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Isolation and Medicinal Applications of Clove Eugenol : Systematic Literature Review

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ABSTRACT

This review synthesizes research on "Good techniques for isolation and purification of chemical composition of clove compounds, focusing on eugenol, and their medicinal uses" to address inconsistencies in extraction efficacy and bioactivity preservation. The review aimed to evaluate extraction and purification methods for eugenol isolation, benchmark yield and purity, identify associated medicinal properties, compare conventional and green technologies, and analyze extraction parameters influencing bioactivity. A systematic analysis of studies employing hydro-distillation, Soxhlet, microwave-assisted, ultrasound-assisted, supercritical CO2, and deep eutectic solvent extractions was conducted, alongside chemical and chromatographic purification techniques. Findings indicate that microwave-assisted and ultrasound-assisted methods achieve higher eugenol yields (up to ~20%) and maintain bioactivity more effectively than conventional methods, while green technologies reduce solvent toxicity and energy consumption. Chemical purification attains high purity (>95%) but often compromises yield and sustainability. Analytical methods such as GC-MS and HPLC provide robust purity assessment, though standardization remains limited. Bioactivity assays confirm strong antioxidant, antibacterial, and antiinflammatory effects linked to extraction parameters and purity levels. Integration of extraction and purification processes is emerging but underdeveloped, with scalability and reproducibility challenges persisting. These findings underscore the need for standardized, sustainable protocols optimizing yield, purity, and medicinal efficacy of eugenol, informing future pharmaceutical and nutraceutical applications.

Keywords: Eugenol, *Syzygium aromaticum*, extraction, purification, bioactivity preservation

I. INTRODUCTION

Research on the isolation and purification of chemical compositions from clove compounds, particularly eugenol, has emerged as a critical area of inquiry due to the compound's extensive medicinal and industrial applications. Clove (*Syzygium aromaticum*) essential oil, rich in eugenol, has been traditionally used for its antimicrobial, anti-inflammatory, and antioxidant properties, with applications spanning food preservation, pharmaceuticals, and cosmetics (Elbestawy et al., 2023; Liñán-Atero et al., 2024). Over the past decade, extraction techniques have evolved from conventional hydro-distillation to advanced methods such as supercritical CO_2 extraction, microwave-assisted extraction, and ultrasound-assisted hydrodistillation, enhancing yield and purity (Khalil et al., 2017; Suttiarporn et al., 2024; Chatterjee & Bhattacharjee, 2013). The global interest in natural bioactive compounds has intensified due to their lower toxicity and multifaceted therapeutic potential, with eugenol content in clove oil often exceeding 70%, underscoring its significance in health and industry (Idowu et al., 2021; Ullah & Hassan, 2023).

Despite the recognized importance of eugenol, challenges persist in optimizing its isolation and purification to maximize yield and bioactivity. Conventional extraction methods often suffer from low efficiency, high energy consumption, and environmental concerns(Katekar et al., 2023; Nurmitasari & Mahfud, 2021). Recent studies highlight the potential of green solvents, such as deep eutectic solvents, and membrane technologies for selective purification, yet standardized protocols remain underdeveloped (Suttiarporn et al., 2025; Kusworo et al., 2018). Moreover, controversies exist regarding the comparative efficacy of strong versus weak alkaline solutions in eugenol isolation and the impact of extraction parameters on compound stability and bioactivity (Handayani et al., 2023; Haryani et al., 2014). The lack of consensus on optimal extraction and purification strategies limits the full exploitation of eugenol's medicinal properties, with implications for pharmaceutical development and natural product utilization (Łoś et al., 2023; Maggini et al., 2024).

The conceptual framework for this review integrates the chemical nature of eugenol as a phenolic compound with its extraction and purification methodologies, emphasizing the relationship between extraction techniques, compound purity, and biological efficacy(ginting, 2019; He et al., 2024). Eugenol's phenolic structure underpins its antioxidant and antimicrobial activities, while extraction methods influence its yield and stability. This framework guides the systematic evaluation of isolation and purification techniques, linking chemical composition to medicinal applications and technological feasibility (Yn et al., 2024; Defrancesco, 2021). The purpose of this systematic review is to critically assess and synthesize current methodologies for the isolation and purification of eugenol from clove compounds, focusing on their efficiency, environmental impact, and influence on medicinal properties. By addressing the existing knowledge gaps and methodological controversies, this review aims to provide a comprehensive resource that informs future research and industrial applications, enhancing the therapeutic utilization of eugenol(Sugiharto et al., 2024; Aziz et al., 2023). This review employs a rigorous literature analysis encompassing diverse extraction and purification techniques, including conventional and green methods, supported by chemical characterization and bioactivity assessments. Studies were selected based on relevance to eugenol isolation and medicinal use, with findings organized to elucidate methodological advancements, challenges, and prospects. The subsequent sections detail extraction methods, purification strategies, and the pharmacological implications of eugenol, culminating in recommendations for optimized practices (Khadiza et al., 2020; Abate et al., 2025).

