REVIEW ARTICLE

Pharmacological Insights into *Zingiber officinale* var. *rubrum* (red ginger): A review of bioactive compounds and medicinal applications

G. Darshan Balaji[1], S. Velmurugan[2], M. Anand[3], S. Marimuthu[4], I. Johnson[5], N. Manikanda Boopathi[6]

[1]Department of Plantation, Spices, Medicinal and Aromatic Crops, HC and RI, TNAU, Coimbatore, Tamil Nadu, India, [2]Department of Spices and Plantation Crops, HC and RI, TNAU, Coimbatore, Tamil Nadu, India, [3]Department of Food Process Engineering, TNAU, Coimbatore, Tamil Nadu, India, [4]Centre for Agricultural Nanotechnology, TNAU, Coimbatore, Tamil Nadu, India, [5]Department of Millets, TNAU, Coimbatore, Tamil Nadu, India, [6]Department of Plant Biotechnology, CPMB and B, TNAU, Coimbatore, Tamil Nadu, India

Abstract

Red ginger (*Zingiber officinale* var. *rubrum* Theilade), commonly known as red ginger or jahe merah, is a distinct variety within the Zingiberaceae family, characterised by its crimson rhizome, elevated essential oil content (2.58–3.90% v/w), and a rich profile of bioactive compounds including gingerols, shogaols, paradols, and variety-specific anthocyanins. This review synthesizes current evidence on the taxonomy, distribution, morphology, ethnopharmacology, nutritional composition, phytochemistry, and pharmacological activities of *Z. officinale* var. *rubrum*. Long established in the Indonesian Jamu tradition, Ayurveda, and Traditional Chinese Medicine, red ginger has been used to treat gastrointestinal disorders, rheumatic pain, fever, and reproductive conditions. Contemporary pharmacological studies have validated these uses, demonstrating antioxidant (nuclear factor erythroid 2-related factor 2/heme oxygenase-1 activation), anti-inflammatory (cyclooxygenase-2/nuclear factor kappa B/mitogen-activated protein kinase inhibition), thrombolytic, antiviral, anthelmintic, gastroprotective (including *Helicobacter pylori* inhibition), and analgesic activities with supporting clinical evidence in dysmenorrhea and osteoarthritis. Preclinical toxicology classifies extracts as practically non-toxic (lethal dose 50% >5,000 mg/kg; World Health Organization Category 5) with a negative genotoxicity profile. Key challenges include a limited clinical trial base, incomplete pharmacokinetic data, and phytochemical variability across sources. Future priorities include well-powered randomised controlled trials, phytochemical standardization, and improved delivery systems to enhance bioavailability. Overall, *Z. officinale* var. *rubrum* represents a promising phytomedicinal resource with significant translational potential across inflammatory, infectious, and pain-related therapeutic areas.

Key words: Anthocyanins, anti-inflammatory, antioxidant, ethnopharmacology, gingerols, jahe merah, phytochemistry, red ginger, shogaols, *Zingiber officinale* var. *rubrum*

INTRODUCTION AND OVERVIEW

Zingiberaceae Zingiber is a genus of aromatic perennial herbs containing over 100 species, with *Zingiber officinale* Roscoe being the most prominent in terms of global medicine, food science and commerce. In this species, the variety of *rubrum,* herein known as red ginger or jahe merah, has gained increasing scientific attention due to its unique crimson-colored rhizome, its significantly greater amount of pungent phenolic compounds, and its long ethnopharmacological history dating back several millennia in South and Southeast Asia.[1] Red ginger (*Z. officinale* var.

Address for correspondence:
G. Darshan Balaji,
Department of Plantation, Spices, Medicinal and Aromatic Crops, HC and RI, TNAU, Coimbatore, Tamil Nadu, India.
E-mail: darshanguna17699@gmail.com

Received: 11-05-2026
Revised: 16-06-2026
Accepted: 24-06-2026

rubrum Theilade) is morphologically and phytochemically differentiated as compared to its congeners, such as the common ginger (*Z. officinale* var. *officinale*) and the Emprit/bitter ginger (*Z. officinale* var. *amarum*).[2] Importantly, comparative phytochemical studies always reveal that red ginger has the highest essential oil content (2.58–3.90% v/w) and the highest concentration of gingerol, shogaol, paradol, and anthocyanin-class pigments among the three major cultivars.[3] These properties make it a highly bioactive type having wide therapeutic opportunities. Red ginger has been used in traditional medical systems such as Ayurveda, Traditional Chinese Medicine and the Jamu healing tradition of Indonesia, over thousands of years to treat a wide range of diseases, including gastrointestinal ailments and rheumatic pain, as well as febrile disease and reproductive disorders. The revitalization of interest in plant-derived therapeutics in the 21st century, due to problems of synthetic drug toxicity, rising antimicrobial resistance and the worldwide epidemic of non-communicable disease, has stimulated renewed interest in exploring the bioactive potential of *Z. officinale* var. *rubrum*.[4] Contemporary pharmacological research has substantiated many of these traditional assertions, demonstrating notable anti-inflammatory, antioxidant, antiviral, anti-ulcer, and analgesic activities attributable to its diverse phytochemical composition. At the same time, nutritional analyses indicate the presence of significant amounts of carbohydrates, dietary fiber, essential minerals (potassium, magnesium, phosphorus) and vitamins that help in determining its nutraceutical value. Red ginger is at the cross-section of its food-grade safety profile and high pharmacological efficacy, making it an ideal candidate to develop into a functional food, to pharmaceutical standardize, and to integrate into clinical practice.[5] Although such promise is present, clinical trial evidence is still rigorous, pharmacokinetic data on key bioactives are yet to be fully characterised, agronomic, geographic and post-harvest differences in phytochemical composition make standardization difficult.[6] The current review thus seeks to bring together existing information on the taxonomy, distribution, morphology, common uses, nutritional composition, and phytochemical constituents of *Z. officinale* var. *rubrum* and hence provide a unified scientific basis on future pharmacological and clinical studies [Figure 1].

TAXONOMY, DISTRIBUTION, AND MORPHOLOGY OF RED GINGER

Taxonomic classification

Botanical clarification has been carried out during the last century concerning the taxonomic identity of red ginger. At first regarded as a separate species, or loosely as part of the larger complex of *Z. officinale*, recent morphological and molecular phylogenetic data indicate conclusively that it is a variety of *Z. officinale* Roscoe, officially recognised as *Z. officinale* var. *rubrum* Theilade.

Table 1 shows the entire taxonomic hierarchy.

Geographic distribution

Red ginger is indigenous to the humid tropical and subtropical zones of South and Southeast Asia. Its primary centers of genetic diversity and cultivation include the Indonesian archipelago, particularly Java, Sumatra, and Kalimantanas well as peninsular Malaysia, Thailand, the Philippines, and parts of southern India and Sri Lanka.[7] Indonesia remains the world's largest producer and consumer of red ginger, where it constitutes a cornerstone ingredient in the traditional medicinal beverage system known as Jamu. In response to increasing international demand, secondary cultivation has expanded into sub-Saharan Africa (Nigeria, Ghana, Tanzania), the Caribbean basin, and parts of tropical South America and Australia.[8] It grows at altitudes ranging from sea level to approximately 1,500 m, in well-drained, loamy-to-clay soils, with mean annual temperatures of 20–30°C, humidity above 70%, and annual rainfall of 1,500–3,000 mm. Cultivation in partial shade, especially within agroforestry systems, is reported to enhance rhizome quality and the yield of bioactive constituents.[1,2]

Morphological characteristics

Red ginger is a strong perennial herb with a height of 0.5–1.5 m, which is typified by straight pseudostems that are made of closely wrapping leaf bases. The leaves are lanceolate to narrowly elliptic 20–40 cm long by 2–4 cm wide, with conspicuous midribs and smooth, glabrous laminae. The

Figure 1: Rhizome morphology of *Zingiber officinale* varieties: (a) var. *rubrum* (red ginger), (b) var. *officinale* (common ginger), and (c) var. *amarum* (Emprit/bitter ginger)

Table 1: Taxonomic classification of *Zingiber officinale* var. *rubrum*.

Taxonomic rank	Classification
Kingdom	Plantae
Division	Tracheophyta
Class	Liliopsida
Order	Zingiberales
Family	Zingiberaceae
Genus	Zingiber
Species	*Zingiber officinale Roscoe*
Variety	*Zingiber officinale var. rubrum Theilade*
Common names	Red ginger, Jahe merah (Indonesia/ Malaysia), Gingembre rouge (French)

superior leaves are dark green on the surface, and light green beneath, pubescent at times along the midrib.[9] The rhizome is the most diagnostically significant and commercially important, irregular, multi-branched structure with a characteristic outer skin that is reddish-brown to dark-red in color. The deep reddish-orange to maroon pigmentation of the cortex and vascular tissue is the characteristic color that differentiates this variety with the pale-yellow of the flesh of *Z. officinale* var. *officinale* in cross-section. This coloration can be explained by the presence of anthocyanins, mostly cyanidin-3-glucoside, in the parenchymatous cells of the rhizome.[10] The fresh rhizome is aromatic, typically pungent and camphoraceous, with a significantly greater spicy heat than in common ginger, which is in line with the high concentration of gingerol and essential oils. The inflorescence is produced directly on the rhizome on another leafless peduncle, producing a compact, ovoid to cylindrical spike 5–10 cm long. A second distinguishing characteristic of the variety is that the bracts are imbricate, broadly ovate, and are usually reddish-green to deep red.[11] The flowers are tubular, of a pale yellow with a purple-spotted labellum, and are carried singly as the bracts of the axil. Fruits, when produced, are trilocular capsules containing black-coated seeds; however, the variety rarely produces viable seed under cultivated conditions and is propagated predominantly by rhizome division.[12]

TRADITIONAL USES OF RED GINGER

Ethnomedicinal context

Z. officinale var. *rubrum* is a medicinal plant with a rich history of application in the indigenous South and Southeast Asian medicine. Jamu is a traditional Indonesian system of healing in which red ginger is one of the oldest and most codified systems in the world and is a building block in a wide variety of formulations.[13] Red ginger is also believed to have warming properties (calorigenic), carminative, tonic, and anti-rheumatic effects by traditional healers and dukun (traditional physicians), used either as freshly squeezed juice, boiled decoctions, common Jamu preparations or as an external poultice. Various traditional medicine systems record the therapeutic uses of red ginger which can be ordered in terms of organ system or disease domain.[14,15] These usage patterns that have been verified to different extents through current bioassay comprise ethnopharmacological evidence base of the contemporary pharmacological inquiry.

NUTRITIONAL AND PHYTOCHEMICAL COMPONENTS

Nutritional composition

The proximate nutritional content of *Z. officinale* var. *rubrum* rhizome/100 g fresh weight has been characterized over various studies. Red ginger has about 78–82 g water, 1.8–2.2 g protein, 0.6–1.0 g total lipid, 15–17 g total carbohydrates (2.0–3.5 g dietary fibre) and also has 60–80 kcal of energy. Notable mineral profile includes potassium (415 mg/100 g), magnesium (43 mg/100 g), phosphorus (34 mg/100 g), and calcium (16 mg/100 g) and trace amounts of iron, zinc, and copper.[16] Vitamins present include ascorbic acid (Vitamin C, ~5 mg/100 g), thiamine (B1), riboflavin (B2), niacin (B3), and pyridoxine (B6).[8,9] It is worth noting that the essential oil level of red ginger (2.58–3.90% v/w) is significantly higher than that of common ginger (1.5–2.5%), which has a direct impact on its high pungency and pharmacological activity.[17]

Phytochemical profile: Bioactive compounds

Z. officinale var. *rubrum* has a rich and structurally diverse set of secondary metabolites upon which the pharmacological actions of the plant are based. These can be classified into five broad phytochemical groups: (1) Gingerols and their homologues; (2) Shogaols; (3) Paradols; (4) Terpenoids (sesquiterpenes and monoterpenes); and (5) Flavonoids and phenolic acids.[18] A sixth class, the anthocyanins largely absent from common ginger is a distinguishing characteristic of the red variety, contributing to its typical coloration and conferring additional antioxidant and anti-inflammatory properties.[19] A complete list of the principal bioactive compounds of *Z. officinale* var. *rubrum*, including their chemical class, reported biological activities, plant-part source, and primary literature reference, is given in [Figure 2].

Phytochemical variability

It should be mentioned that the phytochemical content of *Z. officinale* var. *rubrum* is highly variable under the influence of the genotype, environment and cultivation (altitude, soil type, fertilization regime), harvest maturity, post-harvest handling, and methodology of extraction. The levels of gingerol, e.g., are stated to diminish after 8 months of rhizome maturation, whereas levels of shogaol

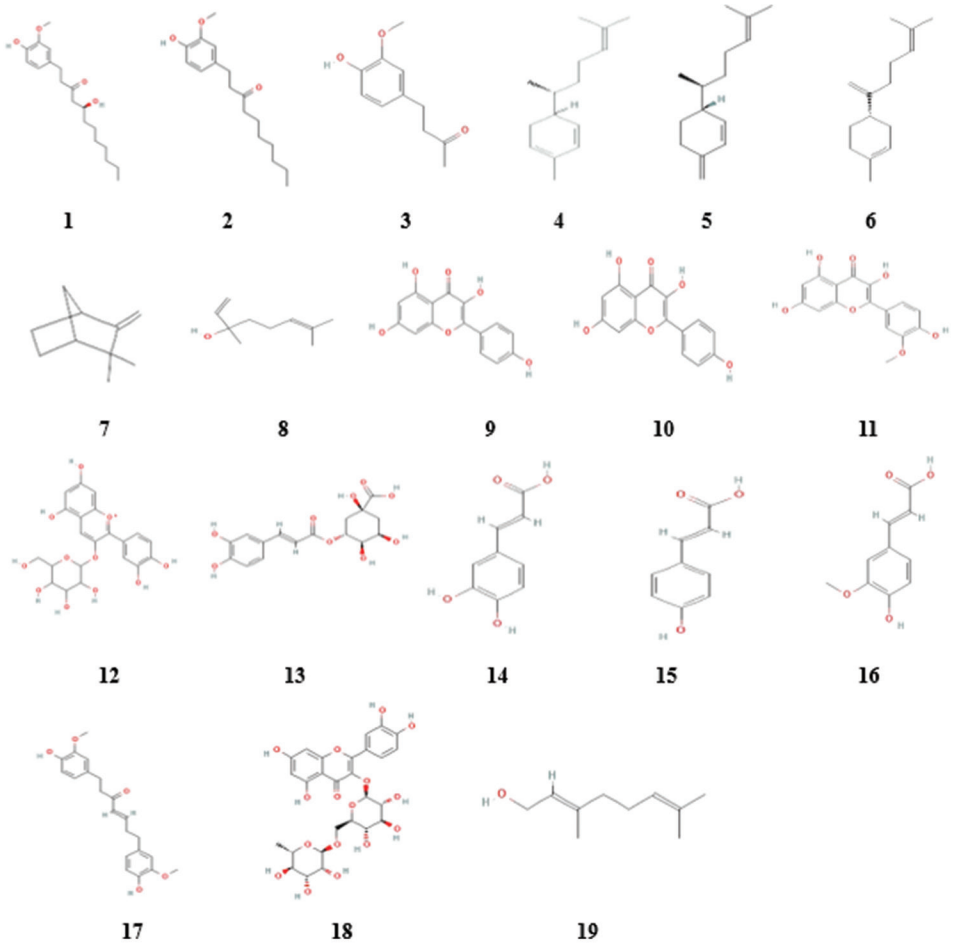

Figure 2: Chemical structures of the major phytochemicals identified in *Zingiber officinale* var. *rubrum* (red ginger): 6-, 8- and 10-gingerol (1), 6-paradol (2), zingerone (3), α-zingiberene (4), β-sesquiphellandrene (5), β-bisabolene (6), camphene (7), linalool (8), kaempferol (9), quercetin (10), isorhamnetin (11), cyanidin-3-glucoside (12), chlorogenic acid (13), caffeic acid (14), *p*-coumaric acid (15), ferulic acid (16), gingerenone A (17), rutin (18) and geraniol (19)

rise a product of thermal or enzymatic drying reactions.[20] The standardization of the quality of the raw materials is thus a crucial requirement to reproducible pharmacological and clinical research. Quality control of red ginger-derived products is increasingly suggested to use chromatographic fingerprinting (high-performance liquid chromatography with a diode array detector [HPLC-DAD], gas chromatography-mass spectrometry) and spectroscopic profiling (nuclear magnetic resonance [NMR], liquid chromatography mass spectrometry [LC-MS/MS]).[21]

ANTIOXIDANT ACTIVITY

Mechanistic basis of antioxidant action

Oxidative stress is an imbalance between the production of reactive oxygen species and the cell's antioxidant defences, and it is a key pathomechanistic mediator of atherosclerosis, Type 2 diabetes mellitus, neurodegeneration, and carcinogenesis.[22] Due to its rich arsenal of hydrogen-donating phenolic compounds gingerols, shogaols, zingerone, flavonoids, phenolic acids, and anthocyanins *Z. officinale* var. *rubrum* is now regarded as one of the most potent antioxidant botanicals studied to date.[23] The principal antioxidant actions reported are: (i) Direct free-radical scavenging through phenolic hydrogen donation; (ii) Prevention of Fenton-type hydroxyl radical formation by chelation of metal ions; (iii) Inhibition of lipid peroxidation chain reactions by trapping peroxyl radicals; and (iv) Stimulation of endogenous antioxidant enzymes (superoxide dismutase, catalase). 6-gingerol activates nuclear factor erythroid 2-related factor 2 (Nrf2) nuclear translocation at concentrations as low as 5 μm in human keratinocytes, driving downstream expression of heme oxygenase-1 (HO-1) and NAD(P)H: quinone oxidoreductase-1.[24] A consistent finding across independent studies is that the antioxidant capacity of *Z. officinale* var. *rubrum* is substantially higher than that of var. *officinale* and var. *amarum* under identical conditions, due to roughly 2.4 times the total phenolic content and the presence of anthocyanins not found in the other varieties [Figure 3].[25]

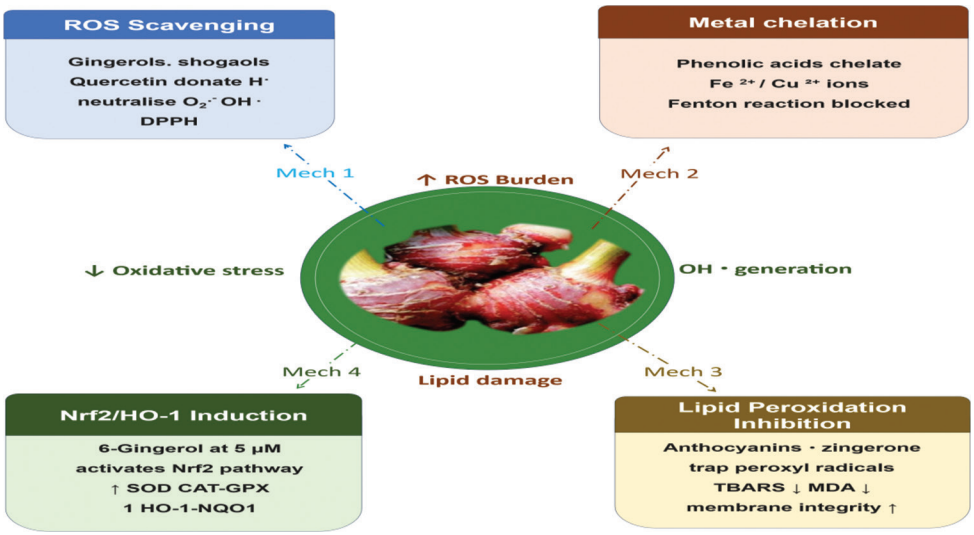

Figure 3: Schematic overview of the four principal antioxidant mechanisms operative in *Zingiber officinale* var. *rubrum* bioactives

ANTI-INFLAMMATORY ACTIVITY

Molecular targets and signaling pathways

The unifying pathophysiological mechanism linking rheumatoid arthritis, inflammatory bowel disease, metabolic syndrome, and carcinogenesis is chronic inflammation. Red ginger exerts multi-target anti-inflammatory effects that parallel and complement those of non-steroidal anti-inflammatory drugs (NSAIDs) while offering a significantly more favorable gastrointestinal safety profile. Its principal molecular targets are the arachidonic acid cascade (cyclooxygenase [COX]-1, COX-2, 5-lipoxygenase [5-LOX]), the nuclear factor kappa B (NF-κB) signaling pathway, and the mitogen-activated protein kinase (MAPK) (ERK, JNK, p38) cascade.[26] 6-Gingerol shows selectivity with a COX-2:COX-1 ratio of approximately 2.3:1, implying a pharmacological profile closer to that of selective COX-2 inhibitors than to non-selective NSAIDs, and thus indicating lower ulcerogenic potential.[27] 6-Shogaol inhibits lipopolysaccharide-induced NF-κB activation in RAW 264.7 macrophages with an IC_{50} of 8.3 µm, suppressing IκBα phosphorylation and the nuclear translocation of p65, which in turn downregulates pro-inflammatory cytokines including tumor necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), IL-6, and IL-8. The diarylheptanoid fraction provides complementary 5-LOX inhibition, preventing leukotriene biosynthesis an action not exerted by traditional NSAIDs but of critical importance in asthmatic and allergic inflammatory processes. Rhizome extracts reduce carrageenan-induced paw edema by 46–55% at 400 mg/kg administered orally [Figure 4].[28]

THROMBOLYTIC ACTIVITY

Arterial thrombosis, the pathological formation of intravascular blood clots, is the proximate cause of myocardial infarction and ischemic stroke, the leading causes of global mortality. *Z. officinale* var. *rubrum* has been investigated for thrombolytic activity, primarily through *in vitro* clot-lysis assays and platelet-aggregation studies, and has demonstrated meaningful, albeit moderate, clot-dissolving and antiplatelet properties.[29] The main thrombolytic mechanisms proposed are: (i) Induction of tissue plasminogen activator (tPA) expression, which drives the conversion of plasminogen to plasmin; (ii) Inhibition of thromboxane A2 production through COX-1 blockade; and (iii) Direct inhibition of platelet aggregation through antagonism of the platelet ADP (P2Y12) receptor. Notably, ginger's pungent constituents inhibit platelet aggregation primarily through the arachidonic acid/COX-1 pathway rather than through platelet-activating factor or thrombin-mediated routes mechanism distinct from, but complementary to, that of aspirin.[30,31] The clot-lysis rates of red ginger extracts (19–41%) are lower than that of streptokinase (~67%), indicating that red ginger is better suited as a preventive antiplatelet agent than as a replacement for acute thrombolytic therapy [Table 2].

ANTIVIRAL ACTIVITY

The antiviral potential of *Z. officinale* var. *rubrum* has attracted growing interest owing to the emergence of viral pathogens, particularly in the wake of the SARS-CoV-2 pandemic. Isolated bioactives and red ginger extracts have demonstrated inhibitory effects against influenza viruses, herpesviruses, hepatitis viruses, respiratory syncytial virus, and surrogate norovirus models.[36] Several antiviral mechanisms have been proposed: (i) A virucidal effect, whereby lipophilic gingerols and terpenoids directly disrupt the viral envelope lipid bilayer; and (ii) Inhibition of viral attachment and cell entry through blockade of surface receptors, as reported for 6-gingerol against Coxsackievirus A16. *In silico* molecular docking assays have identified 6-shogaol and 6-gingerol as potential inhibitors of the SARS-CoV-2 main protease (Mpro), with

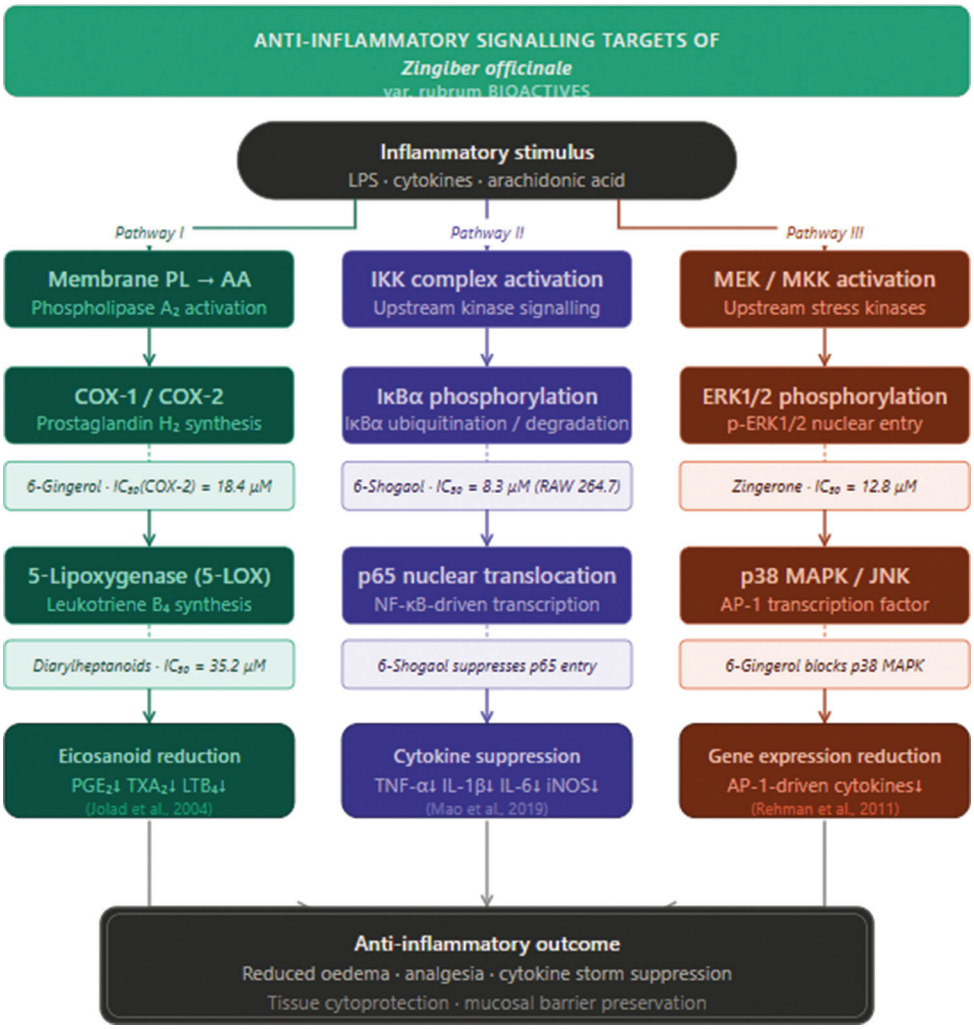

Figure 4: Major anti-inflammatory signaling cascades inhibited by *Zingiber officinale* var. *rubrum* bioactives

Table 2: Thrombolytic and antiplatelet activity of *Zingiber officinale* var. *rubrum* extracts and isolated compounds

Extract/Compound	Concentration	% Activity	Positive control	Assay method	Reference
Rhizome aqueous extract	500 μg/mL	34.6	Streptokinase (67.4%)	*In vitro* clot lysis	[32]
Rhizome ethanolic extract	500 μg/mL	28.2	Streptokinase	*In vitro* clot lysis	[33]
6-Gingerol (pure compound)	200 μm	41.3	Aspirin (52.1%)	Platelet aggregation assay	[34]
Essential oil (α-zingiberene-rich)	100 μg/mL	19.4	Heparin (positive control)	Fibrinolysis assay	[35]

predicted binding energies of −7.8–−8.4 kcal/mol; these computational predictions, however, require experimental and clinical validation [Table 3].[37]

ANTHELMINTIC ACTIVITY

Parasitic helminthiases affect over 1.5 billion people globally, predominantly in tropical and subtropical low-income settings. The emergence of anthelmintic resistance in both veterinary and human medicine has stimulated renewed interest in plant-derived alternatives.[45] *Z. officinale* var. *rubrum* has been evaluated for anthelmintic properties using *in vitro* and *in vivo* experimental models. The anthelmintic mechanism of red ginger is proposed to involve: (i) Disruption of helminth neuromuscular transmission through acetylcholinesterase inhibition or GABA-mimetic effects of zingerone and sesquiterpene constituents; (ii) Membrane permeabilization by amphiphilic gingerols acting on helminth tegument or intestinal epithelium; and (iii) Interference with helminth energy metabolism via inhibition of fumarate reductase an enzyme absent in mammalian mitochondria.[46]

Table 3: Antiviral activity of *Zingiber officinale* var. *rubrum* extracts and bioactive compounds against selected viral pathogens

Target virus	Extract/Compound	IC_{50}/Activity	Experimental model	Reference
Influenza A (H1N1)	Rhizome ethanolic extract	IC_{50}=22.3 μg/mL; SI>10	Plaque reduction assay (MDCK cells)	[38]
HSV-1	6-Gingerol	IC_{50}=35.7 μm; CC50=412 μm	Vero cell infection model	[39]
HCV	Gingerol homologues (6-, 8-, 10-)	IC_{50}=28–54 μm (NS3 helicase)	Enzyme-based *in vitro* assay	[40]
SARS-CoV-2 (*in silico*)	6-Shogaol, 6-Gingerol	Binding energy: −7.8–−8.4 kcal/mol (Mpro)	Molecular docking (AutoDock Vina)	[41]
RSV	Rhizome aqueous extract	IC_{50}=91.5 μg/mL	CPE reduction in HEp-2 cells	[42]
HRV	Zingerone	IC_{50}=48.2 μm	MTT CPE assay	[43]
Feline calicivirus (norovirus surrogate)	6-Gingerol	3 log10 reduction at 200 μm	Plaque assay	[44]

HSV-1: Herpes simplex virus-1, HCV: Hepatitis C virus, HRV: Human rhinovirus, RSV: Respiratory syncytial virus, IC_{50}: Half-maximal inhibitory concentration, MDCK: Madin-Darby Canine kidney, CPE: Cytopathic effect

Reported that rhizome aqueous extract caused significant concentration-dependent paralysis and death of Pheretima posthuma earthworms, though time to paralysis was longer than albendazole reference control, suggesting partial anthelmintic efficacy warranting further investigation.

ANTI-ULCER ACTIVITY

Peptic ulcer disease affects approximately 10% of the global population at some point during their lifetime. Its pathogenesis involves an imbalance between aggressive factors (*H. pylori*, NSAIDs, gastric acid, pepsin) and mucosal defence mechanisms (mucus secretion, prostaglandin E2 [PGE2] production, bicarbonate secretion, epithelial renewal). *Z. officinale* var. *rubrum* is particularly promising as a gastroprotective agent, given its dual capacity to suppress the ulcerogenic NF-κB/COX-2 axis while simultaneously upregulating mucosal cytoprotective prostaglandins.[47] The anti-ulcer mechanisms are multi-pronged. 6-Gingerol and zingerone stimulate mucus secretion from gastric epithelial cells, strengthening the mucosal barrier against acid erosion.[48] Red ginger ethanolic extracts have been shown to inhibit 9 of 19 clinically isolated *H. pylori* strains at a minimum inhibitory concentration of 0.78 mg/mL[49] a clinically significant finding given escalating antibiotic resistance in *H. pylori* management. Upregulation of mucosal PGE2 stimulates mucus and bicarbonate secretion while promoting mucosal blood flow, producing a cytoprotective effect mechanistically analogous to misoprostol.

ANALGESIC ACTIVITY

Preclinical and clinical evidence

Pain is among the most prevalent and debilitating medical complaints encountered in clinical practice. The analgesic properties of *Z. officinale* var. *rubrum* have been evaluated using standardised preclinical models assessing both peripheral (nociceptive) and central (supraspinal/spinal) analgesic activity, as well as in a growing body of randomized controlled clinical trials.[50] The analgesic mechanisms are multi-modal. At the peripheral level, inhibition of prostaglandin synthesis via COX-2 suppression and reduction in bradykinin sensitization of nociceptors mirror the analgesic action of NSAIDs. At the central level, 6-shogaol modulates spinal cord dorsal horn nociception through partial agonism at mu-opioid receptors and inhibition of spinal TRPV1 channel activation, consistent with enhanced latencies observed in hot-plate and tail-flick assays.[51] Anti-neuroinflammatory activity of shogaols reducing microglial activation and spinal TNF-α/IL-1β production contributes to central sensitization reduction in chronic pain models. Clinical trial evidence is particularly notable:[52] demonstrated that standardised red ginger capsules achieved pain relief statistically equivalent to mefenamic acid in primary dysmenorrhea with superior tolerability [Table 4].

TOXICOLOGICAL PROFILE

Safety assessment overview

A comprehensive toxicological assessment is essential before the clinical translation of any botanical therapeutic. For *Z. officinale* var. *rubrum*, the cumulative preclinical safety dataset across acute, sub-acute, and genotoxicity studies is generally reassuring, aligning with centuries of empirical human use without documented serious adverse events.[4] Acute oral toxicity studies in rodents typically classify red ginger extracts as Practically Non-toxic, corresponding to WHO/ Globally Harmonized System (GHS) Category 5 (lethal dose 50% >2,000–5,000 mg/kg).[59,60] Sub-acute and sub-chronic studies establish a NOAEL in the range

Table 4: Analgesic activity of *Zingiber officinale* var. *rubrum*: Preclinical and clinical evidence with quantitative outcomes

Model	Extract/ Compound	Dose	Result	Control	Mechanism	Reference
Acetic acid writhing (mouse)	Rhizome ethanolic extract	100 and 200 mg/kg p.o.	Writhing: 42.3%/61.8%	Aspirin (150 mg/kg): 68.4%	Central +peripheral	[53]
Hot plate test (mouse)	Rhizome aqueous extract	200 and 400 mg/kg p.o.	Latency increase: 1.6–2.1×at 60 min	Morphine: ×3.4 latency increase	Central analgesic	[53]
Tail-flick test (rat)	6-Gingerol (pure)	50 mg/kg p.o.	Reaction time prolonged 2.8-fold (P<0.01)	Indomethacin: 2.1-fold	Opioid pathway partial agonism	[54]
Formalin paw – Phase I (neurogenic)	6-Shogaol	25 mg/kg i.p.	42.1% pain score reduction	Comparable to diclofenac	Central mechanism	[55]
Formalin paw – Phase II (inflammatory)	6-Shogaol	25 mg/kg i.p.	58.4% pain score reduction	Comparable to diclofenac	COX-2/PGE2 inhibition	[56]
Clinical RCT – Dysmenorrhea	Standardised red ginger (500 mg)	×3 daily for 3 days	Pain VAS: 4.2 versus placebo 6.8 (P<0.05)	Mefenamic acid equivalent efficacy	PGs biosynthesis inhibition	[57]
Clinical RCT – Osteoarthritis knee	Ginger extract 255 mg twice daily	6-week RCT, 261 patients	WOMAC pain subscale−63% versus placebo−50%	Statistically significant (P<0.05)	Multi-mechanism	[58]

RCT: Randomized controlled trial, COX-2: Cyclooxygenase 2, PG: Prostaglandin, PEG2: Prostaglandin E2, VAS: Visual Analog Scale, WOMAC: Western Ontario and McMaster Universities

of 200–500 mg/kg/day; however, higher doses have been associated with dose-dependent histopathological changes, including hepatic degeneration and necrosis at 400–800 mg/kg/day, rather than purely reversible biochemical alterations.[61] Genotoxicity profiles, including the Ames test and mammalian chromosomal aberration assays, remain uniformly negative. Principal safety concerns include potential pharmacokinetic interactions with anticoagulants like warfarin (e.g., international normalized ratio elevation) and the risk of embryotoxicity or spontaneous miscarriage at high doses during pregnancy.

FUTURE PERSPECTIVES

Despite strong preclinical evidence for the pharmacological versatility of *Z. officinale* var. *rubrum*, a wide translational gap persists, and several priorities stand out. Most current data derive from *in vitro* and rodent studies, so the field urgently needs adequately powered, double-blind randomized controlled trial sparticularly Phase II/III trials in osteoarthritis, rheumatoid arthritis, metabolic syndrome, chemoprevention, and dysmenorrhea alongside long-term (≥12-month) safety surveillance and pharmacokinetic studies in vulnerable groups such as elderly and metabolically compromised patients.[62,63] Realizing this potential also demands phytochemical standardization: pharmaceutical-grade material defined by specific gingerol and shogaol content (as curcumin is standardised in turmeric), verified through hyphenated analytical methods (LC-MS/MS, HPLC-DAD, NMR metabolomics) and codified in national pharmacopoeias.[64] Because the bioactives suffer from poor water solubility, alkaline instability, and extensive first-pass metabolism, advanced delivery systems lipid nanoparticles, polymeric nanocapsules, self-emulsifying drug delivery systems, cyclodextrin complexes, and co-encapsulation with enhancers like piperine offer 2–8-fold bioavailability gains.[65,66] As a multi-target agent, red ginger is well suited to network-pharmacology approaches that map phytochemical-target relationships and exploit synergistic, polypharmacological effects, notably in neuroinflammatory (Alzheimer's) and NLRP3-driven metabolic-inflammatory pathways.[67,68] Finally, a sustainable supply depends on agronomic investment marker-assisted breeding of high-gingerol cultivars, optimized cultivation and post-harvest processing, and ex situ and in situ conservation of *Z. officinale* var. *rubrum* germplasm from its Indonesian and Malaysian centers of origin.[69]

CONCLUSION

This review has critically synthesised the botanical, ethnopharmacological, phytochemical, and pharmacological dimensions of *Z. officinale* var. *rubrum* (red ginger), spanning its taxonomy, distribution, morphology, traditional

uses, nutritional composition, and reported bioactivities. Collectively, the evidence positions red ginger as pharmacologically distinct from other varieties of *Zingiber officinale*, and from common ginger in particular, owing to its higher gingerol, shogaol, and essential-oil content together with the comparatively unusual presence of anthocyanins. These constituents underpin a broad, mechanistically coherent profile encompassing antioxidant (Nrf2/HO-1 activation, direct radical scavenging), anti-inflammatory (COX-2/NF-κB/MAPK inhibition), thrombolytic (tPA induction, antiplatelet), and antiviral (multi-mechanism, including putative SARS-CoV-2 Mpro inhibition) activities. Preclinical toxicology consistently describes it as practically non-toxic at achievable oral doses, consistent with its long history of human use. Significant gaps nonetheless remain. Translating robust *in vitro* and animal findings into clinical benefit will require well-designed, adequately powered randomised controlled trials, alongside phytochemical standardization, improved bioavailability through advanced delivery systems, and systematic characterization of pharmacokinetics. Critically, the pharmacological distinction between var. *rubrum* and common ginger is variety-specific and must be respected in future work; treating the two interchangeably is a recurring source of interpretive error in the existing literature. In sum, *Z. officinale* var. *rubrum* is a scientifically credible and therapeutically promising phytomedicinal resource. Realizing this potential will depend on sustained, interdisciplinary collaboration among ethnobotanists, pharmacologists, food scientists, clinicians, and regulators across clinical pharmacology, pharmaceutical technology, quality standardization, and agronomy.

REFERENCES

1. Liu Y, Liu J, Zhang Y. Research progress on chemical constituents of *Zingiber officinale* Roscoe. Biomed Res Int 2019;1:5370823.
2. Setyawan AD, Wiryanto S, Bermawie NU. Variation in isozymic pattern of germplasm from three ginger (*Zingiber officinale*) varieties. Nusant Biosci 2014;6:86-93.
3. Kumar Gupta S, Sharma A. Medicinal properties of *Zingiber officinale* Roscoe-a review. J Pharm Biol Sci 2014;9:124-9.
4. Supu RD, Diantini A, Levita J. Red ginger (*Zingiber officinale* var. *rubrum*): Its chemical constituents, pharmacological activities and safety. Fitofarmaka J Ilm Farm 2018;8:25-31.
5. Zhang S, Kou X, Zhao H, Mak KK, Balijepalli MK, Pichika MR. *Zingiber officinale* var. *rubrum*: Red ginger's medicinal uses. Molecules 2022;27:775.
6. Hendra RJ, Rusdi R, Asra R, Misfadhila S. Phytochemical and traditional uses of red ginger: A review (*Zingiber officinale* var. *rubrum*). EAS J Pharm Pharmacol 2022;4:50-65.
7. Suciyati SW, Adnyana IK. Red ginger (*Zingiber officinale* Roscoe var *rubrum*): A review. Pharmacologyonline 2017;2:60-5.
8. Haroen U, Syafwan S, Kurniawan K, Budiansyah A. Determination of total phenolics, flavonoids, and testing of antioxidant and antibacterial activities of red ginger (*Zingiber officinale* var. *rubrum*). J Adv Vet Anim Res 2024;11:114.
9. Windarsih G, Utami DW, Yuriyah S. Morphological characteristics of Zingiberaceae in Serang District, Banten, Indonesia. Biodivers J Biol Divers 2021;22:5507-5529.
10. Syafitri DM, Levita J, Mutakin M, Diantini A. A review: Is ginger (*Zingiber officinale* var. Roscoe) potential for future phytomedicine. Indonesian J Appl Sci 2018;8.
11. Sivasothy Y, Chong WK, Hamid A, Eldeen IM, Sulaiman SF, Awang K. Essential oils of *Zingiber officinale* var. *rubrum* Theilade and their antibacterial activities. Food Chem 2011;124:514-7.
12. Kizhakkayil J, Sasikumar B. Diversity, characterization and utilization of ginger: A review. Plant Genet Resour 2011;9:464-77.
13. Ministry of Health of the Republic of Indonesia. Reference for Traditional Medicine Raw Materials from Medicinal Plants in Indonesia. Jakarta: Directorate General of Pharmacy and Medical Devices; 2017
14. Sugiarti L, Suwandi A, Syawaalz A. Gingerol on the rhizome of red ginger (*Zingiber officinale* Roscoe) with base modified percolation method. J Nat Sci 2011;1:156-65.
15. Jeong CH, Shim KH, Bae HJ. Antioxidant and antimicrobial activities of ginger extracts. Korean J Food Cookery Sci 2009;25:761-7.
16. Adel PR, Prakash J. Chemical composition and antioxidant properties of ginger root (*Zingiber officinale*). J Med Plants Res 2010;4:2674-9.
17. Yaman E, Woerdenbag HJ, Kayser O. Jamu: Indonesian traditional herbal medicine towards rational phytopharmacological. J Herb Med 2014;4:51-73.
18. Dugasani S, Pichika MR, Nadarajah VD, Balijepalli MK, Tandra S, Korlakunta JN. Comparative antioxidant and anti-inflammatory effects of [6]-gingerol, [8]-gingerol, [10]-gingerol and [6]-shogaol. J Ethnopharmacol 2010;127:515-20.
19. Ghasemzadeh A, Jaafar HZ, Rahmat A. Antioxidant activities, total phenolics and flavonoids content in two varieties of Malaysia young ginger (*Zingiber officinale* Roscoe). Molecules 2010;15:4324-33.
20. Zagórska J, Czernicka-Boś L, Kukula-Koch W, Szalak R, Koch W. Impact of thermal processing on the composition of secondary metabolites of ginger rhizome-a review. Foods 2022;11:3484.
21. Maisaroh M, Atmaji P, Astuti, Setianto WB, Restiawaty E, Bindar Y. Headspace Gas Chromatography/mass spectroscopy analysis of volatile organic compounds in red ginger (*Zingiber officinale* var. *rubrum*): Effects of drying on chemical and functional properties. IOP Conf Ser Earth Environ Sci 2025;1477:012068.

22. Hasani H, Arab A, Hadi A, Pourmasoumi M, Ghavami A, Miraghajani M. Does ginger supplementation lower blood pressure? A systematic review and meta-analysis of clinical trials. Phytother Res 2019;33:1639-47.
23. Kochhar SL. Economic Botany in the Tropics. 3rd ed. New Delhi: Macmillan India; 2008.
24. Kim JK, Kim Y, Na KM, Surh YJ, Kim TY. [6]-Gingerol prevents UVB-induced ROS production and COX-2 expression in vitro and *in vivo*. Free Radic Res 2007;41:603-14.
25. Purseglove JW, Brown EG, Green CL, Robbins SR. Spices. Vol. 1 and 2. New York: Longman Scientific and Tecnial Co.
26. Zhu Y, Weng L, Chen L, Cai Y. Review of the anti-inflammatory, analgesic, and antipyretic activities of ginger-derived compounds in herbal medicine. Phytomedicine 2015;22:1054-60.
27. Rehman R, Akram M, Akhtar N, Jabeen Q, Saeed T, Shah SM. *Zingiber officinale* Roscoe (pharmacological activity). J Med Plants Res 2011;5:344-8.
28. Ravindran PN, Nirmal Babu K, editors. Ginger: The Genus Zingiber. Boca Raton: CRC Press; 2016.
29. Pinontoan R, Leke PA, Lesmana JA, Purnomo JS, Dikson D, Samantha A. *In vitro* assessment of thrombolytic potential of red and white ginger (*Zingiber officinale*). Funct Foods Health Dis 2024;14:62-73.
30. Guh J, Ko FN, Jong TT, Teng CM. Antiplatelet effect of gingerol isolated from *Zingiber officinale*. J Pharmacy Pharmacol 1995;47:329-32.
31. Nurtjahja-Tjendraputra E, Ammit AJ, Roufogalis BD, Tran VH, Duke CC. Effective anti-platelet and COX-1 zyme inhibitors from pungent constituents of ginger. Thromb Res 2003;111:259-65.
32. Al-Yahya MA, Rafatullah S, Mossa JS, Ageel AM, Parmar NS, Tariq M. Gastroprotective activity of ginger (*Zingiber officinale* Roscoe) in albino rats. Am J Chin Med 1989;17:51-6.
33. Manju P, Pushpa DA. A study on thrombolytic and cytotoxic activity of methanolic extract of *Zingiber officinale*. Int J Life Sci Pharma Res 2020;10:1-5.
34. Ahmed SH, Gonda T, Agbadua OG, Girst G, Berkecz R, Kúsz N, *et al*. Preparation and evaluation of 6-gingerol derivatives as novel antioxidants and antiplatelet agents. Antioxidants (Basel) 2023;12:744.
35. Akhtar N, Shah SN. *Zingiber officinale* - a traditional herb with significant pharmacological activities. J Pharm Res 2011;4:2986-9.
36. Aminifard MA, Anar MA, Erabi G, Nikzad F, Ghasemi M, Seyfi-Ghale-Jogh M, *et al*. The antiviral potential of *Zingiber officinale* (Ginger): A comprehensive literature review. Curr Tradit Med 2025;11.
37. Shukla Y, Singh M. