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# Unveiling the Therapeutic Potential of Gingerols: A Comprehensive Review of Their Multifaceted Biological Activities in *Zingiber officinale*

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**ABSTRACT :**

Ginger (*Zingiber officinale* Roscoe), a revered medicinal herb in traditional Chinese, Ayurvedic, and Unani systems, owes its therapeutic potential to gingerols, a class of phenolic ketones, with 6-gingerol being the most abundant. This review comprehensively explores the chemical composition, pharmacological properties, and therapeutic applications of gingerols, emphasizing their immunomodulatory, anti-inflammatory, antioxidant, anticancer, antimicrobial, and metabolic effects. Gingerols, characterized by a 4-hydroxy-3-methoxyphenyl group with variable alkyl chains, modulate key signaling pathways, including NF-κB, MAPK, and Nrf2, to mitigate inflammation, oxidative stress, and immune dysregulation. In vitro and in vivo studies demonstrate that 6-gingerol inhibits proinflammatory cytokines (e.g., TNF-α, IL-1β), induces apoptosis in cancer cells (e.g., breast, colorectal), and enhances insulin sensitivity in metabolic disorders. Additionally, gingerols exhibit broad-spectrum antimicrobial and antiparasitic activities, supporting their traditional use in infectious diseases. Despite their promise, challenges such as poor bioavailability and thermal instability limit clinical translation. Advances in nanoformulations, including liposomes and polymeric nanoparticles, offer solutions to enhance solubility and tissue distribution. Ginger's "generally recognized as safe" status and extensive preclinical validation underscore its potential as a source of novel therapeutics. This review highlights the need for standardized formulations, optimized delivery systems, and large-scale clinical trials to fully harness gingerols' multifaceted benefits in managing chronic diseases, infections, and metabolic disorders, bridging traditional knowledge with modern pharmaceutical development.

**Keywords:** Gingerols, Zingiber officinale, Anti-inflammatory, Antioxidant, Immunomodulatory, Anticancer

## Introduction

Ginger (*Zingiber officinale* Roscoe), a prominent member of the Zingiberaceae family, is a perennial herb widely cultivated in tropical and subtropical regions. For over 2,500 years, it has been a cornerstone in traditional Chinese, Ayurvedic, and Unani medicinal systems, employed to treat ailments ranging from digestive disorders and nausea to inflammatory conditions and rheumatism [1, 2]. The rhizome, commonly referred to as ginger root, is valued not only for its culinary versatility but also for its extensive pharmacological properties, which are attributed to a complex array of bioactive compounds, including gingerols, shogaols, paradols, and zingerone [3, 4]. Among these, gingerols, particularly 6-gingerol, are the primary bioactive constituents in fresh ginger, contributing to its characteristic pungency and diverse therapeutic effects [3, 5].

The resurgence of interest in ginger stems from its broad pharmacodynamic profile, encompassing anti-inflammatory, antioxidant, antitumor, antiemetic, antidiabetic, anti-obesity, antinociceptive, immunomodulatory, antimicrobial, and cardioprotective activities [5, 6]. These effects have been substantiated through extensive in vitro and in vivo studies, which validate traditional uses and highlight the potential for gingerol-based therapeutics [5]. Ginger's classification as a "generally recognized as safe" (GRAS) substance by regulatory authorities, such as the U.S. Food and Drug Administration, underscores its low toxicity and favorable safety profile, making it an attractive candidate for pharmaceutical development [7]. This review explores the chemical composition, mechanisms of action, and therapeutic potential of gingerols, with a focus on their immunomodulatory, anti-inflammatory, antioxidant, anticancer, and metabolic effects, while addressing challenges in their clinical application.

## Historical and Cultural Context

Ginger's historical significance spans multiple cultures and medical traditions. In traditional Chinese medicine, ginger is used to "warm the stomach" and alleviate nausea, while in Ayurveda, it is prized for its ability to balance doshas and treat digestive and inflammatory disorders [1, 2]. In Unani medicine, ginger is employed for its warming and stimulant properties, particularly in managing rheumatism and respiratory ailments [2]. These traditional applications are now supported by modern research, which has elucidated the molecular basis of ginger's effects, particularly through gingerols [5, 6]. The integration of traditional knowledge with contemporary science has spurred investigations into ginger's potential in treating chronic diseases, such as cancer, diabetes, and cardiovascular disorders, positioning it as a bridge between ethnopharmacology and modern therapeutics [1, 5].

