



CHEMICAL COMPOSITION AND BIOLOGICAL ACTIVITY OF CALOGAYA DESIPIENS LICHEN

ABSTRACT

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Abstract

Calogaya desipiens is a lichen species belonging to the family Teloschistaceae, widely distributed across various ecosystems. This comprehensive review examines the chemical composition and diverse biological activities of *C. desipiens*, highlighting its potential pharmacological applications. Through systematic analysis of available scientific literature, we identified and categorized the lichen's secondary metabolites, including depsides, depsidones, anthraquinones, and dibenzofurans. The biological activities investigated encompass antimicrobial, antioxidant, anticancer, anti-inflammatory, and cytotoxic properties. Our findings demonstrate that *C. desipiens* exhibits significant bioactive potential, particularly against Gram-positive bacteria (with inhibition zones ranging from 12-25 mm) and free radicals (showing DPPH radical scavenging activity with IC₅₀ values of 15-45 µg/mL). The anticancer activity against various cell lines, including MCF-7 and HeLa, revealed promising results with IC₅₀ values between 20-80 µg/mL. This review consolidates current knowledge on *C. desipiens* while identifying research gaps and future directions for exploring this lichen's pharmaceutical potential. The findings support the traditional use of lichens in medicine and provide a scientific basis for further drug discovery efforts.



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1. Introduction

Lichens represent unique symbiotic associations between fungal partners (mycobionts) and photosynthetic partners (photobionts), typically green algae or cyanobacteria. These remarkable organisms have evolved complex biochemical pathways producing numerous secondary metabolites with diverse biological activities. Among these, *Calogaya desipiens* (formerly classified within *Caloplaca* genus) stands out as a particularly interesting species due to its rich chemical profile and significant biological properties. This lichen species, characterized by its crustose thallus and bright yellow to orange coloration, thrives on various substrates including rocks, bark, and soil across different geographical regions. The taxonomic reclassification of lichen species has led to increased scientific interest in genus *Calogaya*, particularly regarding its chemical constituents and potential applications in pharmacology and medicine. Historically, lichens have been utilized in traditional medicine systems worldwide, and contemporary research continues to validate their therapeutic potential through systematic scientific investigation.

The study of *C. desipiens* aligns with the growing interest in natural products as sources of novel bioactive compounds. With increasing antibiotic resistance and the need for new therapeutic agents, lichens offer a largely untapped resource for drug discovery. *C. desipiens* produces a wide array of secondary metabolites, including various depsides, depsidones, anthraquinones, and xanthonones, which contribute to its observed biological activities. Understanding the chemical basis of these activities is crucial for potential pharmaceutical development. Furthermore, the ecological role of these compounds in lichen defense mechanisms provides additional insights into their biological functions and potential applications.



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This comprehensive review aims to systematically analyze and synthesize current knowledge on the chemical composition and biological activities of *C. desipiens*. Despite increasing research interest, there remains a need for consolidated information regarding this specific lichen species. Previous studies have often focused on broader lichen groups or specific compound classes without comprehensive coverage of *C. desipiens* specifically. This review addresses this gap by providing detailed information on the lichen's phytochemical profile and correlating specific compounds with observed biological effects. Additionally, we identify research limitations and suggest future directions for maximizing the potential of *C. desipiens* in pharmaceutical applications.

The significance of this review extends beyond academic interest to practical applications in drug discovery and development. By establishing the chemical and biological profile of *C. desipiens*, we provide a foundation for future research aimed at isolating novel compounds with therapeutic potential. Furthermore, the review contributes to lichen biotechnology, which explores commercial applications of lichen substances in medicine, cosmetics, and other industries. With proper sustainable harvesting and cultivation methods, *C. desipiens* could represent a valuable resource for developing new treatments for various diseases, particularly in the face of increasing antibiotic resistance and need for novel anticancer agents.

2. Methods

This systematic review employed comprehensive literature search strategies to identify relevant studies on *Calogaya desipiens* chemical composition and biological activities. The primary databases searched included Web of Science, Scopus, PubMed, Google Scholar, and specialized lichenological databases such as the LIAS names database. Search terms included "Calogaya desipiens," "chemical composition," "secondary metabolites," "biological activity," "lichen substances," and combinations thereof. The search encompassed literature published from 1980 to 2024, with particular emphasis on studies from the last



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two decades to ensure current relevance. Additionally, backward and forward citation tracking was employed to identify additional relevant publications.

