distribution

Metabolite Class	Presence in Genus	Evidence in *Z. neesanum*
Phenylbutanoids	Common	Confirmed
phenylpropanoids	Probable	Confirmed
Sesquiterpenes	Very common	Confirmed
Monoterpenes	Common	Minor
Gingerols	Widespread	Not confirmed
Phenolics	Common	Expected
Flavonoids	Common	Probable
Steroids	Occasional	Possible

These comparisons highlight *Z. neesanum*'s unique phenylbutanoid/phenylpropanoid emphasis.

5. Chemotaxonomic Significance

Phytochemical profiles in the genus *Zingiber* delineate distinct lineages: one characterized by **gingerol-rich** compounds (e.g., *Z. officinale*) and another by **terpenoid/phenylbutanoid-rich** profiles (e.g., *Z. cassumunar*, *Z. montanum*). *Z. neesanum* affiliates with the latter through its dominance of phenylbutanoids such as (E)-1-(3′,4′-dimethoxyphenyl) butadiene (31.1%) and (E)-1-(3′,4′-dimethoxyphenyl) but-1-ene (23.1%) in rhizome essential oil, alongside terpenoids like (E)-β-ocimene and β-pinene, supporting chemotaxonomic alignment with phenylbutanoid/terpenoid taxa. Its faint aroma likely results from relatively low volatile terpenoid accumulation compared to strongly aromatic species, potentially modulated by environmental factors like humidity or soil in the Western Ghats. Advanced metabolomic approaches (e.g., untargeted GC-MS/LC-MS profiling) could resolve intraspecific polymorphism and chemotype-environment interactions [4,8].

5.1 Phylogenetic Implications: Chemotaxonomic data corroborate molecular phylogenies within *Zingiber*, where phenylbutanoid-rich profiles correlate with certain clades. *Z. neesanum* shows closer affinity to other Western Ghats endemics like *Z. nimmonii* and *Z. anamalayanum* (formerly confused with *Z. neesanum* in nomenclature), sharing morphological traits (e.g., long-stalked inflorescences) and potential biosynthetic pathways for specialized metabolites. Broader Zingiberaceae phylogenies (e.g., using ITS, matK, or chloroplast genomes) place *Zingiber* in the

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Zingiberoideae subfamily, with endemics from biodiversity hotspots like the Western Ghats forming localized clusters distinct from widespread species like *Z. officinale*. This supports conservation priorities for these narrow-endemic taxa amid habitat threats [6, 22].

5.2 Chemotype Variations: Population-level studies indicate chemotype diversity in *Zingiber* species, driven by abiotic factors such as altitude, soil composition, and microclimate. For *Z. neesanum*, regional comparisons (e.g., Konkan in northern Western Ghats vs. southern populations) reveal variations in phenylpropanoid/phenylbutanoid ratios and essential oil yields, with Konkan samples showing consistent phenylpropanoid dominance and bioactivity (e.g., anti-inflammatory potential via molecular docking). Analogous examples include *Z. roseum*, where altitudinal gradients alter terpenoid profiles (e.g., higher monoterpenes like linalool/pinene at higher elevations) and pesticidal properties, and *Z. officinale* cultivars exhibiting oleoresin/gingerol variations linked to maturity, region, and soil. These patterns suggest edaphic and elevational influences on secondary metabolism, warranting targeted population sampling for chemotype mapping and conservation [11,22].

6. Pharmacological Potential of Zingiber neesanum

Investigations into *Z. neesanum* remain limited but reveal promising therapeutic prospects, particularly from its rhizome essential oil, which is phenylpropanoid-rich in Konkan-region samples with [E]-3,4-Dimethoxy cinnamic acid methyl ester ([E]-3,4-DCME) as the dominant compound (62.09% phenylpropanoids overall). *In-vitro* assays demonstrate strong antimicrobial effects against *Staphylococcus aureus* and *Candida albicans*, antioxidant potency via DPPH and ABTS methods, and superior anti-inflammatory activity through inhibition of albumin denaturation compared to other tests like heat-induced hemolysis and proteinase inhibition. In silico analyses, including molecular docking (binding affinities -7.01 to -8.15 kcal/mol for [E]-3,4-DCME against trypsin), alongside in vivo safety indicators, position the oil as a candidate for novel phytopharmaceuticals, though further clinical validation is needed [11].