## Chemical Composition and Structural Properties of Gingerols

Gingerols are a class of phenolic ketones that form the cornerstone of ginger's pharmacological utility. Structurally, they are analogs of 1-(3-methoxy-4-hydroxyphenyl)-3-hydroxy-5-alkyl ketones, with variations in the alkyl side chain length giving rise to derivatives such as 4-, 6-, 8-, 10-, and 12-gingerol [3, 7]. The most abundant and well-studied is 6-gingerol, which was the first compound isolated from ginger rhizomes and is primarily responsible for the rhizome's pungent flavor [3, 4]. The structural diversity of gingerols, driven by differences in alkyl chain length, influences their lipophilicity, solubility, and biological activity, contributing to their varied pharmacological effects [3, 8].

Gingerols are thermolabile and undergo dehydration during heating or drying, converting into shogaols, which are more pharmacologically potent but exhibit distinct mechanisms of action [3]. This transformation is a β-hydroxy ketone dehydration reaction, resulting in the formation of an α,β-unsaturated ketone in shogaols, which enhances their reactivity and bioactivity [3]. Despite their thermal instability, gingerols remain stable in ethanolic solutions at low temperatures, making them suitable for use in pharmacological formulations and extracts [7]. The stability of gingerols under specific conditions is critical for their application in nutraceuticals and pharmaceuticals, as improper processing can diminish their therapeutic efficacy [3, 7].

The biosynthesis of gingerols occurs via the phenylpropanoid pathway, a complex metabolic route involving multiple enzymatic steps. Phenylalanine is converted into dihydroferulic acid, which undergoes Claisen condensation with malonate and hexanoate to form 6-dehydrogingerdione, the precursor to 6-gingerol [3, 7]. Alternative pathways involving enzymes such as caffeic acid O-methyltransferase and phenylalanine ammonia lyase have been proposed, highlighting the complexity of gingerol biosynthesis [3]. Other structurally related compounds in ginger, such as paradols, gingerdiones, gingerdiols, and acetyl derivatives, contribute synergistically to its pharmacological profile, with each compound exhibiting unique bioactivities [3, 5].

## Phytochemical Constituents and Stability

The phytochemistry of *Zingiber officinale* is remarkably diverse, with over 200 identified compounds, including sesquiterpenes (e.g., zingiberene, β-bisabolene), monoterpenes, and phenolic constituents [5, 6]. Gingerols constitute approximately 23–25% of the total oleoresin in fresh ginger, with 6-gingerol being the most abundant [3, 7]. Other significant bioactive constituents include shogaols (18–25%), paradols, and zingerone, each contributing to ginger's multifaceted biological effects [3, 5]. The relative abundance of these compounds varies depending on the ginger's geographical origin, cultivation conditions, and processing methods, which influence the therapeutic potential of ginger extracts [5].

Gingerols are characterized by a 4-hydroxy-3-methoxyphenyl group linked to a hydrocarbon chain with a β-hydroxy ketone moiety. The alkyl side chain length (e.g., 6-, 8-, 10-, or 12-carbon chains) affects their lipophilicity, which in turn influences their pharmacokinetic and pharmacodynamic properties [3, 8]. For instance, longer alkyl chains, as in 10-gingerol, enhance lipophilicity, potentially improving membrane permeability and bioactivity [8]. However, this also increases susceptibility to metabolic degradation, posing challenges for therapeutic applications [7].

A major limitation of gingerols is their low bioavailability. After oral administration, 6-gingerol is rapidly absorbed in the gastrointestinal tract, metabolized to glucuronide and sulfate conjugates in the liver, and excreted via hepatic and renal pathways [7]. Pharmacokinetic studies in rats have shown that 6-gingerol is distributed to tissues such as the gastrointestinal tract, liver, brain, and kidneys, but its plasma concentrations decline rapidly due to first-pass metabolism [7]. Thermal processing further complicates their stability, as gingerols readily convert to shogaols under heat, altering their pharmacological profile [3, 7]. Strategies to enhance stability and bioavailability, such as nanoencapsulation and liposomal formulations, are discussed later in this review [7].