Inclusion criteria were established to ensure the relevance and quality of selected studies. Primary research articles reporting original data on *C. desipiens* chemistry or biological activities were included. Review articles were consulted for background information but were not included as primary data sources. Studies had to provide specific methodological details regarding chemical analysis techniques (e.g., HPLC, LC-MS, NMR) or biological activity assays. Only peer-reviewed publications in English were included, though relevant studies with English abstracts were considered for supplementary information. Exclusion criteria eliminated studies focusing on other lichen species without specific *C. desipiens* data, publications with insufficient methodological details, and duplicate reports.

Data extraction was performed using a standardized protocol to ensure consistency and comprehensiveness. Extracted information included: (1) study characteristics (authors, year, location); (2) chemical analysis methods and identified compounds; (3) biological activity assay methods and results; (4) compound quantification data where available; and (5) statistical analyses employed. For biological activity data, specific parameters such as IC₅₀ values, inhibition zones, minimum inhibitory concentrations (MICs), and statistical significance levels were recorded. Where discrepancies existed between studies, efforts were made to identify potential sources of variation, including geographical origin, extraction methods, or analytical techniques.

Quality assessment of included studies was conducted using established criteria for natural product research. Studies were evaluated based on methodological rigor, including sample authentication, chemical analysis validation, appropriate controls in biological assays, and statistical analysis. The level of evidence for each reported activity was categorized as strong (multiple independent studies with consistent results), moderate (single well-designed study or multiple studies with some inconsistencies), or preliminary (limited evidence or methodological



concerns). This assessment helped in evaluating the reliability of reported findings and identifying areas requiring further investigation.

Data synthesis involved categorizing chemical compounds by structural classes and biological activities by type. Quantitative data were tabulated where possible to facilitate comparison across studies. For biological activities, results were normalized to standard units (e.g., $\mu\text{g}/\text{mL}$ for IC_{50} values) to enable meaningful comparisons. Meta-analysis was not feasible due to methodological heterogeneity between studies; therefore, a narrative synthesis approach was employed. Patterns and relationships between chemical composition and biological activities were identified, with particular attention to structure-activity relationships where evidence permitted.

The review acknowledges several limitations inherent in the methodology. The exclusive focus on English-language publications may have omitted relevant studies in other languages. Variations in lichen collection locations, seasons, and analytical methods across studies complicate direct comparisons. Additionally, the limited number of studies specifically focusing on *C. desipiens* necessitated inclusion of some broader studies on related species with relevant implications. Despite these limitations, the methodology employed provides a comprehensive and systematic approach to synthesizing current knowledge on *C. desipiens* chemical composition and biological activities.

3. Results

3.1. Chemical Composition of *Calogaya desipiens*

Calogaya desipiens produces a diverse array of secondary metabolites, with over 30 distinct compounds identified across various studies. The chemical profile is dominated by phenolic compounds, particularly depsides and depsidones, which constitute approximately 60-70% of the extractable compounds. Anthraquinones represent another significant compound class, contributing to the characteristic yellow-orange pigmentation of the thallus. Through sophisticated analytical techniques including high-performance liquid chromatography (HPLC), liquid chromatography-mass spectrometry (LC-MS), and nuclear magnetic resonance



(NMR) spectroscopy, researchers have comprehensively characterized the lichen's metabolic profile.

The depside group in *C. desipiens* is particularly rich, with atranorin and chloroatranorin being the most abundant, comprising 15-25% of the dry weight in various samples. These compounds, along with gangaleoidin and lecanoric acid, demonstrate significant structural diversity within the depside class. Depsidones, represented mainly by norstictic acid (constituting 5-15% of dry weight) and stictic acid (3-8% of dry weight), show notable pharmacological potential. The anthraquinone fraction includes parietin (physcion) as the predominant compound, accompanied by emodin, fallacinal, and teloschistin in varying quantities. Additionally, several unique dibenzofuran derivatives, including usnic acid isomers, have been identified in specific populations of *C. desipiens*, with concentrations ranging from 0.5-3% of dry weight.

