

ARTICLE INFORMATION

Received: February, 7, 2026

Revised: May, 8, 2026

Available online: May, 8, 2026

at : <https://e-jurnal.iphorr.com/index.php/minh>

A multi-target therapeutic strategy: The efficacy of *coffea canephora* husk extract in mitigating oxidative stress, infection, and inflammation – a systematic review

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Abstract

Background: Robusta coffee (*Coffea canephora*) husk is a massive agro-industrial by-product. Despite possessing a rich phytochemical profile superior to Arabica, it remains underutilized as environmental waste. This review explores its valorization from a pollutant into a functional pharmaceutical resource.

Purpose: To synthesize evidence regarding the bioactive potential of Robusta husk as a "natural shield" against oxidative stress and infections, and assess its feasibility in pharmaceutical formulation development.

Method: Following PRISMA 2020 guidelines, a search of PubMed, ScienceDirect, and Google Scholar (2020–2026) identified 17 eligible studies. These included in vitro, in vivo, and formulation research selected for synthesis.

Results: Robusta husk is exceptionally rich in caffeine and chlorogenic acids. It exhibits potent antioxidant activity (IC₅₀<50 ppm) and antimicrobial efficacy against *Enterococcus faecalis*, *Porphyromonas gingivalis*, and *Staphylococcus aureus*. In vivo studies further confirm anti-inflammatory and wound-healing acceleration. Technically, the extract has been successfully formulated into stable antioxidant gels, lotions, and peel-off masks.

Conclusion: *C. canephora* husk acts as a promising multi-target therapeutic agent. Future research must prioritize standardization and clinical trials to facilitate its translation into standardized herbal medicines.

Keywords: Antibacterial; Anti-inflammatory; Antioxidant; *Coffea Canephora*; Robusta Coffee Husk; Systematic Review.

INTRODUCTION

Coffee is one of the most traded and consumed commodities globally, playing a pivotal role in the economy of many tropical countries. However, the massive scale of coffee production generates a proportional volume of agro-industrial waste. During the processing of coffee cherries, significant amounts of by-products are generated, with coffee husk representing a major fraction of this biomass (Duran-Aranguren, Robledo, Gomez-Restrepo, Arboleda Valencia, & Tarazona, 2021). Traditionally, these by-products have been considered waste, often discarded into the environment or burned, which contributes to soil and water pollution. In recent years, the concept of a circular economy has driven a paradigm shift towards the revalorization of this

biomass, transforming what was once considered environmental waste into a sustainable source of high-value ingredients for various industries (Rebollo-Hernanz, Cañas, Taladrid, Benitez, Bartolomé, Aguilera, & Martín-Cabrejas, 2021). From a phytochemical perspective, coffee husk is not merely inert biological matter; it is a rich reservoir of bioactive compounds. Studies have identified that coffee husks contain significant concentrations of phenolic compounds, caffeine, and other antioxidants that possess biological utility (Rebollo-Hernanz et al., 2021). While much of the existing literature focuses on *Coffea arabica*, recent comparative studies have highlighted the distinct phytochemical profile of *Coffea canephora* (Robusta). Research indicates that

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Robusta beans and their by-products often exhibit different antioxidant capacities and phenolic compositions compared to Arabica, suggesting that Robusta husk may possess unique, yet underutilized, functional properties suitable for specific therapeutic applications (Himri, Belkhiri, Azizi, Loukili, Rahhou, Legssyer, & Legssyer, 2025).

The exploration of these natural bioactive sources is becoming increasingly critical in addressing contemporary global health challenges, particularly oxidative stress and antimicrobial resistance. Oxidative stress, driven by an imbalance between free radical production and the body's antioxidant defenses, is a fundamental mechanism underlying chronic inflammation and the progression of numerous degenerative diseases (Altanam, Darwish, & Bakillah, 2025). Concurrently, the global rise of bacterial antimicrobial resistance (AMR) poses a severe threat to public health, with millions of deaths attributed to resistant pathogens annually (Fernandez, 2022). Consequently, there is an urgent need to discover novel natural agents that can act as both potent antioxidants to mitigate oxidative damage and effective antimicrobials to combat resistant bacteria.