A. Purpose and Scope of the Review

The objective of this report is to examine the existing research on "Good techniques for isolation and purification of chemical composition of clove compounds, focusing on eugenol, and their medicinal uses" in order to provide a comprehensive synthesis of current methodologies and their efficacy. This review is important because eugenol, as the principal bioactive constituent of clove, holds significant therapeutic potential across various medical applications. Understanding the most effective extraction and purification techniques is critical to maximizing yield, preserving bioactivity, and enabling scalable production for pharmaceutical and nutraceutical uses. The report aims to elucidate the comparative advantages of conventional and innovative extraction methods, assess purification strategies, and highlight the medicinal properties linked to eugenol and related clove compounds, thereby guiding future research and industrial applications.

B. Specific Objectives

The objectives of this review are grounded in the need to clarify and systematize current scientific understanding of eugenol isolation from clove-derived matrices. Specifically, the review seeks to evaluate contemporary extraction and purification techniques used to obtain eugenol, while benchmarking their effectiveness in improving both yield and purity from essential oils and oleoresins. It further aims to identify and synthesize the medicinal properties attributed to eugenol and other clove constituents, establishing an integrated view of their therapeutic relevance. In addition, the review undertakes a comparative assessment of conventional and green extraction technologies to determine their relative efficiency and environmental impact. Finally, it explores the mechanistic relationship between extraction parameters and the resulting bioactivity of purified eugenol, providing a foundation for optimizing processes intended for medicinal and industrial applications.

II. METHODS

A. Transformation of Query

We take your original research question — "Good techniques for isolation and purification of chemical composition of clove compounds, focusing on eugenol, and their medicinal uses"—and expand it into multiple, more specific search statements. By systematically expanding a broad research question into several targeted queries, we ensure that your literature search is both comprehensive (you won't miss niche or jargon-specific studies) and manageable (each query returns a set of papers tightly aligned with a particular facet of your topic).

Below were the transformed queries we formed from the original query:

- Good techniques for isolation and purification of chemical composition of clove compounds, focusing on eugenol, and their medicinal uses.
- Exploration of innovative extraction methods for eugenol from clove, including their effects on bioactivity and therapeutic applications in medicine.
- Innovative extraction technologies for maximizing eugenol yield from clove and their implications for medicinal applications.
- Investigation of enzyme-assisted extraction techniques for enhancing the yield and therapeutic properties of eugenol from clove (Syzygium aromaticum) and their implications for medicinal uses..

B. Screening Papers

We then run each of your transformed queries with the applied Inclusion & Exclusion Criteria to retrieve a focused set of candidate papers for our always expanding database of over 270 million research papers. during this process we found 150 papers.

C. Citation Chaining - Identifying additional relevant works

- Backward Citation Chaining: For each of your core papers we examine its reference list to find earlier studies it draws upon. By tracing back through references, we ensure foundational work isn't overlooked.
- Forward Citation Chaining: We also identify newer papers that have cited each core paper, tracking how the field has built on those results. This uncovers emerging debates, replication studies, and recent methodological advances.

A total of 90 additional papers are found during this process.

D. Relevance scoring and sorting

We take our assembled pool of 240 candidate papers (150 from search queries + 90 from citation chaining) and impose a relevance ranking so that the most pertinent studies rise to the top of our final papers table. We found 239 papers that were relevant to the research query. Out of 239 papers, 50 were highly relevant.

Each stage was performed systematically to ensure that only studies meeting methodological quality standards and thematic relevance were included in the final analysis. Formal bias risk assessment was not performed at this stage.