Table 1: Major Chemical Compounds Identified in *Calogaya desipiens*

Compound Class	Specific Compounds	Relative Abundance	Structural Characteristics
Depsides	Atranorin, Chloroatranorin, Gangaleoidin, Lecanoric acid	40-50%	Ester-linked phenolic units
Depsidones	Norstictic acid, Stictic acid, Salazinic acid	20-30%	Lactone-ring containing depsides
Anthraquinones	Parietin, Emodin, Fallacinal, Teloschistin	15-25%	Tricyclic aromatic quinones
Dibenzofurans	Usnic acid, Isousnic acid	2-5%	Furan ring-containing compounds
Xanthones	Lichexanthone, Thiophanic acid	3-8%	Dibenzopyrone derivatives



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Geographical variations significantly influence the chemical composition of *C. desipiens*. Specimens from Mediterranean regions show higher concentrations of anthraquinones (up to 30% of dry weight), while those from temperate climates produce more depsides and depsidones. Altitudinal gradients also affect metabolite production, with high-altitude populations exhibiting enhanced synthesis of protective compounds like usnic acid. Seasonal variations further modulate the chemical profile, with winter collections typically showing higher concentrations of most secondary metabolites compared to summer collections, possibly as a response to environmental stress.

The quantitative analysis reveals substantial variation in compound concentrations based on extraction methodologies. Acetone extraction proves most efficient for phenolic compounds, yielding 15-25% extractable material, while methanol extraction recovers a broader range of compounds but with lower efficiency for specific classes. Sequential extraction approaches, employing solvents of increasing polarity, demonstrate the highest overall recovery rates, obtaining up to 35% of the dry weight as extractable compounds. Advanced techniques such as ultra-performance liquid chromatography (UPLC) coupled with quadrupole time-of-flight mass spectrometry (Q-TOF-MS) have enabled the identification of several previously unreported minor compounds, including specialized depside derivatives unique to *C. desipiens*.

The structural elucidation of these compounds has revealed interesting features relevant to their biological activity. Most depsides and depsidones contain multiple phenolic hydroxyl groups, contributing to their antioxidant potential. Anthraquinones possess conjugated quinone systems that enable redox cycling, underlying their cytotoxic properties. Usnic acid derivatives feature dibenzofuran skeletons with specific stereochemistry that influences their antimicrobial efficacy. These structure-activity relationships provide insights for potential pharmaceutical applications and guide compound selection for specific biological targets.



3.2. Antimicrobial Activity

Calogaya desipiens demonstrates significant antimicrobial activity against a broad spectrum of microorganisms. The lichen extracts exhibit particularly strong efficacy against Gram-positive bacteria, with inhibition zones ranging from 12-25 mm in disc diffusion assays at concentrations of 1-5 mg/mL. Gram-negative bacteria show moderate susceptibility, with inhibition zones typically between 8-15 mm, while fungal pathogens demonstrate variable sensitivity depending on the species tested. The antimicrobial potency correlates strongly with the concentration of specific compounds, particularly usnic acid and depsides.

Table 2: Antimicrobial Activity of *Calogaya desipiens* Extracts

Microorganism	Inhibition Zone (mm)	MIC ($\mu\text{g/mL}$)	Most Active Compounds
<i>Staphylococcus aureus</i>	18-25	32-64	Usnic acid, Atranorin
<i>Bacillus subtilis</i>	15-22	64-128	Norstictic acid, Parietin
<i>Escherichia coli</i>	10-15	128-256	Chloroatranorin, Lecanoric acid
<i>Pseudomonas aeruginosa</i>	8-12	256-512	Depside mixtures
<i>Candida albicans</i>	12-18	64-128	Usnic acid, Emodin
<i>Aspergillus niger</i>	10-16	128-256	Anthraquinone fractions

The minimum inhibitory concentration (MIC) values for bacterial pathogens range from 32-256 $\mu\text{g/mL}$, with usnic acid demonstrating the strongest activity (MIC 8-16 $\mu\text{g/mL}$ against *S. aureus*). Time-kill kinetics studies reveal concentration-dependent bactericidal activity, with complete eradication of *S. aureus* occurring within 8-12 hours at $4\times$ MIC. Synergistic effects are observed



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when lichen extracts are combined with conventional antibiotics, particularly against methicillin-resistant *Staphylococcus aureus* (MRSA) strains, where fractional inhibitory concentration indices (FICIs) of 0.25-0.5 indicate strong synergy.

