

Review

## Health-Promoting Potential of Hemp (*Cannabis sativa*) Root Extracts: Phytochemical Composition, Biological Activities, and Nutraceutical Applications

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### Abstract

Despite industrial hemp (*Cannabis sativa* L.) being long recognized for its diverse bioactive phytochemicals, most scientific studies have predominantly focused on aerial tissues, leaving the roots relatively underexplored. This review provides a comprehensive overview of the phytochemical architecture, biological functionalities, and nutraceutical prospects of hemp root extracts. Characterized by a unique metabolic profile featuring pentacyclic triterpenoids, phytosterols, specialized alkaloids, and neolignans, hemp roots have demonstrated promising antioxidant, anti-inflammatory, antinociceptive, cytotoxic, and cell-protective activities, primarily in preclinical studies. We further examine how advancements in extraction and formulation technologies, such as nano-encapsulation, are overcoming historical barriers to stability and bioavailability. By addressing current regulatory landscapes and research limitations, this review highlights the potential of hemp roots as a sustainable, high-value resource for the functional food and cosmeceutical industries. It proposes prospects for metabolomics-guided discovery and clinical validation.



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## Keywords

Hemp root extract; *Cannabis sativa*; phytochemicals; antioxidant activity; anti-inflammatory activity; anti-cancer activity; nutraceuticals

## 1. Introduction

The global demand for natural plant-derived ingredients with health-promoting properties has increased rapidly in recent years, driven by growing consumer interest in functional foods, nutraceuticals, and preventive healthcare strategies. Plant extracts represent a major source of bioactive compounds, including polyphenols, terpenoids, alkaloids, and phytosterols, which exhibit antioxidant, anti-inflammatory, antimicrobial, and metabolic regulatory activities. These properties have positioned botanical extracts as key components in the development of functional food products and dietary supplements aimed at reducing the risk of chronic diseases associated with oxidative stress and inflammation [1-3].

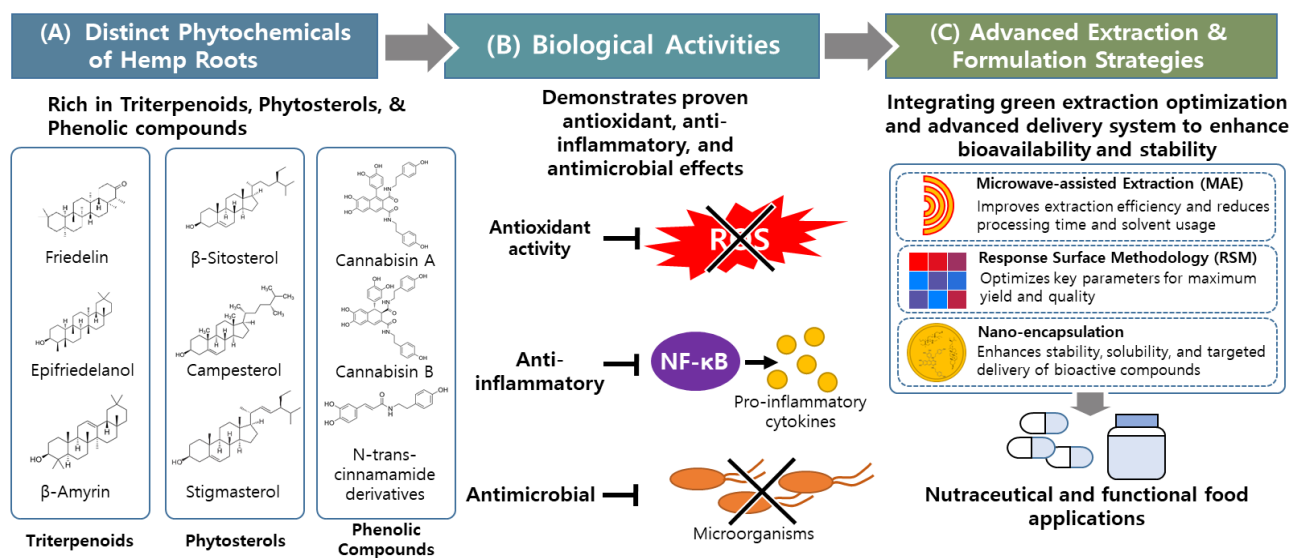
Hemp (*Cannabis sativa* L.) is a versatile crop that has attracted substantial scientific and industrial attention due to its rich phytochemical diversity and broad range of applications in food, medicine, cosmetics, and biomaterials. Most research on hemp-derived bioactives has focused on aerial tissues, particularly flowers and leaves, which are known to accumulate cannabinoids, flavonoids, and terpenes. In contrast, hemp roots have received relatively limited scientific attention despite their long-standing use in traditional medicine systems, where root preparations have historically been used to manage pain, inflammation, fever, and skin disorders [4, 5]. This knowledge gap highlights the need for systematic evaluation of hemp roots as a potential source of functional bioactive compounds.