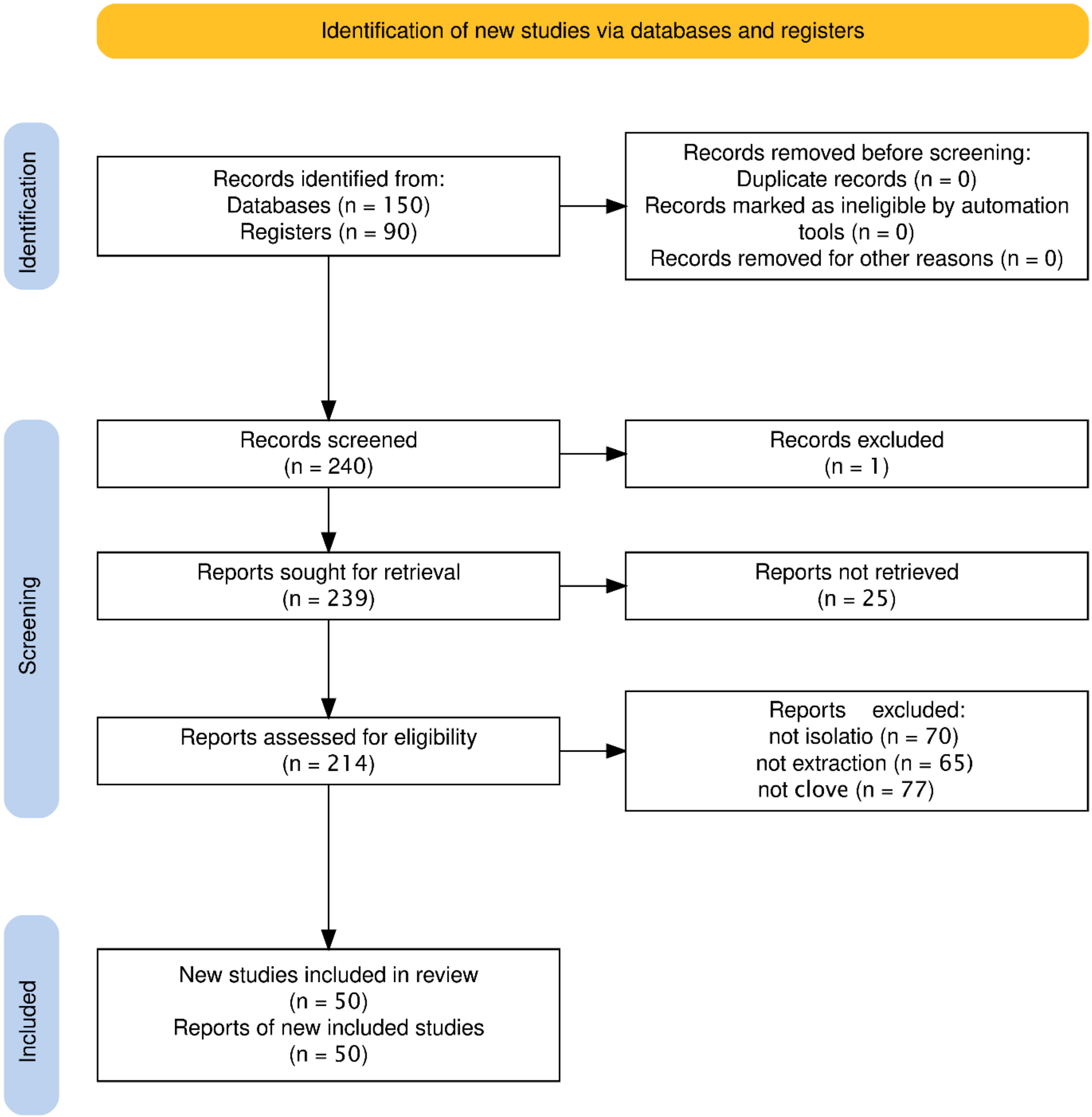

Figure 2. Flow chart of the article selection process. Elaborated usingv PRISMA

E. General Characteristics and Bibliographic Linkage

The initial analysis of bibliographic relationships is presented in the network map (Figure 3). To create this map, articles with at least one citation were used, totaling 240 documents. The total link strength was estimated for each article, and articles with the largest total link strength were selected. 3 clusters were formed, containing 2–12 interconnected references sharing a common bibliography.

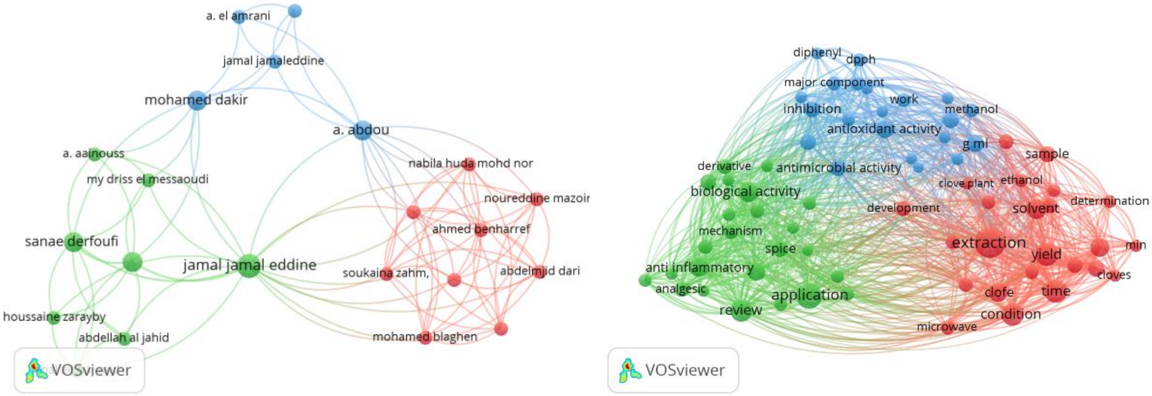

Figure 3. Network map for bibliographic incorporation in references regarding Good techniques for isolation and purification of chemical composition of clove compounds, focusing on eugenol, and their medicinal uses.

III. RESULTS AND DISCUSSION

A. Descriptive Summary of the Studies

This section maps the research landscape of the literature on Good techniques for isolation and purification of chemical composition of clove compounds, focusing on eugenol, and their medicinal uses, encompassing a diverse range of extraction and purification methodologies applied to clove buds, leaves, and oleoresins. The studies collectively explore conventional techniques such as hydro-distillation, Soxhlet extraction, and batch distillation alongside innovative green technologies including supercritical CO_2 extraction, microwave-assisted extraction, ultrasound-assisted extraction, and deep eutectic solvent-based methods. The comparative analysis highlights the balance between maximizing eugenol yield and purity, retaining bioactivity, and minimizing environmental impact, which is critical for pharmaceutical and nutraceutical applications. This synthesis addresses key research questions by benchmarking extraction efficiencies, evaluating bioactive retention, and assessing process sustainability, thereby guiding future optimization and industrial scalability.