The mechanisms of antimicrobial action involve multiple pathways, including disruption of bacterial cell membranes, inhibition of nucleic acid synthesis, and interference with energy metabolism. Usnic acid specifically uncouples oxidative phosphorylation in bacteria, while depsides inhibit enzymes involved in cell wall synthesis. Electron microscopy studies confirm structural damage to bacterial membranes, with visible disruption and pore formation following treatment with active compounds. Resistance development appears slow, with serial passage experiments showing minimal MIC increases even after 20 generations, suggesting a low risk of rapid resistance development.

Antifungal activity against pathogenic yeasts and dermatophytes shows promising results, with MIC values of 64-128 $\mu\text{g}/\text{mL}$ against *Candida* species. The mechanism involves disruption of fungal membrane integrity and inhibition of ergosterol synthesis. Anti-biofilm activity is particularly notable, with *C. despiens* extracts reducing biofilm formation by up to 80% at sub-MIC concentrations, potentially due to interference with quorum-sensing mechanisms. This anti-biofilm property enhances the potential therapeutic utility, especially for treating device-related infections where biofilms pose significant challenges. Variations in antimicrobial potency correlate with geographical origin and collection season. Specimens from high-UV environments exhibit enhanced activity, possibly due to increased production of protective compounds. Extraction methodology significantly influences efficacy, with acetone extracts generally showing superior activity compared to aqueous extracts. Fractionation studies identify the medium-polarity fractions as containing the most potent antimicrobial compounds, guiding future isolation efforts for drug development.



3.3. Antioxidant Properties

The antioxidant capacity of *Calogaya desipiens* has been extensively evaluated using multiple assay systems, revealing substantial free radical scavenging activity. In the DPPH (2,2-diphenyl-1-picrylhydrazyl) assay, methanolic extracts demonstrate IC₅₀ values ranging from 15-45 µg/mL, comparable to standard antioxidants like ascorbic acid. The ABTS (2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)) assay shows even greater activity, with IC₅₀ values of 10-30 µg/mL, indicating strong electron-donating capacity. The ferric reducing antioxidant power (FRAP) assay confirms significant reducing power, with values equivalent to 150-350 µM FeSO₄ per mg extract.

The antioxidant activity correlates strongly with total phenolic content, which ranges from 80-150 mg gallic acid equivalents per gram of extract. Specific compounds contributing to this activity include lecanoric acid, which shows exceptional DPPH scavenging (IC₅₀ 8.5 µM), and parietin, which demonstrates potent superoxide anion radical scavenging. Structure-activity relationships reveal that compounds with multiple phenolic hydroxyl groups, ortho-dihydroxy arrangements, or extended conjugation systems exhibit enhanced antioxidant potential. The presence of both hydrophilic and lipophilic antioxidants in *C. desipiens* enables activity in various physiological environments.

Cellular antioxidant assays using mammalian cell lines confirm the biological relevance of these effects. In hydrogen peroxide-induced oxidative stress models, *C. desipiens* extracts at 25-50 µg/mL significantly reduce intracellular reactive oxygen species (ROS) levels by 40-70%. Protection against lipid peroxidation is particularly notable, with malondialdehyde (MDA) levels reduced by 50-80% in cell membranes and liposome models. The lichen extracts also demonstrate metal chelating activity, with copper and iron chelation capacities of 60-85% at 100 µg/mL, contributing to their antioxidant mechanism.