Recent studies have revealed that hemp roots contain diverse classes of phytochemicals, including triterpenoids, sterols, phenolic acids, alkaloids, and root-specific metabolites that differ substantially from those found in aerial tissues [6, 7]. These compounds have been reported to exhibit antioxidant, anti-inflammatory, antimicrobial, and cell-protective activities *in vitro* and in cell-based models, suggesting that hemp root extracts may modulate cellular redox balance and inflammatory signaling pathways [8]. Although evidence from animal studies and human clinical trials remains limited, such biological activities are directly relevant to nutraceutical applications targeting metabolic disorders, immune regulation, and age-related diseases.

In parallel with advances in phytochemical profiling, improvements in extraction technologies and formulation strategies have enhanced the stability, safety, and bioavailability of plant-derived compounds. Techniques such as solvent optimization, green extraction methods, and nano- or micro-encapsulation have enabled more efficient recovery and delivery of bioactive constituents from plant matrices [9-11]. These developments further expand the potential of hemp root extracts for incorporation into functional foods and dietary supplements [12, 13].

Despite these advances, comprehensive reviews specifically focusing on hemp root extracts remain scarce. Existing literature is fragmented across phytochemical, pharmacological, and applied nutrition studies, making it difficult to obtain an integrated understanding of their health-related potential [4, 7]. Therefore, this review summarizes current knowledge on hemp root phytochemistry and biological activity while critically evaluating the available evidence, which is

derived predominantly from *in vitro* studies with limited support from *in vivo* investigations. By integrating phytochemical, mechanistic, and regulatory perspectives, this review provides a focused, up-to-date synthesis that specifically addresses hemp root extracts as distinct from other hemp-derived materials. In addition, current challenges, safety considerations, and future research directions are highlighted to support the sustainable utilization of hemp roots as a novel plant-derived resource for health-promoting applications. The overall framework of this review, encompassing the phytochemical profiling, biological activities, and potential nutraceutical applications of hemp root extracts, is conceptually illustrated in Figure 1.



**Figure 1** Conceptual framework illustrating the phytochemical composition, biological activities, and advanced extraction and formulation strategies of hemp (*Cannabis sativa* L.) roots. (A) Phytochemical diversity of hemp roots (triterpenoids, phytosterols, and phenolic compounds). (B) Core biological activities (antioxidant, anti-inflammatory, and antimicrobial activities). (C) Advanced extraction and formulation strategies, including microwave-assisted extraction (MAE), response surface methodology (RSM) optimization, and nano-encapsulation, to enhance phytochemical recovery, bioavailability, stability, and nutraceutical or functional food applications.

## 2. Phytochemical Composition of Hemp Root Extracts

Hemp roots possess a distinct phytochemical profile that differs substantially from aerial tissues such as flowers and leaves. Unlike inflorescences, which are rich in cannabinoids and volatile terpenes, hemp roots primarily accumulate triterpenoids, phytosterols, phenolic compounds, alkaloids, and root-specific secondary metabolites. Recent phytochemical investigations have further expanded the chemical characterization of hemp roots by isolating and structurally elucidating several neolignans and related phenolic compounds, many of which have demonstrated anti-inflammatory activity *in vitro* [14, 15]. However, quantitative information regarding individual neolignan constituents remains limited, highlighting the need for future studies employing standardized quantitative analytical methods. Among these, pentacyclic triterpenoids such as friedelin, epifriedelanol, and  $\beta$ -amyrin have been frequently reported and are considered major contributors to the biological activity of root extracts. These pentacyclic triterpenoids, particularly

friedelin and epifriedelanol, serve as key markers for the therapeutic potential of the root extracts (Table 1). Quantitative analysis of cannabis root extracts has identified friedelin and epifriedelanol at levels of approximately 12.8 mg/kg (0.00128%) and 21.3 mg/kg (0.00213%), respectively [4]. These compounds are known for their potent antioxidant and anti-inflammatory properties, as validated in recent isolation studies.