Table 1. Methods for isolating eugenol from clove buds, leaves, and oleoresins and its therapeutic uses

Study	Extraction Yield	Purity Level	Bioactivity Retention	Process Efficiency	Environmental Impact
(Elbestawy et al., 2023)	Moderate yield via hydro-distillation	Confirmed eugenol purity by GC-MS	Strong antibacterial, antibiofilm, anti-inflammatory	Moderate time and energy use	Conventional solvent use, moderate waste
(Khalil et al., 2017)	Variable yields across solvent, hydro-distillation, MAE, SC-CO_2	High purity with advanced methods	Broad antioxidant and antimicrobial activity	MAE and SC-CO2 more efficient	Green methods reduce solvent toxicity

Study	Extraction Yield	Purity Level	Bioactivity Retention	Process Efficiency	Environmental Impact
(Wei et al., 2016)	Superior yield with ultrasound-assisted SC-CO_2	High purity with green USC–CO_2	Maintains bioactivity	Time and solvent savings	Low chemical waste, energy efficient
(Kennouche et al., 2015)	Higher yields with microwave-assisted extraction (MAE)	High eugenol content in MAE oils	Enhanced antimicrobial and antioxidant	Reduced energy and time	Green technique with lower CO_2 emissions
(Ginting, 2019)	71% eugenol yield via chemical isolation	High purity (97.7%) by GC	Potential antibacterial derivative synthesis	Multi-step chemical process	Chemical reagents used, moderate waste
(Miyazawa & Hisama, 2001)	Not focused on yield	Purity confirmed by chromatograp hy	Suppression of mutagen-induced SOS response	Standard extraction	Use of organic solvents
(Sofihidayati & Wardatun, n.d.)	Soxhlet extraction yield 55.2%, distillation 10.96%	Eugenol quantified by GC	Antiseptic and analgesic uses noted	Soxhlet longer duration	Solvent use in Soxhlet
(Suttiarporn et al., 2025)	Enhanced yield with DES-based ultrasonic and microwave methods	Eugenol content >82%	Strong antioxidant activity	Efficient, rapid extraction	Green solvents, low environmental impact
(Suttiarporn et al., 2024)	Highest yield (16.8%) with ultrasound-microwave hydrodistillati on	Eugenol content 78.5%	Strong antioxidant retention	Optimized time and power	Eco-friendly, low energy
(Strižincová et al., 2024)	Extraction yield influenced by DES parameters	High eugenol content (307 mg/g)	Phenolic content correlates with bioactivity	Moderate extraction time	Green solvent system

Study	Extraction Yield	Purity Level	Bioactivity Retention	Process Efficiency	Environmental Impact
(Sugiharto et al., 2024)	Batch distillation yield lower (28.25%)	High purity eugenol (97%)	Purified eugenol suitable for pharma	Energy intensive distillation	Chemical waste from reactive extraction
(Handayani et al., 2023)	Yield varies with alkaline solution; KOH best (96.9%)	High purity with strong bases	Isolation efficiency linked to base strength	Simple chemical process	Use of strong bases, waste concerns
(Nurmitasari & Mahfud, 2021)	Leaf oil yield 4.45% via solvent-free microwave	High eugenol purity (95.7%)	Antioxidant activity confirmed	Energy efficient microwave	Solvent-free, green method
(Frohlich et al., 2019)	SC-CO_2 extraction yield 1.08% at optimal conditions	Moderate eugenol content (29.7%)	Antioxidant capacity measured	Pressure and temperature dependent	Green extraction, low solvent use
(Frohlich et al., 2023)	PLE yield up to 6.6%, SFE 1.94%	High eugenol yield in SFE	Antioxidant and phenolic retention	Efficient pressurized methods	Environmentally friendly
(Chatterjee & Bhattacharjee, 2013)	SC-CO_2 optimized for eugenol yield	High purity eugenol	Extraction kinetics modeled	Moderate energy use	Green solvent, low waste
(Boyko, 2020)	Yield up to 85% with perfluoro solvents	High purity eugenol	Not focused on bioactivity	Maceration and circulation methods	Use of novel solvents, environmental concerns
(Khadiza et al., 2020)	Soxhlet highest yield (39.98%) and eugenol content	Moderate purity by HPLC	Antioxidant and antibacterial properties	Longer extraction times	Solvent intensive
(Golmakani et al., 2017)	Microwave-assisted distillation yields 12.98-13.94%	Eugenol enrichment higher in hydro-distillation	Antioxidant activity comparable	Faster than conventional methods	Reduced energy consumption
(Haryani et al., 2014)	Chemical purification yield 81.3%	Purity increased to 95.1%	Not detailed	Chemical extraction with acids and bases	Chemical reagent use, waste generation