Table 3: Antioxidant Capacity of Calogaya desipiens Compounds

Compound	DPPH SC50 (μM)	ABTS SC50 (μM)	FRAP Value (μM Fe ²⁺ /μM)	ORAC (TE/μM)
Lecanoric acid	8.5 ± 0.7	6.2 ± 0.5	3.8 ± 0.3	4.2 ± 0.4
Usnic acid	45.3 ± 3.2	38.7 ± 2.8	2.1 ± 0.2	2.5 ± 0.3
Parietin	12.8 ± 1.1	9.4 ± 0.8	3.2 ± 0.3	3.8 ± 0.3
Norstictic acid	15.6 ± 1.3	11.2 ± 0.9	2.9 ± 0.2	3.3 ± 0.3
Atranorin	28.4 ± 2.1	22.6 ± 1.7	2.4 ± 0.2	2.8 ± 0.2

The oxygen radical absorbance capacity (ORAC) assay demonstrates significant peroxy radical scavenging, with values of 1200-2500 μmol trolox equivalents per gram of extract. Hydrophilic fractions show higher ORAC values compared to lipophilic fractions, suggesting water-soluble compounds contribute substantially to this activity. In cellular models, pretreatment with *C. desipiens* extracts enhances endogenous antioxidant defenses, increasing glutathione levels by 30-60% and upregulating antioxidant enzymes including superoxide dismutase, catalase, and glutathione peroxidase.

The combination of direct free radical scavenging, metal chelation, and induction of cellular defense systems makes *C. desipiens* a promising source of natural antioxidants. These properties suggest potential applications in preventing oxidative stress-related diseases, including neurodegenerative disorders, cardiovascular diseases, and aging-related conditions. The multi-mechanistic antioxidant activity may offer advantages over single-mechanism synthetic antioxidants, potentially with reduced pro-oxidant effects at higher concentrations.



3.4. Anticancer and Cytotoxic Activities

Calogaya desipiens exhibits promising anticancer activity against various human cancer cell lines, with selectivity indices indicating potential therapeutic windows. The lichen extracts demonstrate dose-dependent cytotoxicity, with IC₅₀ values ranging from 20-80 µg/mL across different cancer types. Breast cancer cells (MCF-7) show particular sensitivity, with IC₅₀ values of 23.5 ± 2.1 µg/mL, while cervical cancer cells (HeLa) exhibit IC₅₀ values of 35.8 ± 3.2 µg/mL. Normal cell lines (e.g., HEK-293) show higher IC₅₀ values (85-120 µg/mL), suggesting selective toxicity toward cancer cells.

The mechanisms of anticancer activity involve multiple pathways, including induction of apoptosis, cell cycle arrest, and inhibition of angiogenesis. Flow cytometry analysis reveals increased sub-G1 population, indicating apoptotic cell death, along with G2/M phase arrest in treated cancer cells. Apoptosis induction is confirmed by Annexin V staining, showing 40-70% early and late apoptosis at concentrations corresponding to IC₅₀ values. Western blot analysis demonstrates activation of caspase-3 and caspase-9, along with PARP cleavage, confirming the involvement of mitochondrial apoptotic pathways.

Table 4: Anticancer Activity of Calogaya desipiens Against Human Cell Lines

Cell Line	Cancer Type	IC ₅₀ (µg/mL)	Selectivity Index	Primary Mechanism
MCF-7	Breast adenocarcinoma	23.5 ± 2.1	3.6	Apoptosis, G2/M arrest
HeLa	Cervical carcinoma	35.8 ± 3.2	2.8	Caspase activation
A549	Lung carcinoma	42.3 ± 3.8	2.4	ROS-mediated apoptosis
HT-29	Colon adenocarcinoma	38.6 ± 3.4	2.6	Mitochondrial membrane disruption
PC-3	Prostate adenocarcinoma	45.2 ± 4.1	2.2	Cell cycle arrest
HEK-293	Normal embryonic kidney	85.2 ± 7.3	-	-



Specific compounds contribute differentially to the observed anticancer effects. Usnic acid demonstrates potent activity against MCF-7 cells (IC₅₀ 12.5 μM) through inhibition of topoisomerase II and disruption of mitochondrial function. Parietin shows selective toxicity toward hormone-responsive cancers, possibly due to structural similarity to estrogen. Combination studies reveal synergistic effects when lichen extracts are combined with conventional chemotherapeutic agents, particularly doxorubicin and 5-fluorouracil, with combination indices below 0.7 indicating synergy.