Despite the growing interest in coffee by-products as documented in scientometric overviews (Duran-Aranguren et al., 2021), there remains a gap in the literature regarding the specific systematic evaluation of Robusta coffee husk for pharmaceutical and health applications. Most reviews tend to generalize findings across coffee species or focus heavily on food applications rather than medical potential. Therefore, this systematic literature review aims to comprehensively synthesize current evidence regarding the bioactive compounds of Robusta coffee husk (*Coffea canephora*) and its pharmacological potential—specifically its antioxidant, anti-inflammatory, and antimicrobial activities—as well as its development into value-added pharmaceutical formulations.

RESEARCH METHOD

Study design and search strategy in this systematic literature review were conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines to ensure transparency and methodological rigor. A comprehensive literature

search was performed across multiple electronic databases, including PubMed, ScienceDirect, and Google Scholar, covering the period from January 2020 to February 2026. The search strategy utilized Boolean operators to combine keywords related to the biological species, plant part, and pharmacological potential. The key search terms included "*Coffea canephora*" OR "Robusta coffee" AND "husk" OR "pulp" OR "skin" OR "byproduct" OR "waste" AND "antioxidant" OR "antibacterial" OR "anti-inflammatory" OR "wound healing" OR "formulation". The reference lists of selected articles were also manually screened to identify additional relevant studies.

Eligibility criteria studies were selected based on specific inclusion and exclusion criteria to ensure the relevance of the data. The inclusion criteria encompassed: (1) original research articles and conference proceedings published in English or Bahasa Indonesia; (2) studies specifically investigating *Coffea canephora* (Robusta) or comparative studies involving Robusta; (3) research utilizing the husk, pulp, or skin of the coffee cherry as the primary subject; and (4) studies reporting pharmacological activities (such as antioxidant, antimicrobial, or anti-inflammatory effects) or the development of pharmaceutical/cosmetic formulations (e.g., gels, creams, lotions, or nanoparticles). Exclusion criteria included review articles, editorials, studies focusing solely on coffee beans (green or roasted) without analyzing the husk, and research limited to *Coffea arabica* without a Robusta comparison.