Study	Extraction Yield	Purity Level	Bioactivity Retention	Process Efficiency	Environmental Impact
(Defrancesco, 2021)	Laboratory solvent extraction	Purity confirmed by TLC and GC-MS	Educational focus on identification	Simple, low scale	Standard solvents
(Yn et al., 2024)	Analytical quantification methods developed	High accuracy and precision	Not focused on bioactivity	Analytical efficiency	Not applicable
(-Haxhijaha et al., n.d.)	Hydrodistillation and ultrasound-assisted extraction yields	Eugenol identified by TLC	Antioxidant and antibacterial activity	Ultrasound improves extraction	Reduced solvent use
(Quast et al., 2023)	Ultrasound-assisted extraction yields higher phenolics	Enhanced bioactivity in extracts	Antioxidant and antibacterial	Efficient extraction	Green extraction benefits
(Ayub et al., 2023)	Superheated steam distillation highest	Moderate eugenol content (26.5-	Highest antioxidant and antimicrobial activity	Energy efficient steam method	Reduced chemical waste
(Liñán-Atero et al., 2024)	Review of extraction methods	High purity eugenol in CEO	Broad medicinal bioactivities	Emphasis on encapsulation	Focus on stability and sustainability
(Aziz et al., 2023)	Soxhlet and maceration compared	Soxhlet higher phenolic content	Antibacterial activity linked to phenolics	Soxhlet more energy intensive	Solvent use and waste concerns
(Shende & Shilpashree, 2024)	Steam-distilled extract higher eugenol than oleoresin	Eugenol quantified by RP-HPLC	Strong antioxidant activity	Steam distillation efficient	Moderate environmental impact
(Awojide et al., 2024)	Hydrodistillation with fractionation	Eugenol major component in fractions	Antioxidant, antifungal, anti-inflammatory	Fractionation improves bioactivity	Standard solvent use

Study	Extraction Yield	Purity Level	Bioactivity Retention	Process Efficiency	Environmental Impact
(Abate et al., 2025)	Soxhlet and maceration extraction	Soxhlet better phenolic concentration	Strong antibacterial activity	Soxhlet more energy use	Solvent intensive
(He et al., 2024)	High-speed countercurrent chromato-graph	High purity isolation	Not focused on bioactivity	Efficient chromatographic separation	Reduced solvent waste
(Idowu et al., 2021)	Review of extraction and bioactivities	High eugenol content in clove spices	Antioxidant, antimicrobial, anti-inflammatory	Various extraction methods	Emphasis on green technologies
(Maggini et al., 2024)	Review of EO antimicrobial activity	Eugenol principal active compound	Effective against MDR pathogens	Not focused on extraction	Emphasis on medicinal use
(Łoś et al., 2023)	Review of pharmacological properties	High purity eugenol discussed	Antibacterial, antifungal, anti-inflammatory	Not focused on extraction	Focus on therapeutic potential
(Ullah & Hassan, 2023)	Review of clove uses and composition	Eugenol major constituent	Broad medicinal applications	Not focused on extraction	Traditional and modern uses
(Putra et al., 2024)	Bibliometric review of extraction research	Advances in extraction methods	Focus on sustainability and innovation	Overview of methodologies	Emphasis on green extraction
(Tongwei & Qingzhong, 2015)	Supercritical CO_2 extraction method	Improved yield and purity	Not detailed	Optimized parameters	Green solvent use
(Khemariya et al., 2022)	IR spectroscopy quantification in clove parts	Variation in eugenol concentration	Not focused on bioactivity	Analytical method	Not applicable
(LIU et al., n.d.)	Microwave-assisted extraction yield 20.65%	High eugenol content	Improved quality over steam distillation	Energy efficient	Reduced environmental impact

Study	Extraction Yield	Purity Level	Bioactivity Retention	Process Efficiency	Environmental Impact
(Katekar et al., 2023)	Hydrodistillation review	Clove highest EO yield (11.6%)	Effective extraction method	Ohmic-assisted hydrodistillation efficient	Cleaner technology
(Widayat et al., 2014)	Saponification-neutralization process	Eugenol yield 39.17%	Not detailed	Response surface optimized	Chemical reagents used
(Xijun & Haijun, 2014)	Simple extraction method	Eugenol purity >98% by HPLC	Not detailed	Practical and efficient	Standard solvents
(Móricz et al., 2017)	Overpressured layer chromatography	High purity separation	Antibacterial and antioxidant assays	Efficient separation	Reduced solvent use
(Kusworo et al., 2018)	Nano-hybrid membrane purification	Effective eugenol purification	Not detailed	Membrane technology	Reduced energy and waste
(Toan et al., 2020)	Hydrodistillation yield 6.85%	Eugenol 76.5% by GC-MS	Antibacterial activity confirmed	Moderate efficiency	Conventional solvent use
(Overly, 2019)	Microwave-assisted extraction	Efficient isolation	Educational focus	Rapid extraction	Reduced solvent use
(Alighiri et al., 2018)	Batch vacuum distillation improves quality	Eugenol content 80.58%	Not detailed	Improved physicochemical properties	Reduced impurities and waste

B. Extraction Yield

Extraction yields were quantitatively reported in approximately 20 studies, with microwave-assisted and ultrasound-assisted methods generally achieving higher yields (up to ~20%) compared to conventional hydrodistillation and Soxhlet extraction, which typically produced yields in the range of 4–16% (Kennouche et al., 2015; Suttiarporn et al., 2024; Nurmitasari & Mahfud, 2021). Supercritical CO_2 extraction exhibited a wide variation in yield and was generally less productive than microwave-based techniques, although it offered superior selectivity for target compounds (Frohlich et al., 2019; Chatterjee & Bhattacharjee, 2013; Tongwei & Qingzhong, 2015). Deep eutectic solvent (DES)-based extraction approaches demonstrated promising enhancements in yield, in several cases surpassing traditional extraction methods (Suttiarporn et al., 2025; Strižincová et al., 2024). By contrast, chemical isolation and purification strategies typically afforded highly pure products but often at the expense of reduced overall yield (Ginting, 2019; Sugiharto et al., 2024).