**Table 1** Phytochemical profile, quantitative abundance, and biological activities of major bioactive constituents identified in hemp (*Cannabis sativa* L.) root extracts.

Compound Class	Major Constituents	Reported Conc. <sup>a</sup>	Biological Activities	Proposed Mechanisms	Ref.
<b>Triterpenoids</b>	Friedelin	12.8 mg/kg	• Anti-inflammatory	• Inhibition of NF-κB and MAPK signaling	[4, 8]
	Epifriedelanol	21.3 mg/kg	• Antioxidant	• Activation of Nrf2/HO-1 pathway	
	β-Amyrin	N.D. <sup>b</sup>	• Antinociceptive	• Modulation of pain receptors	
<b>Phytosterols</b>	β-Sitosterol	1.5% <sup>c</sup>	• Anti-inflammatory	• Inhibition of NF-κB signaling	[4]
	Campesterol	0.78% <sup>c</sup>	• Cholesterol-lowering activity	• Competitively inhibit cholesterol absorption in the human intestine	
	Stigmasterol	0.56% <sup>c</sup>	• Antimicrobial		
<b>Phenolic Compounds &amp; Neolignans</b>	Cannabisin derivatives (Neolignans)	N.D. <sup>b</sup>	• Anti-cancer	• Induction of apoptosis in malignant cells	[14, 15]
	N-trans-cinnamamide derivatives	1.6 mg/kg	• Anti-inflammatory • Antioxidant	• Free radical scavenging • Inhibition of NO production	
<b>Alkaloids</b>	Cannabisativine	2.5 mg/kg	• Cell-protective	• Modulation of cellular signaling	[4, 6]
	Anhydrocannabisativine	0.3 mg/kg	• Antipruritic	• Interaction with specific membrane receptors	

<sup>a</sup> Concentrations are based on dry weight (dw) or specific extract fractions as reported in key references.

<sup>b</sup> Not Determined or Not fully quantified.

<sup>c</sup> Percentage values represent the relative abundance within the total sterol fraction, not the dry weight of the root.

Phytosterols, including  $\beta$ -sitosterol (1.5%), campesterol (0.78%), and stigmasterol (0.56%), have also been detected in hemp root tissues [4]. These molecules are structurally similar to cholesterol and are associated with cholesterol-lowering effects and anti-inflammatory activity, supporting the potential nutritional relevance of hemp root-derived extracts. In addition, phenolic acids, including specialized nitrogenous constituents such as N-(p-hydroxy- $\beta$ -phenylethyl)-p-hydroxy-trans-cinnamamide (1.6 mg/kg), and flavonoid derivatives present in hemp roots contribute to free radical scavenging capacity and metal chelation, which are important mechanisms in oxidative stress mitigation [14]. Recent metabolomics-based analyses have further revealed the presence of unique root-associated metabolites, such as the alkaloids cannabistatine (2.5 mg/kg) and anhydrocannabistatine (0.3 mg/kg), which are absent or present at low concentrations in aerial tissues [6].

While triterpenoids like friedelin are found in various medicinal plants, hemp roots are distinguished by their high concentration of these compounds without the regulatory burden of psychoactive cannabinoids, a distinct advantage over other traditional roots like *Panax ginseng* (ginsenosides) or *Glycyrrhiza glabra* (glycyrrhizin). Furthermore, unlike many medicinal roots that require years of maturation, hemp roots can be harvested as a high-value co-product within a single growing season, offering superior economic sustainability.