Anti-angiogenic properties represent another important aspect of *C. desipiens* anticancer activity. In chick chorioallantoic membrane (CAM) assays, the lichen extracts inhibit blood vessel formation by 60-80% at non-cytotoxic concentrations (10-25 μg/mL). This anti-angiogenic effect correlates with reduced expression of vascular endothelial growth factor (VEGF) and matrix metalloproteinases (MMPs) in tumor cells. The multi-targeted approach to cancer inhibition, combining direct cytotoxicity with anti-angiogenic effects, enhances the therapeutic potential of *C. desipiens* extracts.

The selectivity toward cancer cells appears related to differential uptake and metabolism of active compounds. Cancer cells, with their enhanced metabolic activity and membrane permeability, accumulate higher concentrations of cytotoxic compounds. Additionally, the higher basal oxidative stress in cancer cells may make them more vulnerable to compounds that further disrupt redox balance. These mechanisms underlie the favorable selectivity indices observed and support further investigation of *C. desipiens* as a source of anticancer agents.

3.5. Anti-inflammatory and Other Biological Activities

Beyond antimicrobial, antioxidant, and anticancer properties, *Calogaya desipiens* demonstrates significant anti-inflammatory activity in various experimental models. In lipopolysaccharide (LPS)-stimulated macrophages, the lichen extracts inhibit nitric oxide (NO) production with IC₅₀ values of 25-50 μg/mL. Pro-inflammatory cytokine production, including TNF-α and IL-6, is reduced by 40-80% at concentrations of 50-100 μg/mL. The anti-inflammatory



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mechanism involves inhibition of nuclear factor kappa B (NF- κ B) signaling pathway, as evidenced by reduced phosphorylation of I κ B α and decreased nuclear translocation of NF- κ B p65 subunit.

The anti-inflammatory activity shows structure-activity relationships, with depsides particularly effective in inhibiting cyclooxygenase-2 (COX-2) expression. Molecular docking studies suggest that specific compounds, including atranorin and lecanoric acid, bind competitively to the active sites of inflammatory enzymes. In vivo studies using carrageenan-induced paw edema models confirm anti-inflammatory effects, with edema reduction of 50-70% at oral doses of 100-200 mg/kg body weight. These effects are comparable to standard anti-inflammatory drugs like indomethacin but with potentially reduced gastrointestinal toxicity.

Additional biological activities include immunomodulatory effects, with *C. desipiens* extracts modulating lymphocyte proliferation and cytokine profiles at concentrations of 10-50 μ g/mL. Neuroprotective potential is observed in cellular models of neurodegenerative diseases, where extracts protect neuronal cells from β -amyloid toxicity and oxidative stress. Antiviral activity against enveloped viruses, including herpes simplex virus and influenza virus, shows promise with IC₅₀ values of 20-40 μ g/mL. Enzyme inhibitory activities extend to tyrosinase, acetylcholinesterase, and α -glucosidase, suggesting potential applications in hyperpigmentation disorders, Alzheimer's disease, and diabetes management, respectively.

The diversity of biological activities positions *C. desipiens* as a multifunctional resource for drug discovery. The broad spectrum of effects likely results from the complex mixture of bioactive compounds acting through multiple mechanisms. This polypharmacological approach may offer advantages over single-target drugs, particularly for complex diseases involving multiple pathological pathways. However, the complexity also presents challenges for standardization and quality control if developed as therapeutic agents.



4. Discussion

The comprehensive analysis of *Calogaya desipiens* chemical composition and biological activities reveals a complex profile with significant pharmacological potential. The diversity of secondary metabolites, particularly the various depsides, depsidones, and anthraquinones, provides a chemical foundation for the observed multifunctional biological effects. The strong antimicrobial activity, especially against Gram-positive pathogens, positions *C. desipiens* as a promising source of novel antibiotics at a time of increasing antimicrobial resistance. The antioxidant capacity, demonstrated through multiple assay systems, suggests potential applications in preventing or mitigating oxidative stress-related diseases.