C. Purity Level

High-purity eugenol (>95%) has been obtained using batch distillation, chemical purification, and chromatographic techniques (Sugiharto et al., 2024; Handayani et al., 2023; He et al., 2024). Microwave-assisted and ultrasound-assisted extraction methods have also been shown to maintain relatively high eugenol purity, frequently exceeding 75% eugenol content (Kennouche et al., 2015; Suttiarporn et al., 2024; Liu et al., n.d.). In addition, deep eutectic solvent (DES) systems and supercritical CO_2 extraction have yielded highly purified eugenol fractions with minimal thermal or oxidative degradation (Suttiarporn et al., 2025; Frohlich et al., 2019). Across these studies, analytical techniques such as HPLC, GC–MS, and TLC were routinely employed to verify eugenol purity and characterize the chemical profile of the extracts (Yn et al., 2024; Defrancesco, 2021).

D. Bioactivity Retention

The preservation of biological activity following extraction and purification is a critical determinant of the functional value of clove-derived compounds, particularly eugenol. Across 25 studies, antioxidant, antibacterial, and anti-inflammatory activities were consistently retained in post-extraction samples, with eugenol-rich fractions demonstrating especially strong bioactivity (Elbestawy et al., 2023; Quast et al., 2023; Awojide et al., 2024). Emerging evidence indicates that green extraction technologies—such as ultrasound-assisted, microwave-assisted, and supercritical CO_2 methods—preserve these bioactivities more effectively than conventional, prolonged thermal extractions (Suttiarporn et al., 2024; Frohlich et al., 2023). Moreover, targeted fractionation has been shown to enhance specific biological activities by enriching eugenol and related phenolic constituents (Awojide et al., 2024). Although certain chemical purification approaches prioritize compound integrity over biological performance, they nonetheless maintain the structural stability of eugenol and associated metabolites (Ginting, 2019; Sugiharto et al., 2024).

E. Process Efficiency

In recent years, increasing attention has been directed toward optimizing extraction and purification strategies for clove-derived compounds, particularly eugenol, with an emphasis on process efficiency, energy demand, and environmental impact. Comparative studies have demonstrated that microwave-assisted and ultrasound-assisted extraction techniques substantially reduce extraction time and energy consumption relative to conventional Soxhlet extraction and hydro-distillation, while maintaining satisfactory extraction performance (Kennouche et al., 2015; Suttiarporn et al., 2024; Liu et al., n.d.). Supercritical CO_2 extraction, although requiring careful optimization of operating parameters such as pressure and temperature, has been shown to provide favorable extraction kinetics and high process efficiency (Chatterjee & Bhattacharjee, 2013; Tongwei & Qingzhong, 2015). By contrast, batch distillation and chemical purification routes are generally more energy-intensive and time-consuming, limiting their sustainability and scalability (Sugiharto et al., 2024; Widayat et al., 2014). More recently, deep eutectic solvent (DES)-based methods have emerged as promising alternatives, offering a compromise between extraction efficiency and the use of greener, less toxic solvents (Suttiarporn et al., 2025; Strižincová et al., 2024).

F. Environmental Impact

Recent advances in extraction science have increasingly emphasized the importance of environmentally responsible methodologies for isolating bioactive compounds from natural products such as clove. Green extraction technologies—including deep eutectic solvents, supercritical CO_2 systems, ultrasound-assisted processes, and microwave-assisted techniques—have demonstrated clear advantages in reducing solvent toxicity, minimizing waste generation, and lowering overall carbon footprints (Wei et al., 2016; Suttiarporn et al., 2025; Fröhlich et al., 2019). In contrast, conventional solvent-based extraction and chemically intensive purification approaches present significant environmental drawbacks due to their heavy reliance on organic solvents and the production of hazardous chemical waste (Ginting, 2019; Haryani et al., 2014). Emerging purification strategies, particularly membrane-based separation and advanced chromatographic methods, offer promising avenues for further reducing energy consumption and waste output while maintaining high levels of selectivity and efficiency (He et al., 2024; Kusworo et al., 2018). Recent reviews reinforce the growing consensus that sustainable practices are essential for future developments in clove oil extraction and processing, underscoring the need for methodologies that balance efficiency with ecological responsibility (Liñán-Atero et al., 2024; Putra et al., 2024).

G. Critical Analysis and Synthesis

The reviewed literature presents a comprehensive examination of various extraction and purification techniques for eugenol from clove, alongside evaluations of its medicinal properties. A prominent theme is the comparison between conventional and green extraction methods, highlighting advancements in yield, purity, and environmental sustainability. However, inconsistencies in methodological parameters and limited standardization across studies pose challenges for direct comparison and scalability. Additionally, while the bioactivity of eugenol is well-documented, the influence of extraction parameters on its medicinal efficacy requires further elucidation. The integration of novel purification technologies and analytical methods also reflects ongoing efforts to optimize eugenol isolation for pharmaceutical applications.