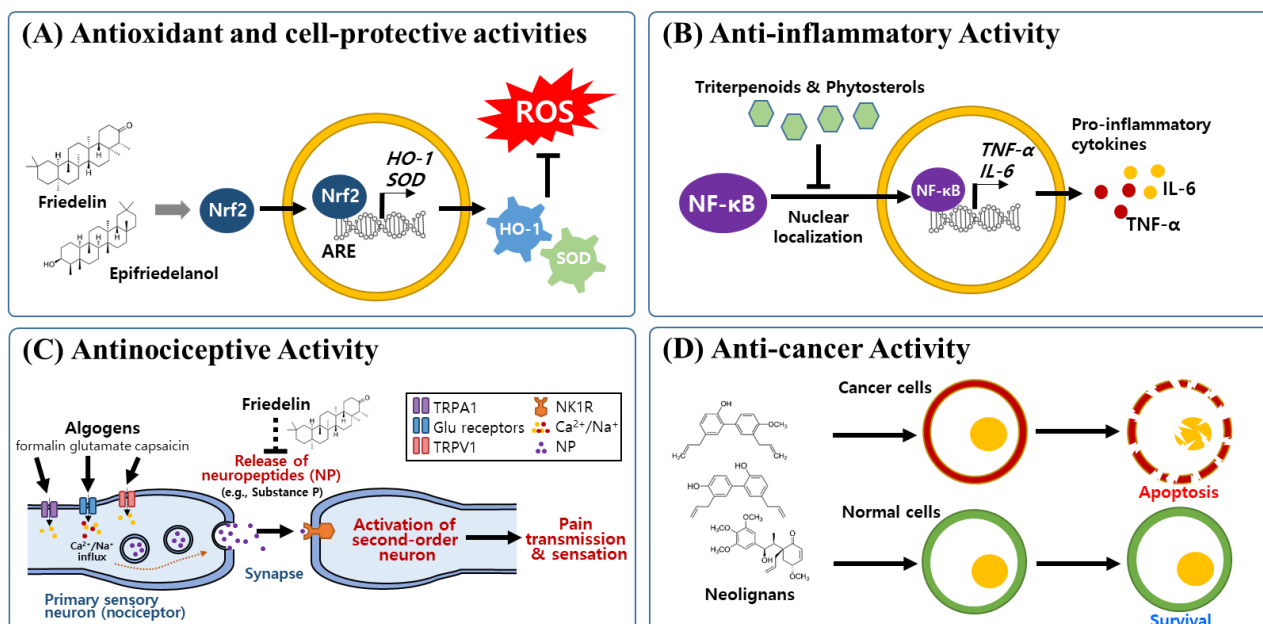
The quantitative composition of hemp root extracts is influenced by cultivar, cultivation conditions, harvest stage, and extraction methodology. Particularly, the choice between soil-based cultivation and hydroponic systems plays a critical role in metabolic variation. Hydroponic systems are increasingly favored for industrial applications because they provide a controlled environment that ensures chemical consistency and enables the enrichment of specific secondary metabolites, such as phenolics and alkaloids, which may vary significantly in heterogeneous soil conditions [16]. Standardization of controlled cultivation systems and elicitation strategies is crucial, as triterpenoid accumulation can be significantly influenced by culture conditions and elicitor treatments. For example, hairy root cultures treated with salicylic acid (75  $\mu$ M) accumulated approximately 1.95-fold higher friedelin and 1.4-fold higher epifriedelanol than untreated controls, demonstrating the potential of elicitation to improve phytochemical consistency and production efficiency [16]. Nevertheless, standardized comparative studies evaluating different cultivation systems, elicitation strategies, and analytical methodologies are still needed to establish reliable phytochemical benchmarks for hemp root production.

Furthermore, the choice of the extraction method is as critical as the cultivation condition for maximizing yield. Recent comparisons indicate that advanced techniques, such as microwave-assisted extraction (MAE) and response surface methodology (RSM) optimization, significantly enhance the recovery of bioactive fractions compared with conventional maceration [9, 10]. Solvent polarity, extraction temperature, and processing duration further affect the recovery of bioactive constituents, highlighting the importance of standardized extraction protocols for reproducible nutraceutical applications. The major bioactive constituents identified in hemp roots, along with their respective biological activities and underlying mechanisms, are summarized in Table 1. Although the term “entourage effect” has been widely used in cannabinoid research to describe synergistic interactions among cannabis phytochemicals, direct experimental evidence demonstrating comparable synergistic interactions among hemp root constituents (e.g., friedelin, phytosterols, and phenolic compounds) is currently lacking. Therefore, any potential synergistic

effects within the hemp root matrix should be regarded as a hypothesis requiring further experimental validation.