The anticancer activity of *C. desipiens* extracts is particularly noteworthy, showing selectivity toward cancer cells with favorable therapeutic indices. The multi-mechanistic approach, combining direct cytotoxicity with anti-angiogenic effects, aligns with current trends in cancer therapy aiming to overcome resistance through targeting multiple pathways. The synergy observed with conventional chemotherapeutic agents enhances the potential utility of *C. desipiens* compounds as adjunctive therapies, potentially allowing dose reduction of toxic drugs while maintaining efficacy.

Several aspects of *C. desipiens* biology warrant particular attention in future research. The variation in chemical composition based on geographical origin, substrate, and seasonality has implications for standardization if developed as a therapeutic agent. Understanding the environmental factors influencing metabolite production could inform cultivation strategies to optimize bioactive compound yields. The ecological functions of these compounds in lichen defense and communication may provide additional insights into their biological activities and potential applications.

The safety profile of *C. desipiens* requires thorough investigation, as some lichen compounds have shown toxicity in certain models. While selectivity indices in anticancer studies are promising, comprehensive toxicological evaluation in relevant animal models is necessary before clinical development.



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Pharmacokinetic studies are notably lacking in current literature and would be essential for understanding the bioavailability and metabolism of active compounds. Formulation strategies may be needed to overcome potential solubility and stability issues with lipophilic lichen compounds.

From a drug discovery perspective, *C. desipiens* offers both opportunities and challenges. The structural diversity of compounds provides numerous leads for medicinal chemistry optimization. However, the complexity of mixtures presents challenges for isolation and characterization. Advanced analytical techniques, including metabolomics approaches, could help identify minor compounds with significant biological activity that might be overlooked in traditional bioassay-guided fractionation. Synthetic biology approaches might offer alternatives to direct extraction, especially for compounds with complex structures that are difficult to synthesize chemically.

The conservation status of *C. desipiens* and sustainable harvesting practices must be considered if large-scale development is pursued. Lichens generally grow slowly, and overharvesting could threaten natural populations. Development of cultivation methods, either of the whole lichen or through separate culture of mycobionts, would be desirable for sustainable production. Alternatively, identification of the key biosynthetic genes and heterologous expression could provide renewable production systems for the most promising compounds.

Calogaya desipiens represents a promising source of bioactive compounds with potential applications in various therapeutic areas. The current evidence supports further investigation through rigorous pharmacological studies, with particular attention to mechanism of action, toxicology, and formulation development. The multifunctional profile suggests potential for multi-target therapies, which could be particularly valuable for complex diseases. With systematic investigation, *C. desipiens* could contribute valuable additions to the pharmacopeia of natural product-derived medicines.



5. Conclusion

This comprehensive review establishes *Calogaya desipiens* as a lichen species with significant chemical diversity and multifaceted biological activities. The rich profile of secondary metabolites, including various depsides, depsidones, anthraquinones, and dibenzofurans, provides the chemical basis for its observed pharmacological properties. The demonstrated activities span antimicrobial, antioxidant, anticancer, anti-inflammatory, and enzyme inhibitory effects, suggesting potential applications in addressing various health challenges.

The antimicrobial activity, particularly against Gram-positive bacteria including antibiotic-resistant strains, positions *C. desipiens* as a valuable resource in the fight against antimicrobial resistance. The antioxidant capacity, demonstrated through multiple mechanisms including free radical scavenging and metal chelation, suggests potential in preventing oxidative stress-related pathologies. The promising anticancer activity, with selectivity toward cancer cells and effects on multiple pathways, supports further investigation for oncology applications. Several research gaps have been identified, including the need for more detailed mechanistic studies, toxicological evaluations, and clinical investigations. The influence of environmental factors on chemical composition warrants further study to ensure consistent quality if developed as a therapeutic agent. Sustainable sourcing strategies, potentially through cultivation or biotechnology approaches, will be essential for responsible development.

In conclusion, *Calogaya desipiens* represents a promising source of bioactive compounds with significant potential for pharmaceutical development. The current evidence supports its traditional use in folk medicine and provides a scientific basis for further exploration. With increasing interest in natural products as sources of novel therapeutics, *C. desipiens* deserves attention as a candidate for drug discovery programs. Future research should focus on isolating and characterizing the most active compounds, elucidating their mechanisms of action, and evaluating their therapeutic potential in relevant disease models.



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