6.1 Antimicrobial Activity: The rhizome essential oil exhibits potent antimicrobial activity, with excellent inhibition against gram-positive *Staphylococcus aureus* (via broth and agar dilution) and the fungus *Candida albicans*, primarily attributed to synergistic effects of phenylbutanoids like DMPBD and terpenoids such as β-pinene (7.4%). Rhizome extracts, particularly chloroform and ethyl acetate, show effective antibacterial action against pathogens including *Pseudomonas aeruginosa* (0.5 cm inhibition zone in chloroform extract), *Bacillus subtilis*, *Actinomycetes sp.*, and *Serratia sp.*, while isopropanol extracts target gram-negative *Enterococcus faecalis* (21.7 ± 0.6 cm zone) due to high tannin content. Antifungal potential is highlighted by activity against *Mucor rouxii* (9.7 ± 0.6 cm), underscoring the plant's broad-spectrum microbicidal efficacy for potential therapeutic applications [4,8,11].

6.2 Antioxidant Activity: *Z. neesanum* rhizome extracts display robust antioxidant capacity, with isopropanol extracts yielding high total tannin (55.261 ± 6.623 mg TAE/100 g DW) and ethyl acetate extracts rich in flavonoids (681.94 ± 33.87 mg CE/100 g DW), contributing to effective free radical scavenging in DPPH (IC_{50} 0.74 mg/mL) and FRAP assays, often comparable to standards like ascorbic acid. This activity is linked to polyphenolics and terpenoids, including those identified via GC-MS, which mitigate oxidative stress through electron donation and metal chelation mechanisms. Essential oil from Konkan samples also shows excellent performance in DPPH and ABTS assays, supporting its role in preventing oxidative damage-related disorders [8,11].

6.3 Anti-inflammatory Activity: Anti-inflammatory effects are pronounced in the rhizome oil, with superior inhibition of albumin denaturation (best among tested methods) and proteinase activity, reflecting modulation of inflammatory pathways by phenylbutanoids such as (E)-1-(3′,4′-dimethoxyphenyl) butadiene (31.1%, potential anti-inflammatory via COX inhibition). Molecular docking studies reveal strong binding affinities (-7.01 to -8.15 kcal/mol) for [E]-3,4-DCME against trypsin, involving H-bonding, Van der Waals, and π-alkyl interactions with active site residues, corroborating in vitro results. These findings align with traditional uses for pain and swelling, suggesting potential for anti-inflammatory drug development [4,11].

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6.4 Pharmacokinetics and Toxicity: ADME profiling via Swiss-ADME indicates favorable pharmacokinetics for key compounds like [E]-3,4-DCME, including high gastrointestinal (GI) absorption, no violations of Lipinski's rule of five, and a good bioavailability score (0.55), facilitating oral administration potential. These parameters, combined with zero blood-brain barrier penetration for peripheral applications, affirm the safety profile for further therapeutic exploration [11].

6.5 Other Potential Activities: Preliminary GC-MS data highlight immunosuppressive potential from Deoxyspergualin (12.55%), known for inhibiting immune responses, and antineoplastic effects from Actinomycin C2 (8.57%), which targets cell proliferation via DNA intercalation. Additional bioactives like 2-Methyl-7-nonadecene (13.99%) contribute to broader antimicrobial roles, while overall polyphenolic richness suggests applications in cancer chemoprevention or immunomodulation. Though in vitro-focused, these findings warrant in vivo studies to validate therapeutic efficacy against neoplastic and immune-related [8].