### 3. Biological Activities of Hemp Root Extracts

The diverse biological effects of hemp root extracts are mediated by various molecular pathways, including antioxidant defense, modulation of inflammation, and apoptotic signaling. The molecular mechanisms underlying these biological activities are schematically illustrated in Figure 2.



**Figure 2** Schematic representation of the molecular mechanisms underlying the biological activities of hemp (*Cannabis sativa* L.) root extracts. (A) Antioxidant and cell-protective activities. Friedelin and other extract components trigger Nrf2 translocation into the nucleus and bind to the Antioxidant Response Element (ARE), upregulating the expression of antioxidant enzymes such as Heme Oxygenase-1 (HO-1) and Superoxide Dismutase (SOD), thereby neutralizing reactive oxygen species (ROS). (B) Anti-inflammatory Activity. Upon inflammatory stimulation (e.g., by LPS), triterpenoids and phytosterols suppress NF-κB activation and its nuclear translocation, thereby downregulating the transcriptional expression of pro-inflammatory cytokines (TNF-α and IL-6). (C) Antinociceptive activity. Friedelin may attenuate nociceptive signaling by suppressing neuropeptide release (e.g., substance P) from primary sensory neurons following algogen-induced activation of nociceptive receptors/ion channels (e.g., TRPV1), thereby reducing activation of second-order neurons involved in pain transmission. NK1R: Neurokinin 1 receptor [6, 7]. (D) Anti-cancer Activity. Neolignans induce cytotoxicity and apoptosis in cancer cells.

### **3.1 Antioxidant Activity**

Oxidative stress is a major contributor to the development of chronic diseases, including cardiovascular disorders, neurodegenerative diseases, and metabolic syndromes [17]. Hemp root extracts have demonstrated notable antioxidant activity in multiple *in vitro* assays, such as DPPH radical scavenging, ABTS assays, and ferric reducing antioxidant power (FRAP) tests [4, 7, 18]. These effects are largely attributed to the high content of phenolic compounds and triterpenoids, particularly friedelin and epifriedelanol, which function as electron or hydrogen donors to neutralize reactive oxygen species (ROS) [7, 18].

Cell-based studies further support the antioxidant potential of hemp root extracts by demonstrating reduced intracellular ROS accumulation and enhanced cellular resistance to oxidative damage. Specifically, triterpenoid-rich fractions have been shown to maintain the activity of endogenous antioxidant enzymes, such as superoxide dismutase (SOD) and glutathione peroxidase (GPx), under chemically induced oxidative stress [8]. Such properties are particularly relevant for nutraceutical applications aimed at improving cellular redox balance and preventing oxidative stress-related tissue damage. However, it is important to note that most evidence remains limited to *in vitro* systems, and extensive *in vivo* validation is still required to confirm systemic antioxidant efficacy.

### **3.2 Anti-Inflammatory and Immunomodulatory Effects**

Chronic low-grade inflammation is closely associated with metabolic disorders, aging, and immune dysfunction [19]. Several studies have reported that hemp root-derived compounds, particularly friedelin and specific lignan derivatives, significantly suppress the production of pro-inflammatory mediators, including nitric oxide (NO), tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), and interleukin-6 (IL-6), in lipopolysaccharide (LPS)-stimulated macrophages [14]. These effects are mediated by modulating key signaling pathways, specifically the inhibition of nuclear factor kappa-light-chain-enhancer of activated B cells (NF- $\kappa$ B) and mitogen-activated protein kinases (MAPK) [20]. Furthermore, a recent network pharmacology study combined with experimental validation demonstrated that friedelin alleviated ulcerative colitis in a mouse model by inhibiting NF- $\kappa$ B activation and modulating inflammatory signaling pathways, thereby providing preliminary *in vivo* evidence for its therapeutic potential in gastrointestinal inflammation [20].

Recent mechanistic insights have further elucidated that hemp root extracts activate the Nrf2 (Nuclear factor erythroid 2-related factor 2) signaling pathway, which upregulates endogenous antioxidant enzymes and mitigates oxidative stress-driven inflammation. Specifically, the translocation of Nrf2 to the nucleus triggers the expression of heme oxygenase-1 (HO-1), providing a robust cell-protective response against inflammatory insults.