Table 2. Reviewed techniques for eugenol extraction and purification and their medicinal evaluation

Aspect	Strengths	Weaknesses
Extraction Techniques	The literature showcases a diverse array of extraction methods, including hydro-distillation, microwave-assisted extraction (MAE), supercritical CO_2 extraction (SC-CO_2), and deep eutectic solvent (DES)-based methods, demonstrating significant improvements in eugenol yield and purity. Innovative green techniques such as ultrasound- assisted supercritical CO_2 extraction and DES-MHD have been shown to enhance extraction efficiency while reducing environmental impact (Wei et al., 2016; Suttiarporn et al., 2025; Suttiarporn et al., 2024). Microwave-assisted methods notably reduce extraction time and energy consumption, yielding high-quality oils with elevated eugenol content (Kennouche et al., 2015; Liu et al.).	Despite the variety of methods, there is a lack of standardized protocols, making it difficult to compare results across studies. Some conventional methods like Soxhlet extraction, while yielding high eugenol content, are energy- intensive and less environmentally friendly(Khadiza et al., 2020)(Abate et al., 2025). Additionally, optimization parameters such as temperature, pressure, and solvent ratios vary widely, limiting reproducibility and industrial scalability(Frohlich et al., 2019)(Chatterjee & Bhattacharjee, 2013). The economic feasibility of some advanced methods remains underexplored(Suttiarporn et al., 2024).

Aspect	Strengths	Weaknesses
Purification Strategies	Chemical purification approaches, including reactive extraction with alkaline and acidic reagents and batch distillation, have achieved high eugenol purity levels (up to 97%) (Sugiharto et al., 2024; Handayani et al., 2023; Haryani et al., 2014). Membrane-based nanohybrid technologies offer promising low- energy alternatives for purification, addressing solvent compatibility issues (Kusworo et al., 2018). Analytical techniques such as GC-MS, HPLC, and OPLC coupled with bioactivity assays provide robust characterization and quality control of purified eugenol(Elbestawy et al., 2023; Yn et al., 2024; Móricz et al., 2017).	Many purification methods involve multiple steps with potential losses in yield and require careful control of reaction conditions(Sugiharto et al., 2024; Widayat et al., 2014). Chemical extraction processes may generate hazardous waste and require neutralization steps, impacting sustainability (Haryani et al., 2014). Membrane technologies, while innovative, face challenges related to membrane fouling and eugenol solubility, limiting their current industrial application(Kusworo et al., 2018). There is also limited integration of purification with extraction in continuous processes.
Chemical Composition and Purity Assessment	Studies employ advanced chromatographic and spectroscopic techniques to accurately quantify eugenol and related compounds, ensuring high purity and detailed chemical profiling(Elbestawy et al., 2023)(Yn et al., 2024; Khemariya et al., 2022). The use of GC-MS and HPLC-DAD allows differentiation between eugenol and its derivatives, critical for medicinal applications (Defrancesco, 2021; Yn et al., 2024). Validation of analytical methods according to international guidelines enhances data reliability (Yn et al., 2024).	Variability in analytical methods and lack of uniform reporting standards complicate cross- study comparisons. Some studies rely on indirect or less sensitive methods, potentially underestimating impurities or minor constituents (Khadiza et al., 2020; Haxhijaha et al., n.d.). The influence of extraction solvents and conditions on chemical stability during analysis is not always addressed, which may affect accuracy (Shende & Shilpashree, 2024).

Aspect	Strengths	Weaknesses
Medicinal Properties and Bioactivity Correlation	The literature robustly documents eugenol's antibacterial, antioxidant, anti-inflammatory, and antifungal activities, supporting its therapeutic potential(Elbestawy et al., 2023)(Awojide et al., 2024)(Maggini et al., 2024)(Łoś et al., 2023). Several studies link enhanced extraction purity and optimized processing parameters to improved bioactivity, such as stronger DPPH radical scavenging and inhibition of resistant bacterial strains (Suttiarporn et al., 2025; Suttiarporn et al., 2024; Quast et al., 2023). Synergistic effects of eugenol with other clove constituents are also explored, highlighting the complexity of bioactivity (Awojide et al., 2024).	Few studies systematically investigate how variations in extraction and purification directly influence medicinal efficacy, leaving gaps in understanding the structure-activity relationship(Khalil et al., 2017)(Łoś et al., 2023). Most bioactivity assessments are in vitro, with limited clinical validation. The stability of bioactive compounds during processing and storage is insufficiently addressed, which may affect therapeutic outcomes(Liñán-Atero et al., 2024).
Environmental and Economic Considerations	Green extraction methods, including DES-based and ultrasound-assisted techniques, demonstrate reduced solvent use, lower energy consumption, and minimized chemical waste, aligning with sustainability goals (Wei et al., 2016; Suttiarporn et al., 2025; Suttiarporn et al., 2024). Economic analyses highlight microwave-assisted hydrodistillation as cost-effective for scale-up (Suttiarporn et al., 2024). The adoption of renewable energy sources in hydrodistillation further enhances environmental benefits(Katekar et al., 2023).	Comprehensive life cycle assessments and cost- benefit analyses are scarce, limiting understanding of the true environmental and economic impacts of various methods(Aziz et al., 2023)(Katekar et al., 2023). Some green technologies require specialized equipment and expertise, potentially restricting accessibility in resource-limited settings (Suttiarporn et al., 2025). The trade-offs between yield, purity, and sustainability are not fully quantified.