7. Research Gaps and Future Perspectives

Current phytochemistry of *Z. neesanum* remains predominantly oil-centric (essential oil via GC-MS/GC-FID), with limited exploration of non-volatile secondary metabolites such as polyphenols, curcuminoids, or other polar compounds that require advanced techniques like LC-MS, HRMS, or NMR for comprehensive profiling. Pharmacological studies are sparse and primarily *in vitro/in silico*-focused (e.g., antimicrobial, antioxidant, anti-inflammatory via DPPH, FRAP, albumin denaturation, and docking), lacking robust preclinical validation including cytotoxicity (e.g., against cancer cell lines), antidiabetic (glucose uptake/lipase inhibition), or neuroprotective screens. Ecological variability across the Western Ghats (e.g., Konkan vs. southern populations) influences chemotypes, necessitating metabolomic comparisons to map intraspecific polymorphism and environmental drivers. Multidisciplinary approaches, integrating biotechnology for micropropagation/clonal propagation to address conservation needs, ethnobotanical surveys for sustainable use, and omics for pathway elucidation, could unlock greater utility for this understudied endemic species, potentially leading to novel phytopharmaceuticals while supporting biodiversity conservation in a hotspot region [4,8,11,23].

7.1 Advanced Analytical Needs: To overcome the volatile bias, integrate multi-omics platforms: untargeted LC-HRMS or UHPLC-QTOF-MS/MS for non-volatile profiling (as applied in related *Zingiber montanum* for curcuminoids/phenylbutenoids), NMR for structural elucidation of novel isolates, and combined GC-MS/LC-MS metabolomics with chemometrics to distinguish chemotypes across Ghats populations. Such approaches would enable high-throughput screening of bioactive fractions, quality control standardization, and identification of polymorphism-linked markers, addressing current gaps in comprehensive metabolite coverage beyond essential oils [24].

7.2 Clinical Translation: Preclinical expansion is essential: advance promising anti-inflammatory formulations (e.g., phenylpropanoid-rich oil) to in vivo models (e.g., carrageenan-induced paw edema or adjuvant arthritis) and toxicity studies beyond ADME predictions. Screen for additional activities like cytotoxicity (MTT assays on cancer lines), antidiabetic (α-glucosidase inhibition, insulin signaling), or neuroprotective (e.g., against oxidative stress in neuronal models), building on genus-wide evidence from Zingiber spp. (e.g., gingerols/zerumbone analogs). This could facilitate formulation development (e.g., nanoemulsions for topical/oral use) and bridge to clinical trials for pain, inflammation, or oxidative stress-related disorders [25].

7.3 Conservation-Linked Research: As a Western Ghats endemic facing habitat fragmentation and potential pathogen pressures (e.g., Pythium susceptibility in related endemics), prioritize ethnobotanical surveys among local communities for traditional uses, informing sustainable harvesting and ex-situ conservation (e.g., via botanical gardens or tissue culture). Genetic diversity studies (e.g., AFLP or SSR markers) combined with metabolomics could link chemotype variations to ecological factors, supporting in-situ protection and biotechnology for propagation to reduce wild collection pressure. This aligns with broader calls for adaptive strategies in hemiclonal/sexual Zingiber populations amid ecological threats [26].

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8. Conclusion

Zingiber neesanum features a distinctive phenylbutanoid-dominant rhizome essential oil, with major compounds DMPBD, (E)-1-(3',4'-dimethoxyphenyl) but-1-ene, and regional [E]-3,4-DCME, aligning it with terpenoid/phenylpropanoid-rich chemotypes (e.g., *Z. cassumunar*) rather than gingerol- or zerumbone-dominant species. In vitro antimicrobial, antioxidant, and anti-inflammatory activities—driven by synergistic phenylbutanoids and terpenoids—support its traditional Western Ghats uses, with low toxicity and favorable pharmacokinetics. Preliminary bioactives like Actinomycin C2 and Deoxyspergualin hint at antineoplastic and immunosuppressive potential.

Despite these advances, research is largely limited to volatiles, with key gaps in non-volatile profiling, population chemotype variation, and in vivo validation. As a vulnerable Western Ghats endemic, *Z. neesanum* urgently requires integrated metabolomics, preclinical expansion, ethnobotanical surveys, and biotechnology-driven propagation to conserve its biodiversity and realize its therapeutic and natural product value.

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