These findings suggest that hemp root extracts may be multi-target candidates for the prevention of chronic inflammatory disease; however, further *in vivo* and clinical studies are required to confirm these effects. The anti-inflammatory activity of hemp root extracts is particularly attractive for nutraceutical development, aligning with the growing demand for natural alternatives to synthetic anti-inflammatory agents. Moreover, the absence of psychoactive cannabinoids in root tissues enhances the regulatory acceptability of hemp root-based products compared to aerial part derivatives [4]. However, these conclusions are derived predominantly from

cell culture studies, and further *in vivo* and clinical investigations are required before translational claims can be substantiated.

### **3.3 Antinociceptive and Analgesic Potential**

Historically, hemp root preparations were frequently applied topically to alleviate joint pain and gout [4]. As one of the major pentacyclic triterpenoids identified in hemp roots, friedelin may contribute to the traditional analgesic properties attributed to hemp root preparations. Although direct nociceptive studies on hemp root extracts are limited, friedelin isolated from *Combretum duarteanum* has demonstrated antinociceptive activity in rodent models, significantly reducing formalin-, glutamate-, and capsaicin-induced nociceptive responses [21]. These pharmacological findings suggest that friedelin may modulate nociceptive signaling, possibly by suppressing neuropeptide release (e.g., substance P) from primary sensory neurons, thereby reducing activation of second-order neurons involved in pain transmission [21]. Given the central role of TRPV1 in nociceptive signaling [22], it remains to be determined whether friedelin directly modulates TRPV1-related pathways. These findings provide preliminary support for the traditional use of hemp root preparations in pain management; however, direct experimental evidence for hemp root extracts remains limited, and further preclinical and mechanistic studies are warranted to validate these proposed mechanisms.

### **3.4 Antimicrobial, Cell-Protective, and Anti-Cancer Properties**

Hemp root extracts have also shown antimicrobial activity against selected bacterial strains *in vitro*, suggesting potential applications in food preservation and gut health modulation. Research indicates that specific fractions of hemp root extracts exhibit inhibitory effects against pathogens such as *Staphylococcus aureus* and *Escherichia coli*, likely due to the synergistic action of triterpenoids and sterols [23].

In cellular interactions, hemp root extracts exhibit a dual nature depending on the target cell type. In healthy cells, cell-protective effects have been reported; root-derived compounds improved cell viability under stress conditions and reduced apoptosis induced by oxidative or chemical stressors in human keratinocytes and microglial cells [8].

Beyond their cell-protective role in healthy tissues, recent *in vitro* investigations have highlighted the potential anticancer effect of neolignans isolated from hemp roots [15]. However, these findings remain limited to preclinical evidence, and further *in vivo* studies are required to determine their therapeutic relevance.

## **4. Nutraceutical, Functional Food, and Cosmeceutical Applications**

The expanding functional food and nutraceutical markets offer new opportunities for the utilization of hemp root extracts as value-added ingredients. Due to their potent antioxidant and anti-inflammatory properties, hemp root-derived bioactives are increasingly viewed as viable candidates for dietary supplements targeting immune health, metabolic regulation, and healthy aging [13, 24]. Although synergistic interactions among hemp root constituents have been hypothesized by analogy with the “entourage effect” described for aerial cannabis tissues, such interactions have not yet been experimentally demonstrated [4, 13]. Consequently, the functional

value of hemp root extracts should currently be interpreted primarily based on the biological activities of their individual constituents, pending further studies investigating potential synergistic effects.

However, the effective incorporation of these bioactives requires overcoming significant physicochemical challenges. Advances in formulation technologies have been instrumental in improving the applicability of hemp root extracts. Encapsulation strategies, such as lipid-based carriers, polymer nanoparticles, and microemulsions, have been shown to enhance compound stability, protect sensitive phytochemicals (e.g., friedelin and phytosterols) from oxidative degradation, and significantly increase bioavailability [11, 25]. These delivery systems enable controlled release and targeted absorption in the gastrointestinal tract, thereby improving the physiological efficacy of plant-derived nutraceuticals.