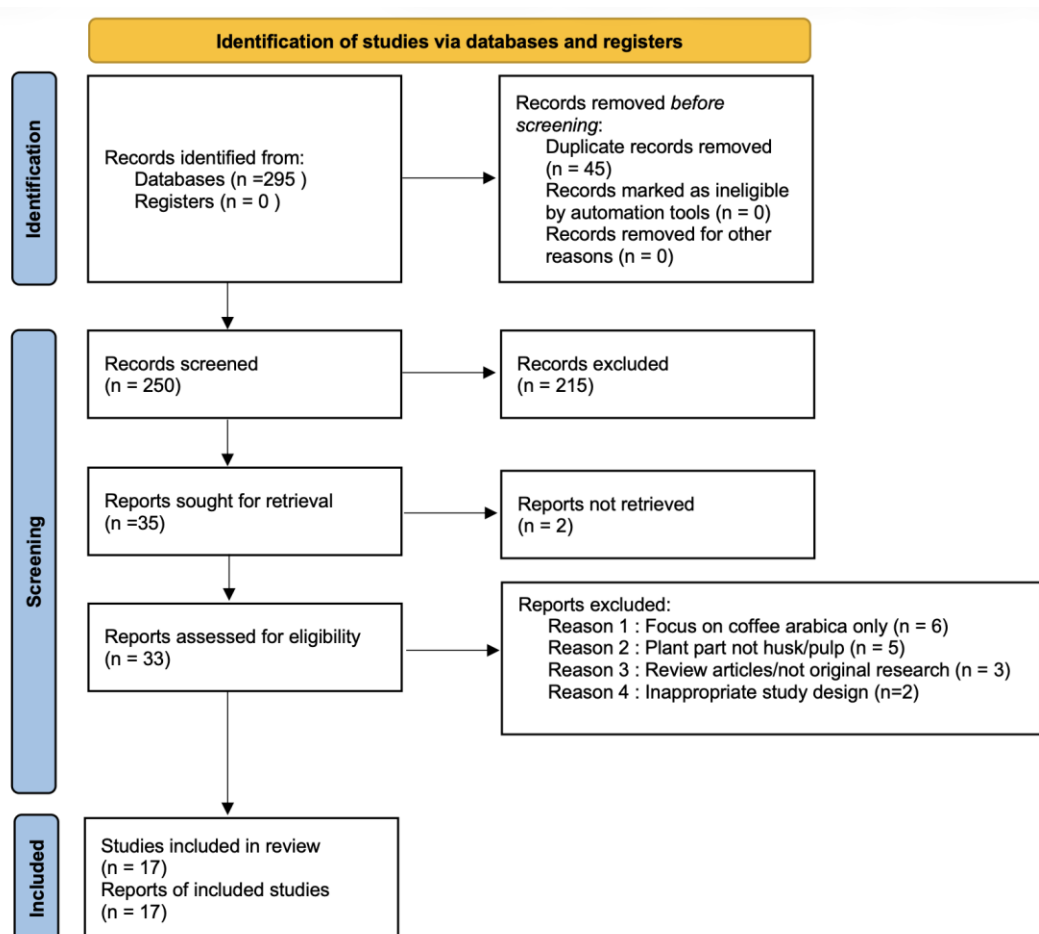
The screening process involved a two-stage review: initially screening titles and abstracts to remove duplicates and irrelevant topics, followed by a full-text review of potentially eligible articles. From the final selection of 17 included studies, data were extracted using a standardized form capturing the following details: first author, year of publication, study location, extraction method (e.g., maceration, Soxhlet, ultrasound-assisted extraction), type of assay (in vitro, in vivo, or in silico), specific phytochemical compounds identified (e.g., phenols, flavonoids, caffeine), and key outcomes regarding biological activity or physical stability of formulations. The data were then synthesized qualitatively to categorize the pharmacological potential of Robusta coffee husk into antioxidant activity, antimicrobial efficacy, and pharmaceutical product development.

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DOI: <https://doi.org/10.33024/minh.v9i2.2537>

RESEARCH RESULTS



Picture PRISMA 2020 Algorithm

A total of 17 studies met the stringent inclusion criteria for this systematic review. The temporal distribution of the selected articles, spanning from 2020 to early 2026, indicates a growing scientific interest in the valorization of Robusta coffee husk (*Coffea canephora*). Notably, the majority of the studies were published between 2023 and 2026, reflecting a recent surge in research focus towards sustainable pharmaceutical ingredients and the circular economy. Geographically, the research is predominantly concentrated in major coffee-producing nations in Southeast Asia, specifically Indonesia and Vietnam. This geographical trend suggests a strong regional effort to address the agro-industrial waste challenges inherent to these countries by transforming local coffee by-products into

value-added health commodities. Regarding the study design and methodological approaches, the included literature can be classified into four distinct categories: in vitro experimental studies, in vivo animal models, pharmaceutical formulations, and in silico computational analyses.

In vitro experimental studies, the largest proportion of the included studies employed an in vitro design to evaluate the fundamental biological activities and phytochemical profiles of Robusta coffee husk. Ten studies focused on extraction optimization, chemical characterization, and preliminary efficacy testing against pathogens or free radicals. For instance in previous research provided comprehensive analyses of antioxidant capacity and caffeine content (Fitriansyah, Saonah, Baroroh,