## Mechanisms of Action and Immunomodulatory Activity

Gingerols exert their biological effects through modulation of multiple signaling pathways, with a particular emphasis on immunomodulatory and anti-inflammatory activities. These compounds influence both innate and adaptive immune responses by regulating macrophage activation, cytokine production, and lymphocyte proliferation [7, 9]. The primary molecular targets include nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB), mitogen-activated protein kinase (MAPK), and phosphatidylinositol 3-kinase (PI3K)/Akt pathways, which are central to inflammation and immunity [7].

In vitro studies have demonstrated that 6-gingerol inhibits nitric oxide (NO) production, inducible nitric oxide synthase (iNOS) expression, and proinflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin (IL)-1β, and IL-12 in lipopolysaccharide (LPS)-stimulated macrophages [7]. These effects are mediated through the suppression of NF-κB and protein kinase C (PKC) signaling, which regulate inflammatory gene expression [7]. Additionally, 6-gingerol inhibits calcium mobilization and MAPK activation, reducing Th1 and Th2 cytokine production and mast cell degranulation, which are critical in allergic responses [7]. In models of allergic rhinitis, 6-gingerol attenuated c-fos expression and prevented NF-κB nuclear translocation, suggesting a role in modulating T-helper cell differentiation [7].

Gingerols also enhance immune function by promoting natural killer (NK) cell activity, B- and T-cell proliferation, and anti-inflammatory cytokine production, such as IL-10 [7, 10]. In rat models, 6-gingerol increased antibody titers and delayed-type hypersensitivity responses, indicating its potential in boosting humoral and cell-mediated immunity [10]. These immunomodulatory effects position gingerols as promising agents for managing inflammatory, autoimmune, and infectious diseases [7, 11].

## Immunomodulation in Specific Disease Models

The immunomodulatory effects of gingerols have been extensively studied in models of infectious and inflammatory diseases. In *Mycobacterium tuberculosis*-infected mice, 6-gingerol reduced bacterial loads in the lungs, liver, and spleen by enhancing innate immune responses and modulating cytokine profiles [7]. Similarly, in sepsis-induced acute kidney injury models, 6-gingerol and 10-gingerol attenuated proinflammatory cytokine levels

(e.g., IL-1β, TNF-α) and oxidative stress, improving renal histopathology [7]. These findings suggest that gingerols may have therapeutic applications in infectious diseases and sepsis-related organ damage.

In autoimmune disease models, such as rheumatoid arthritis, gingerols have shown promise by suppressing proinflammatory mediators and restoring immune balance [2, 11]. The ability of gingerols to modulate T-cell differentiation and cytokine production makes them potential candidates for managing conditions like multiple sclerosis and systemic lupus erythematosus, although further clinical studies are needed [11].

## Anti-inflammatory Activity

The anti-inflammatory properties of gingerols, particularly 6-gingerol, have been rigorously investigated in both in vitro and in vivo models. Inflammation is a critical immune response, but chronic or dysregulated inflammation contributes to diseases such as arthritis, inflammatory bowel disease, and cardiovascular disorders [11]. Gingerols mitigate inflammation by suppressing proinflammatory mediators and enhancing anti-inflammatory cytokines [8, 7, 1].

At the molecular level, 6-gingerol inhibits cyclooxygenase-2 (COX-2) and lipoxygenase (LOX), enzymes responsible for producing prostaglandins and leukotrienes, respectively [8]. Tjendraputra et al. found that 10-gingerol exhibited the highest COX-2 inhibitory activity, followed by 6-, 8-, and 12-gingerol, with potency linked to alkyl side chain length [8]. This structural variation influences the binding affinity of gingerols to COX-2, highlighting the importance of chemical diversity in their anti-inflammatory effects [8].

In TNF-α-induced osteoblast-like MG63 cells and RAW 264.7 macrophages, 6-gingerol reduced inflammatory markers such as prostaglandin E2 (PGE2), TNF-α, and IL-6 by downregulating receptor activator of nuclear factor kappa-B ligand (RANKL) expression and NF-κB signaling [7]. These effects suggest potential applications in bone-related inflammatory conditions, such as osteoporosis and osteoarthritis [7]. In LPS-induced macrophages, 6-gingerol suppressed iNOS and proinflammatory gene expression through a COX-2-independent pathway involving NF-κB and activator protein 1 (AP-1) transcription factors [7].

In vivo studies further validate these findings. In dextran sulfate sodium (DSS)-induced colitis models, 6-, 8-, and 10-gingerol alleviated colonic inflammation by reducing malondialdehyde levels, increasing superoxide dismutase activity, and lowering serum TNF-α and IL-1β levels [7]. Histological analysis revealed improved mucosal integrity, suggesting a role for gingerols in managing inflammatory bowel diseases [7]. Similarly, in thioacetamide-induced liver fibrosis models, 6-gingerol reduced inflammatory and fibrotic markers, supporting its hepatoprotective effects [12].

## Anti-inflammatory Mechanisms in Chronic Diseases

The anti-inflammatory effects of gingerols extend to chronic diseases such as cardiovascular disease and neurodegenerative disorders. In models of myocardial ischemia/reperfusion injury, 10-gingerol reduced infarct size and inflammatory markers by modulating the JAK2/STAT3 signaling pathway [7]. In neuroinflammatory models, 6-gingerol attenuated microglial activation and cytokine production, suggesting potential in managing Alzheimer's disease and Parkinson's disease [7, 11]. These effects are mediated through the inhibition of NF-κB and MAPK pathways, which are implicated in chronic inflammation and oxidative stress [7, 11].

## Antioxidant and Anticancer Properties

Oxidative stress, caused by an imbalance between reactive oxygen species (ROS) and antioxidant defenses, contributes to cancer, aging, and degenerative diseases. Gingerols, particularly 6-gingerol, exhibit potent antioxidant properties by activating the nuclear factor erythroid 2–related factor 2 (Nrf2) pathway, a master regulator of cellular antioxidant responses [7, 13]. This pathway upregulates antioxidant enzymes such as superoxide dismutase and catalase, reducing oxidative damage and protecting cells from ROS-mediated injury [7].

The anticancer potential of gingerols has been demonstrated across various cancer cell lines, including breast, colorectal, lung, and ovarian cancers [14, 15, 16]. 6-Gingerol induces apoptosis and cell cycle arrest by inhibiting anti-apoptotic proteins (e.g., Bcl-2), activating caspases, and suppressing Akt, extracellular signal-regulated kinase (ERK), and NF-κB pathways [7, 15]. In colon cancer cells, 6- and 10-gingerol inhibited proliferation, induced G2/M cell cycle arrest, and reduced migration and invasion by downregulating matrix metalloproteinases (MMP-2 and MMP-9) [7, 17]. In breast cancer (MDA-MB-231) cells, 6-gingerol inhibited cell classification and metastasis-associated protein expression, highlighting its antimetastatic potential [14].

Gingerols also enhance the efficacy of chemotherapeutic agents. In A549 lung cancer cells, 6-gingerol synergized with tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) to enhance apoptosis by impairing autophagy flux and increasing oxidative stress [7]. Similarly, 10-gingerol increased the Bax/Bcl-2 ratio and activated caspase pathways, promoting intrinsic apoptosis in cancer cells [7]. These findings suggest that gingerols could be used as adjuvants in cancer therapy to enhance treatment efficacy and reduce resistance [7, 16].

## Anticancer Mechanisms and Clinical Potential

The anticancer effects of gingerols are mediated through multiple mechanisms, including cell cycle regulation, apoptosis induction, and inhibition of angiogenesis and metastasis [7, 15, 17, 16]. In pancreatic cancer cells, 6-gingerol inhibited proliferation and invasion by blocking the STAT3 signaling pathway, a key driver of tumor growth [15]. In ovarian cancer cells, ginger extract modulated cell cycle and apoptosis regulatory proteins, further supporting its anticancer potential [16].

The clinical translation of gingerols in cancer therapy is promising but requires further investigation. Preclinical studies suggest that gingerols could be used in combination with conventional chemotherapies to enhance efficacy and reduce toxicity [7]. However, challenges such as poor bioavailability and rapid metabolism must be addressed to optimize their therapeutic potential [7].

## Gingerols in In Vivo Models of Inflammation and Immunity

The immunomodulatory and anti-inflammatory effects of gingerols have been validated in various in vivo models. In *Mycobacterium tuberculosis*-infected mice, 6-gingerol reduced bacterial loads and modulated immune responses, enhancing macrophage activity and cytokine production [7]. In sepsis-induced acute kidney injury models, 6- and 10-gingerol attenuated inflammatory and oxidative stress markers, improving renal function and histopathology [7]. These effects were attributed to the restoration of antioxidant defenses and suppression of ROS generation [7].

In DSS-induced colitis models, 6-, 8-, and 10-gingerol alleviated colonic damage by reducing proinflammatory cytokines and oxidative stress markers while enhancing antioxidant enzyme activity [7]. Histological improvements in mucosal integrity suggest that gingerols could be therapeutic in inflammatory bowel diseases, such as ulcerative colitis and Crohn's disease [7]. In radiation-exposed murine models, 6-gingerol enhanced macrophage viability, spleen weight, and immune responses, including antibody titers and delayed-type hypersensitivity, highlighting its potential in immune restoration [7, 10].

## In Vivo Models of Other Diseases

Gingerols have also been studied in models of liver injury and fibrosis. In CCl4-induced acute liver failure models, ginger oil containing gingerols reduced hepatic inflammation and oxidative stress, improving liver function [13]. In thioacetamide-induced liver fibrosis models, 6-gingerol exhibited antifibrotic effects by reducing inflammatory and fibrotic markers [12]. These hepatoprotective effects are mediated through the modulation of oxidative stress and inflammatory pathways, making gingerols potential candidates for managing liver diseases [12, 13].

## Neuroprotective and Cardioprotective Roles of Gingerols

Gingerols exhibit significant neuroprotective and cardioprotective effects, primarily through their antioxidant and anti-inflammatory properties. In H9c2 cardiomyocytes exposed to $CoCl_2$-induced hypoxia, 6-gingerol reduced oxidative stress by activating the Nrf2 pathway and inhibiting p38 and NF-κB signaling, enhancing cell survival [7]. In myocardial ischemia/reperfusion injury models, 10-gingerol reduced infarct size, preserved cardiac enzyme levels, and inhibited apoptotic markers through modulation of the JAK2/STAT3 pathway [7]. These cardioprotective effects suggest potential applications in managing ischemic heart disease and heart failure [7].

The neuroprotective potential of gingerols is linked to their ability to modulate neuroinflammatory signaling and oxidative stress. In preclinical models of neuroinflammation, 6-gingerol attenuated microglial activation and cytokine production, suggesting therapeutic potential in Alzheimer's disease, Parkinson's disease, and other neurodegenerative disorders [7, 11]. Although clinical studies are limited, the ability of gingerols to cross the blood-brain barrier and modulate NF-κB and cytokine pathways supports their potential in neurological applications [7].

## Neuroprotective Mechanisms

The neuroprotective effects of gingerols are mediated through multiple pathways. By activating Nrf2, gingerols upregulate antioxidant enzymes, reducing oxidative damage in neuronal cells [7]. Additionally, their inhibition of NF-κB and MAPK pathways reduces neuroinflammation, a key driver of neurodegenerative diseases [7, 11]. These effects are particularly relevant in conditions characterized by chronic inflammation and oxidative stress, such as Alzheimer's disease and stroke [11].

## Antimicrobial and Antiparasitic Activities

Gingerols exhibit broad-spectrum antimicrobial activity against Gram-positive and Gram-negative bacteria, with fresh ginger extracts showing greater potency than dried ones due to the thermal instability of gingerols [1]. The antibacterial activity is attributed to the disruption of bacterial cell membranes and inhibition of biofilm formation, making gingerols potential candidates for combating antibiotic-resistant infections [1].

Antifungal activity is primarily attributed to gingerols and gingerdiols, with studies demonstrating efficacy against multiple fungal species, including *Candida albicans* and *Aspergillus* species [1]. Ginger powder extracts have been used traditionally to treat fungal skin infections, and modern studies support their antifungal potential [1]. The mechanisms involve disruption of fungal cell walls and inhibition of ergosterol biosynthesis, a critical component of fungal membranes [1].

Gingerols also exhibit antiparasitic properties. Methanolic extracts of *Zingiber officinale* have shown significant activity against trypanosomiasis in vivo, reducing parasite burden and modulating immune responses [1]. Gingerol-enriched fractions have been particularly effective, suggesting their potential in managing parasitic infections such as African trypanosomiasis [1].

## Gingerols in Metabolic Disorders and Other Health Conditions

Gingerols have demonstrated significant potential in managing metabolic disorders, including diabetes, obesity, and dyslipidemia. In high-fat diet-induced obese mice, 6-gingerol reduced plasma glucose and insulin levels by activating AMP-activated protein kinase (AMPK) and enhancing insulin sensitivity in muscle and adipose tissues [1]. These effects improve glycemic control and reduce the risk of diabetes-related complications [1].