Hemp root extracts may also be integrated into functional beverages, protein supplements, and plant-based food matrices. Nevertheless, the successful development of such products depends on the careful optimization of sensory characteristics, particularly the masking of bitterness associated with certain triterpenoids, and managing solubility issues [26]. Furthermore, the anti-inflammatory and cell-protective properties of hemp root extracts make them attractive candidates for cosmeceutical applications, particularly in formulations designed to soothe sensitive skin or support skin barrier integrity against environmental stressors [27]. As the industry moves towards sustainable, plant-based solutions, hemp roots represent a promising, yet underutilized, resource for next-generation functional foods and personal care products.

## 5. Safety, Regulatory Considerations, and Current Limitations

Safety evaluation is a critical prerequisite for the commercialization of hemp root-derived nutraceuticals. Although hemp roots contain negligible levels of psychoactive cannabinoids compared to aerial parts, comprehensive toxicological assessments are still required to confirm long-term safety and potential interactions with pharmaceuticals [4, 6]. The quantitative composition of hemp root extracts varies substantially depending on cultivar, cultivation system, harvest stage, and extraction methodology. Reported concentrations of major triterpenoids, such as friedelin, range widely across studies, reflecting differences in extraction solvents and environmental conditions [7, 18]. This variability poses a significant challenge to commercial standardization and highlights the urgent need for validated chemical fingerprinting approaches and batch-to-batch consistency protocols [28]. While *in vitro* cytotoxicity assays have generally indicated favorable safety profiles at nutritionally relevant concentrations, human clinical data remain limited [8].

Regulatory frameworks governing hemp-derived products vary across global jurisdictions. In many regions, including the European Union and North America, industrial hemp is permitted under strict delta-9-tetrahydrocannabinol (THC) thresholds (typically <0.3 or <0.2), and non-psychoactive plant parts such as roots are often subject to fewer regulatory constraints than cannabinoid-rich flowers [4, 29]. Nevertheless, the standardization of raw materials, rigorous quality control procedures, and clear labeling requirements remain essential to ensure consumer safety and regulatory compliance [13, 28].

Despite promising preliminary findings, several translational gaps persist, including variability in phytochemical composition arising from cultivation and elicitation conditions [16], the lack of

standardized extraction protocols [17-19], and the limited availability of clinical validation studies. Addressing these gaps will be critical for the sustainable development of hemp root-based nutraceuticals. Standardization through controlled cultivation systems, such as hydroponics or aeroponics, will be essential to overcome the current challenges of phytochemical variability, ensuring a consistent 'chemical fingerprint' that meets the stringent requirements of the functional food and pharmaceutical industries [16].

## 6. Conclusion

This review highlights the emergence of hemp (*Cannabis sativa* L.) roots as a distinct and valuable reservoir of bioactive compounds, diverging from the cannabinoid-centric focus of aerial plant parts. The unique accumulation of pentacyclic triterpenoids—most notably friedelin and epifriedelanol—along with phytosterols and specialized alkaloids, underpins the potent antioxidant, anti-inflammatory, and cell-protective properties of hemp root extracts, which are mechanistically supported by Nrf2/HO-1 activation and NF- $\kappa$ B modulation. However, the translation of these findings into commercial applications is currently impeded by significant phytochemical variability and the lack of standardized chemical fingerprinting protocols. To facilitate their successful translation, priority should be given to standardizing extraction methods and quality-control procedures to ensure the consistent production of bioactive compounds. In addition, well-designed animal studies and human clinical trials are needed to validate their efficacy and safety. In contrast, long-term toxicological and safety assessments are essential to support their safe application in nutraceutical and functional food products. As an initial step toward clinical translation, pilot clinical studies evaluating topical hemp root formulations for inflammatory skin disorders and musculoskeletal pain may serve as practical, scientifically justified models based on the currently available preclinical evidence. Ultimately, the valorization of hemp roots represents a transformative opportunity to convert an agricultural by-product into a sustainable, high-value functional ingredient that complements established medicinal botanicals in the preventive nutrition and cosmeceutical landscapes.

## Author Contributions

HWC conducted all the research work for this study.

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## Competing Interests

The author has declared that no competing interests exist.

## AI-Assisted Technologies Statement

Artificial intelligence (AI) tools were used solely for basic grammar correction and language refinement in the preparation of this manuscript. All scientific content, data interpretation, and conclusions were developed independently by the author. The authors have thoroughly reviewed and edited the AI-assisted text to ensure its accuracy and accept full responsibility for the content of the manuscript.

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