Aspect	Strengths	Weaknesses
Methodological Robustness and Reproducibility	Several studies employ rigorous experimental designs, including response surface methodology and orthogonal experiments, to optimize extraction parameters and validate results (Nurmitasari & Mahfud, 2021; Chatterjee & Bhattacharjee, 2013; Widayat et al., 2014). The use of standardized bioassays and analytical validations strengthens the reliability of findings (Yn et al., 2024; Awojide et al., 2024).	Heterogeneity in sample preparation, clove source, and extraction conditions introduces variability. Many studies lack detailed reporting on replicates, statistical analyses, and control experiments, which undermines reproducibility (Khadiza et al., 2020; Defrancesco, 2021). The influence of clove part (buds, leaves, stems) on extraction outcomes is inconsistently considered (Khemariya et al., 2022).
Integration of Extraction and Purification Processes	Emerging research explores combined extraction-purification approaches, such as ultrasound-assisted supercritical CO_2 extraction coupled with chromatographic analysis, enhancing process efficiency and product quality (Wei et al., 2016; He et al., 2024). The development of continuous and scalable methods is addressed in techno-economic studies (Sugiharto et al., 2024; Suttiarporn et al., 2024).	Integration remains limited, with most studies treating extraction and purification as discrete steps. This separation may lead to inefficiencies and increased costs. There is a paucity of pilot- scale or industrial-scale validations, hindering translation from laboratory to commercial production (Sugiharto et al., 2024; Kusworo et al., 2018). The impact of integrated processes on bioactivity preservation is underexplored.

H. Theoretical and Practical Implications

Eugenol, the principal bioactive constituent of clove (*Syzygium aromaticum*), has attracted sustained research interest due to its diverse pharmacological properties and its central role as a value-added product in pharmaceutical, nutraceutical, and food-related applications. However, the efficiency, selectivity, and sustainability of its extraction and purification remain highly dependent on the interplay between plant matrix characteristics, process parameters, and the choice of conventional versus green technologies. Against this backdrop, the present review not only consolidates current knowledge on eugenol isolation and purification, but also distills its broader implications at both theoretical and practical levels. Theoretically, the findings refine existing concepts regarding how extraction conditions shape the chemical profile, purity, and bioactivity of clove-derived compounds, offering mechanistic insight into solvent–solute interactions, membrane phenomena, and constituent synergy within complex essential oil matrices. Practically, the results provide evidence-based guidance for the design and optimization of scalable, environmentally responsible processes, encompassing advanced extraction (e.g., ultrasound-, microwave-, and supercritical CO_2-based techniques), green solvent systems such as deep eutectic solvents, and state-of-the-art purification strategies including chromatographic and membrane-based approaches. Together, these implications establish a conceptual and operational framework for developing standardized, high-performance protocols that maximize yield, purity, and therapeutic efficacy of eugenol, while simultaneously addressing industrial, regulatory, and sustainability demands.

IV. CONCLUSION

The collective body of research on the isolation and purification of eugenol from clove underscores a clear advancement in both conventional and green extraction methodologies aimed at optimizing yield, purity, and bioactivity retention. Traditional techniques such as hydro-distillation and Soxhlet extraction continue to serve as accessible, well-established methods but are generally associated with lower efficiencies, longer processing times, and higher environmental footprints. In contrast, innovative approaches including microwave-assisted extraction, ultrasound-assisted extraction, supercritical CO2 extraction, and deep eutectic solvent-based methods demonstrate significant improvements in extraction yield, purification efficacy, and preservation of eugenol's bioactive properties, while simultaneously aligning with sustainability goals. Microwave and ultrasound technologies stand out for their ability to drastically reduce extraction time and energy consumption, yielding oils with high eugenol content and strong antioxidant and antimicrobial activities. Supercritical CO2 extraction, although sometimes yielding lower total volumes, offers superior selectivity and environmental advantages by obviating the use of organic solvents.

Purification strategies have evolved to complement these extraction techniques, with batch distillation, chemical purification via alkaline and acid treatment, and chromatographic methods achieving eugenol purities exceeding 95%. Emerging membrane technologies provide promising low-energy alternatives, though challenges related to membrane compatibility with eugenol and scalability remain. Analytical methods such as GC-MS, HPLC, and TLC achieve reliable chemical profiling and purity confirmation, yet disparities in methodology and reporting standards hinder full comparability among studies.

Regarding medicinal efficacy, the literature consistently confirms eugenol's potent antioxidant, antibacterial, anti-inflammatory, and antifungal activities, which are largely preserved or enhanced when green extraction methods are employed. However, there is a notable gap in systematic investigations directly correlating extraction and purification parameters with variations in therapeutic efficacy, particularly in clinical contexts. The stability of eugenol and its bioactivity during processing and storage also warrants deeper exploration.

Environmental and economic considerations increasingly influence method selection, with green technologies demonstrating reduced solvent use, lower emissions, and improved cost-effectiveness in pilot-scale assessments. Still, comprehensive lifecycle analyses and economic viability studies at industrial scales are limited. Overall, the integration of optimized extraction and purification processes, supported by robust analytical techniques, holds promise for scalable production of high-purity eugenol with preserved bioactivity. Future research should focus on standardizing protocols, advancing continuous integrated processing systems, and elucidating the structure-activity relationships of eugenol in medicinal applications to fully harness its therapeutic potential.

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