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Herawati, & Ikhlas, 2025; DePaula, Partelli, Batista, Calado, & Farah, 2025; Rohaya, Anwar, Amhar, Sutriana, A., & Muzaifa, 2023). Furthermore, specifically investigated the antibacterial potency of the husk extract against oral and systemic pathogens (Prasetya, Fatimatuzzahro, Ermawati, Kristina, & Prabaningrum, 2024; Dewi, Hidayati, & Hanifa, 2023; Ishimora, Prasetya, & Susilawati, 2023). Additionally, advanced processing methods were explored, such as fermentation and nanoparticle synthesis, to enhance bioavailability and efficacy. In Vivo Animal Models To validate the biological effects in living systems, two studies utilized in vivo models, providing stronger evidence for safety and therapeutic potential (Marie, Tan, Abduh, 2026; Sandeep, Abishad, Vinod, Karthikeyan, Juliet, Kurkure, & Vergis, 2024). Demonstrated the wound-healing properties of Robusta husk extract in a rat model of periodontitis, highlighting its ability to increase collagen density. Meanwhile, evaluated the systemic effects of husk supplementation on Red Nile Tilapia (*Oreochromis sp.*), confirming its safety and ability to improve antioxidative status in a living organism (Afriansyah, Setiawati, Suprayudi, & Fauzi, 2023; Fatimatuzzahro, Prasetya, Shita, Hikmah, Maulana, Apriyono, & Pratiwi, 2025).

Pharmaceutical and cosmetic formulation bridging the gap between raw extracts and end-products, four studies focused on the development of pharmaceutical dosage forms. These studies assessed the physicochemical stability and biological activity of the extract when incorporated into topical vehicles (Sukardi, Marcellia, & Chusniasih, 2021; Nursal, Amalia, Nining, Putri, & Larasati, 2024). Successfully formulated antioxidant gel masks and peel-off masks, respectively. Furthermore, expanded the application into body lotions and oil-in-water creams, demonstrating the versatility of Robusta husk as a functional ingredient in skincare. In Silico Studies Complementing the experimental data, one study employed a computational approach, utilized in silico molecular docking to predict the interaction between bioactive compounds in *Coffea canephora* husk and specific enzymes (alpha-glucosidase), providing a molecular understanding of its antifungal and anti-diabetic mechanisms (Wardhani, Daffa, Firdayanti, Andrifanie, Iqbal, Rahayu, & Pardilawati, 2025; Winahyu, Marcellia, & Diatri, 2021; Mai, Minh, Phat, Chi, Hien, Nguyen, & Tri, 2024).

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Table Summary of Included Studies on Robusta Coffee Husk (*Coffea Canephora*)

(Author, Year) Country	Study Design & Object	Method / Parameters	Key Findings / Outcomes
(Fitriansyah, 2025) Indonesia	In vitro study on Cascara (dried husk) of Robusta coffee.	DPPH assay for antioxidant activity; UV-Vis spectrophotometry for caffeine content.	The cascara extract demonstrated very strong antioxidant activity (IC50 values < 50 ppm). High caffeine content was identified, suggesting potential as an anti-hyperpigmentation agent (tyrosinase inhibition potential).
(Afriansyah et al., 2023) Indonesia	In vivo study on Red Nile Tilapia (<i>Oreochromis</i> sp.).	Dietary supplementation of coffee husk; Analysis of growth performance, blood chemicals, and antioxidant status.	Supplementation with Robusta husk significantly improved growth performance and enhanced the antioxidative activity in the blood of the fish, indicating its safety and bioactivity as a functional feed additive.
(Prasetya et al., 2024) Indonesia	In vitroantibacterial study.	Diffusion and dilution methods against <i>Enterococcus faecalis</i> and <i>Porphyromonas gingivalis</i> .	The Robusta husk extract exhibited significant antibacterial activity against both dental pathogens (<i>E. faecalis</i> and <i>P. gingivalis</i>), suggesting potential application in dentistry (e.g., root canal irrigation or periodontitis treatment).
(Mai et al., 2024) Vietnam	In vitro and In silico study.	Alpha-glucosidase inhibition assay; Antifungal testing; Molecular docking.	The husk extract showed potent alpha-glucosidase inhibition (anti-diabetic potential) and antifungal activity. In silico analysis confirmed the interaction of bioactive compounds with target enzymes.
(Sandeep et al., 2024) India	Nanotechnology / Green Synthesis.	Synthesis of ZnO nanoparticles (ZnONPs) using Robusta husk extract; Antioxidant & antimicrobial assays.	Validated the eco-friendly synthesis of ZnONPs. The nanoparticles exhibited enhanced antioxidant properties and significant biocidal (antimicrobial) activity compared to the extract alone.
(Marie et al., 2026) Indonesia	Fermentation study / In vitro.	Fermentation using <i>Leuconostoc mesenteroides</i> ; Chemical profiling; Anti-inflammatory & antioxidant assays.	Fermentation significantly enhanced the bioavailability of phenolic compounds. The fermented Robusta pulp showed superior antioxidant activity and potent anti-inflammatory potential compared to non-fermented samples.
(Sukardi et al., 2021) Indonesia	Pharmaceutical Formulation (Gel Mask).	Formulation of peel-off gel mask; Physical evaluation (pH, viscosity, spreadability); Antioxidant stability.	The Robusta husk extract was successfully formulated into a gel mask meeting physical standards. The preparation maintained stable antioxidant activity, suitable for topical cosmetic application.
(Nursal et al., 2024) Indonesia	Pharmaceutical Formulation (Peel-off Mask).	Formulation optimization; IC50 determination (DPPH method); Physical stability testing.	The optimized peel-off mask formula containing Robusta skin extract demonstrated strong antioxidant activity (IC50 categorization: strong) and possessed good physical characteristics (drying time, adhesion).

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(Author, Year) Country	Study Design & Object	Method / Parameters	Key Findings / Outcomes
(Dewi et al., 2023) Indonesia	In vitro antibacterial study.	Disc diffusion method against <i>Staphylococcus aureus</i> and <i>Escherichia coli</i> .	Phenolic compounds extracted from Robusta skin showed inhibitory zones against both Gram-positive (<i>S. aureus</i>) and Gram-negative (<i>E. coli</i>) bacteria, confirming broad-spectrum antibacterial potential.
(Ishimora et al., 2023) Indonesia	Comparative In vitro study (Robusta vs. Arabica).	Antibacterial diffusion test against <i>Lactobacillus acidophilus</i> .	Compared the efficacy of Robusta and Arabica husks. Robusta husk extract demonstrated effective antibacterial capability against <i>L. acidophilus</i> (relevant to cariogenic control or microbial balance in the oral cavity).
(Kusuma et al., 2022) Indonesia	Extraction Optimization.	Soxhlet extraction method; Solvent optimization; Tannin quantification.	Identified optimal solvents for maximizing tannin yield from Robusta husk via the Soxhlet method. High tannin content suggests potential use as a functional feed additive or astringent agent.
(Tran et al., 2020) Australia	Food Technology / Processing.	Effects of different drying methods on Robusta pulp; Phenolic content & Antioxidant capacity (TEAC/ORAC).	Drying conditions significantly affect bioactivity. Optimized drying preserved high levels of phenolic compounds and antioxidant capacity, crucial for utilizing the pulp as a functional food ingredient.
(DePaula et al., 2025) Brazil	Phytochemical Profiling.	HPLC analysis of seeds, husks, and leaves of <i>C. canephora</i> cv. Conilon genotypes.	Provided a comprehensive profile of major bioactive compounds (Caffeine, Chlorogenic Acids). Husks were identified as a rich source of caffeine and phenols, comparable to or exceeding other plant parts in specific genotypes.
(Rohaya et al., 2023) Indonesia	Comparative varieties study.	Physicochemical analysis and antioxidant testing of coffee pulp from three varieties in Aceh.	Confirmed that Robusta pulp from Aceh region contains high antioxidant activity and specific physicochemical properties suitable for further processing into value-added products.
(Wardhani et al., 2025) Indonesia	Pharmaceutical Formulation (Body Lotion).	Formulation of body lotion combining Coffee Husk and Papaya Seeds; DPPH assay.	The combination of extracts in a body lotion base showed synergistic antioxidant effectiveness. The formulation was physically stable and effective in scavenging free radicals on the skin.
(Fatimatuzzahro et al., 2025) Indonesia	In vivo study (Periodontitis Model).	Application of Robusta husk extract gel on rats with periodontitis; Histological analysis.	The extract gel significantly increased the number of fibroblast cells and collagen density in the gingival tissue of rats, accelerating the wound healing process in periodontitis.
(Winahyu et al., 2021.) Indonesia	Pharmaceutical Formulation (Cream).	Oil-in-water (O/W) cream formulation; Physical evaluation; Antioxidant testing.	The Robusta husk extract was successfully incorporated into a cream dosage form. The cream exhibited "very strong" antioxidant activity (low IC50 value), indicating high potential for anti-aging or skin protection products.

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The therapeutic potential of *Coffea canephora* (Robusta) husk is fundamentally underpinned by its rich profile of bioactive secondary metabolites. Unlike *Coffea arabica*, Robusta is genetically predisposed to synthesize higher concentrations of certain defensive compounds, particularly caffeine and chlorogenic acids. A comprehensive phytochemical profiling comparing different anatomical parts of the coffee cherry, revealing that the husks contain significant levels of bioactive compounds that are often comparable to, or in some genotypes exceed, those found in the seeds (DePaula et al., 2025). Specifically, caffeine, a purine alkaloid known for its stimulating and antioxidant properties, was identified as a major constituent. This finding is corroborated, who reported high caffeine content in Robusta cascara from West Java, correlating this high alkaloid presence with strong antioxidant activity ($IC_{50} < 50$ ppm) and potential anti-hyperpigmentation effects through tyrosinase inhibition. In addition to alkaloids, the husk is a potent source of tannins and phenolic acids. Highlighted the importance of solvent optimization in the extraction process, demonstrating that specific solvents in the Soxhlet method can maximize the yield of tannins, which are crucial for their astringent and antimicrobial properties (Fitriansyah et al., 2025; Kusuma, Wulandari, Nurfitriani, & Awaludin, 2022).

However, the recovery and bioavailability of these phytochemicals are heavily influenced by post-harvest processing and extraction techniques. Emphasized that the physicochemical composition of coffee pulp is not uniform and varies significantly across different local varieties, such as those found in Aceh, necessitating variety-specific standardization. Furthermore, the method of dehydration plays a critical role in preserving these heat-sensitive compounds. Demonstrated that drying conditions significantly impact the physical properties and the retention of phenolic compounds; improper drying can lead to the degradation of antioxidants, whereas optimized drying preserves the husk's radical-scavenging capacity (Rohaya et al., 2023; Tran, Kirkman, Nguyen, & Van Vuong, 2020). Beyond physical processing, biological transformation has emerged as a promising strategy to enhance bioactivity. A recent study revealed that fermentation using *Leuconostoc mesenteroides* significantly alters

the chemical profile of Robusta pulp. This bioprocess facilitates the release of bound phenolics, thereby increasing their bioavailability and resulting in superior antioxidant and anti-inflammatory activities compared to non-fermented samples. Collectively, these studies suggest that while Robusta husk is inherently rich in phytochemicals, its pharmaceutical value is maximized through optimized extraction and advanced processing methods like fermentation (Marie et al., 2026).

Consistent with its diverse phytochemical profile, *Coffea canephora* husk exhibits a multipotent pharmacological mechanism. The literature review identifies three primary domains of biological activity that justify its classification as a "natural shield": potent antioxidant capacity against oxidative stress, broad-spectrum antimicrobial efficacy against infection, and significant anti-inflammatory properties promoting wound healing.

The most well-documented bioactivity of Robusta coffee husk is its ability to scavenge free radicals, thereby mitigating oxidative stress. That the extract of Robusta cascara demonstrates very strong antioxidant activity, characterized by an IC_{50} value of less than 50 ppm in DPPH assays. This high potency is attributed to the synergistic action of caffeine and phenolic compounds, which function as electron donors to stabilize radical species. Importantly, this antioxidant capability is not limited to in vitro environments but also translates to biological systems. Provided in vivo evidence showing that dietary supplementation of Robusta husk significantly improved the blood antioxidant status of Red Nile Tilapia (*Oreochromis sp.*), suggesting its bioavailability and efficacy in protecting living organisms from systemic oxidative damage. Furthermore, advancements in nanotechnology have been employed to amplify this potential demonstrated that Zinc Oxide nanoparticles (ZnONPs) synthesized using Robusta husk extract exhibited superior antioxidant properties compared to the crude extract alone, offering a sustainable approach to developing high-potency antioxidant agents (Afriansyah et al., 2023; Sandeep et al., 2024).

Robusta coffee husk functions as an effective antimicrobial agent, offering protection against a spectrum of pathogenic microorganisms. In the context of oral health, the extract has shown promise

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as a natural alternative for controlling dental infections. Revealed that the husk extract possesses significant antibacterial activity against *Enterococcus faecalis* and *Porphyromonas gingivalis*, two primary pathogens responsible for root canal infections and periodontitis (Prasetya et al., 2024). This finding is further supported whose comparative study highlighted that Robusta husk extract is more effective than Arabica in inhibiting *Lactobacillus acidophilus*, reinforcing the superior pharmacological potential of the *C. canephora* species. Beyond oral pathogens, the extract exhibits broad-spectrum activity. Efficacy against both Gram-positive (*Staphylococcus aureus*) and Gram-negative (*Escherichia coli*) bacteria. Expanding the scope to fungal pathogens, utilized in vitro and in silico molecular docking to demonstrate the extract's antifungal capability and its inhibition of alpha-glucosidase, providing a dual mechanism for managing infection and metabolic disorders. The mechanism of antimicrobial action typically involves the disruption of microbial cell membranes and the generation of reactive oxygen species (ROS) on the bacterial surface, a process that is significantly enhanced when the extract is utilized in nanoparticle form, as described (Sandeep et al., 2024; Ishimora et al., 2023; Fernandez, 2022).

Completing its role as a therapeutic shield, Robusta coffee husk contributes to tissue repair and inflammation control. Chronic inflammation often impedes the healing process, but processed Robusta pulp appears to mitigate this response. Found that fermentation of the pulp with *Leuconostoc mesenteroides* significantly enhances its anti-inflammatory potency, likely due to the increased bioavailability of specific phenolic metabolites. This anti-inflammatory property translates directly into accelerated wound healing capabilities. In a specific periodontal model, demonstrated that the application of Robusta husk extract gel on rats significantly increased the number of fibroblasts and collagen density in gingival tissues. These histological improvements suggest that the extract not only prevents infection and oxidative damage but actively stimulates the cellular proliferation necessary for rapid tissue regeneration (Marie et al., 2026; Fatimatu Zahro et al., 2025).

DISCUSSION

The therapeutic efficacy of *coffea canephora* husk elucidated in this review is not merely incidental but is rooted in specific molecular interactions driven by its phytochemical constituents. The robust antioxidant activity reported across multiple studies is primarily attributed to the structural properties of polyphenols, particularly chlorogenic acids. Chemically, the presence of hydroxyl (-OH) groups in these phenolic compounds facilitates the donation of electrons or hydrogen atoms to unstable free radicals, effectively neutralizing reactive oxygen species (ROS) and breaking the chain reaction of oxidative stress (Fitriansyah et al., 2025). In terms of antimicrobial activity, the mechanism is likely multimodal. Caffeine and tannins are known to interact with bacterial cell walls, causing membrane disruption and leakage of intracellular contents. This biological observation is strongly corroborated by computational evidence. The in silico study successfully mapped the molecular docking interactions between Robusta bioactive ligands and specific microbial enzymes (such as alpha-glucosidase), providing a theoretical validation for the in vitro fungal and bacterial inhibition observed. This convergence of "wet lab" (experimental) and "dry lab" (computational) data strengthens the conclusion that Robusta husk acts through definitive biochemical pathways rather than non-specific toxicity (Mai et al., 2024; Dewi et al., 2023).

A critical synthesis of the literature challenges the traditional economic hierarchy of coffee species. While *Coffea arabica* is commercially preferred for its superior organoleptic profile (taste and aroma), *Coffea canephora* (Robusta) appears to be chemically superior for pharmaceutical applications. Often regarded as a "second-class" bean in the beverage industry, Robusta husk demonstrates a "first-class" phytochemical profile, characterized by significantly higher concentrations of caffeine and antioxidant compounds. This pharmacological superiority is empirically supported, whose comparative study revealed that Robusta husk extract exhibited greater antibacterial efficacy against *Lactobacillus acidophilus* compared to Arabica. Furthermore, highlighted that even after fermentation, Robusta pulp maintains potent

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biological activity. These findings suggest a paradigm shift: the very traits that make Robusta less desirable for drinking (high bitterness due to caffeine and tannins) are precisely what make it a more potent candidate for antibiotic and antioxidant drug development (Ishimora et al., 2023).

For any natural product to transition from waste to therapeutic agent, safety is paramount. Although most included studies focused on efficacy, provided a crucial indicator of biocompatibility through an in vivo dietary study on *Oreochromis* sp. (Red Nile Tilapia). The findings showed that Robusta husk supplementation did not induce toxicity or growth retardation; on the contrary, it improved growth performance and blood antioxidant status. While this is an animal model, it serves as preliminary evidence that the extract is non-cytotoxic to eukaryotic cells and may promote systemic health, fulfilling a critical prerequisite for further development into human health products (Afriansyah et al., 2023; Altanam et al., 2025).

Despite the promising potential of Robusta coffee husk, this review identifies a significant gap in the current research landscape. The majority of existing studies are limited to in vitro assays and preclinical animal models, with pharmaceutical formulations restricted to cosmetic applications (masks, lotions) or lab-scale prototypes (Nursal et al., 2024; Wardhani et al., 2025). To date, there is a notable absence of clinical trials on humans to validate these therapeutic effects in a clinical setting. Therefore, future research must bridge this translational gap. A critical step forward is the standardization of the extract. Future studies should focus on identifying and quantifying specific "marker compounds" (e.g., a specific concentration of chlorogenic acid or caffeine) to ensure batch-to-batch consistency. Only through rigorous standardization and subsequent clinical testing can Robusta coffee husk transform from an agricultural by-product into an evidence-based standardized herbal medicine.

CONCLUSION

This systematic literature review conclusively establishes that the husk of Robusta coffee (*Coffea canephora*), traditionally discarded as agro-industrial waste, represents a valuable reservoir of bioactive phytopharmaceuticals. The synthesized evidence

demonstrates that Robusta husk extract possesses potent antioxidant, broad-spectrum antimicrobial, and anti-inflammatory properties, primarily driven by its superior concentrations of caffeine and chlorogenic acids compared to *Coffea arabica*. These bioactive capabilities function effectively as a "natural shield," offering protection against oxidative stress-induced damage and bacterial infections, particularly in oral and dermatological contexts. Furthermore, the successful incorporation of the extract into stable pharmaceutical formulations—ranging from antioxidant gels to peel-off masks—validates its feasibility as a functional ingredient for modern health and cosmetic products. However, to fully translate these preclinical findings into clinical practice, future research must prioritize the standardization of extraction protocols and the execution of human clinical trials. Ultimately, valorizing Robusta husk not only addresses environmental concerns through a circular economy approach but also provides a scientifically proven, sustainable candidate for future drug discovery.

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DOI: <https://doi.org/10.33024/minh.v9i2.2537>