Gingerols also reduce advanced glycation end products (AGEs), such as N'-carboxymethyl-lysine, which are implicated in diabetic complications like nephropathy and retinopathy [1]. The mechanism involves Nrf2 activation and inhibition of oxidative stress pathways, highlighting the therapeutic potential of gingerols in preventing diabetic complications [1].

In dyslipidemia, gingerols reduce total cholesterol, low-density lipoprotein (LDL), and triglycerides by inhibiting lipid peroxidation and protecting against atherosclerotic plaque formation [1]. These hypolipidemic effects are mediated through the antioxidant properties of gingerols, which prevent oxidative damage to lipids and vascular tissues [1]. In obesity models, gingerols promote thermogenesis, suppress appetite, and enhance fat oxidation, contributing to weight loss and metabolic health [1].

## Additional Therapeutic Applications

Gingerols have shown promise in other health conditions, such as nausea and vomiting. Their antiemetic effects are well-documented, particularly in chemotherapy-induced nausea and pregnancy-related morning sickness [5, 1]. The mechanisms involve modulation of serotonin receptors and inhibition of nausea-inducing pathways in the central nervous system [5]. Additionally, gingerols have been explored for their analgesic properties, with studies suggesting efficacy in managing musculoskeletal pain and migraines [2].

## Pharmacokinetics and Delivery Challenges

The clinical translation of gingerols is hindered by their poor bioavailability and rapid metabolism. After oral administration, 6-gingerol undergoes extensive first-pass metabolism in the liver, forming glucuronide and sulfate conjugates that are excreted via bile and urine [7]. Pharmacokinetic studies in rodents show that 6-gingerol is rapidly absorbed and distributed to tissues but has a short plasma half-life due to metabolic clearance [7].

To address these challenges, researchers have developed advanced drug delivery systems, such as nanoencapsulation, liposomes, and polymeric nanoparticles [7]. Nanoformulations improve the solubility, stability, and gastrointestinal absorption of gingerols, enhancing their bioavailability and tissue distribution [7]. For example, liposomal encapsulation of 6-gingerol has been shown to protect against degradation and improve delivery to target tissues, increasing therapeutic efficacy [7]. These advancements are critical for translating gingerols into effective clinical therapies.

## Future Directions in Drug Delivery

Emerging drug delivery strategies, such as targeted nanoparticles and micellar systems, offer promising avenues for optimizing gingerol pharmacokinetics [7]. Targeted delivery to specific tissues, such as tumors or inflamed sites, could enhance the therapeutic index of gingerols while minimizing systemic side effects [7]. Additionally, combination therapies with other bioactive compounds or drugs could synergize with gingerols to improve efficacy in complex diseases like cancer and chronic inflammation [7].

## Safety Profile and Clinical Considerations

Gingerols are generally well-tolerated, with ginger classified as GRAS by regulatory authorities [7]. Clinical studies have reported minimal adverse effects, primarily mild gastrointestinal discomfort at high doses [5]. However, the safety of long-term, high-dose gingerol administration requires further investigation, particularly in vulnerable populations such as pregnant women and individuals with bleeding disorders, as ginger may have mild anticoagulant effects [5, 1].

Clinical trials have explored ginger's efficacy in conditions such as osteoarthritis, nausea, and metabolic syndrome, with promising results [5, 1]. However, variability in ginger extract composition and dosing regimens has led to inconsistent outcomes, highlighting the need for standardized formulations [5]. Future clinical studies should focus on optimizing dosing, assessing long-term safety, and evaluating gingerols in combination with conventional therapies [5, 7].

## Conclusion

Gingerols, the principal bioactive compounds of *Zingiber officinale*, exhibit a remarkable range of biological activities, including anti-inflammatory, antioxidant, anticancer, antimicrobial, antidiabetic, and immunomodulatory effects. Their ability to modulate key molecular pathways, such as NF-κB, MAPK, and Nrf2, underlies their therapeutic potential in managing chronic diseases, infections, and metabolic disorders. Extensive preclinical studies have validated these effects, and traditional medicine systems have long harnessed ginger's benefits, providing a strong foundation for modern therapeutic development.

However, challenges such as poor bioavailability, rapid metabolism, and thermal instability limit the clinical utility of gingerols. Advances in drug delivery technologies, particularly nanotechnology-based approaches, offer promising solutions to enhance their pharmacokinetic profile and therapeutic efficacy. With growing interest in plant-based therapeutics, gingerols represent a compelling candidate for further pharmaceutical development and clinical investigation. Future research should focus on optimizing delivery systems, conducting large-scale clinical trials, and exploring combination therapies to fully realize the potential of gingerols in modern medicine.

**REFERENCES**


1. Sindhoora D, Bhattacharjee A. A brief review on pharmacological profile of *Zingiber officinale*. *RGUHS J Pharm Sci*. 2020;10(2):1–6.
2. Srivastava KC, Mustafa T. Ginger (*Zingiber officinale*) in rheumatism and musculoskeletal disorders. *Med Hypotheses*. 1992;39(4):342–8.
3. Semwal RB, Semwal DK, Combrinck S, Viljoen A. Gingerols and shogaols: Important nutraceutical principles from *Zingiber officinale*. *Phytochemistry*. 2015;117:554–68.
4. Li W, Wang W, Huang H, et al. S-6-gingerol suppresses hepatic inflammation and oxidative stress in IL1β-stimulated hepatocytes. *Int Immunopharmacol*. 2013;15(1):74–9.
5. Mao QQ, Xu XY, Cao SY, et al. Bioactive compounds and bioactivities of ginger (*Zingiber officinale* Roscoe). *Foods*. 2019;8(6):185.
6. Kukula-Koch W, Czernicka L. Application of *Zingiber officinale* and its active compounds in the treatment of inflammatory diseases. *Nutrients*. 2020;12(6):1920.
7. Yücel Ç, Karatoprak GŞ, Açıkara ÖB, et al. Immunomodulatory and anti-inflammatory therapeutic potential of gingerols and their nanoformulations. *Front Pharmacol*. 2022;13:902551. doi:10.3389/fphar.2022.902551
8. Dugasani S, Pichika MR, Nadarajah VD, et al. Comparative antioxidant and anti-inflammatory effects of [6]-gingerol, [8]-gingerol, [10]-gingerol and [6]-shogaol. *J Ethnopharmacol*. 2010;127(2):515–20.
9. Farhath S, Sujatha R, Hazeena Begum V. Immunomodulatory effects of 6-gingerol on humoral and cell-mediated immune responses in rats. *Int J Pharma Bio Sci*. 2013;4(3):748–54.
10. Rasmussen B, Johnson M, Wray J, et al. Ginger extract inhibits cell growth and modulates cell cycle and apoptosis regulatory proteins in ovarian cancer cells. *BMC Complement Altern Med*. 2019;19(1):1–9.
11. Hitomi Y, Watanabe Y, Tsuchiya N, et al. Ginger extract prevents alcohol-induced liver injury by scavenging free radicals and suppressing inflammatory cytokines. *PLoS ONE*. 2017;12(9):e0185580.
12. Algandaby MM, Ashour OM, Al-Abbasi FA. Antifibrotic and anti-inflammatory role of 6-gingerol in thioacetamide-induced liver fibrosis in rats. *Can J Physiol Pharmacol*. 2016;94(6):607–17.
13. Lee TY, Lee KC, Chen SY, et al. Protective effects of ginger oil on hepatic injury and inflammation in mice with CCl4-induced acute liver failure. *Evid Based Complement Alternat Med*. 2015;2015:231387.
14. Lee HS, Seo EY, Kang NE, et al. [6]-Gingerol inhibits metastasis of MDA-MB-231 human breast cancer cells. *J Nutr Biochem*. 2008;19(5):313–9.
15. Wang S, Zhang C, Yang G, et al. The inhibitory effect of [6]-gingerol on proliferation and invasion of human pancreatic cancer cells through blocking STAT3 signaling pathway. *Oncol Rep*. 2018;39(3):1320–8.
16. Tahir M, Sultana S. Role of ginger extract in chemoprevention of kidney tumors: histopathological and immunohistochemical analysis. *Asian Pac J Trop Med*. 2015;8(3):207–15.
17. Hu R, He Z, Liu M, et al. [8]-Gingerol inhibits colorectal cancer cell proliferation and migration via EGFR/STAT pathway. *J Cell Biochem*. 2020;121(2):1645–56.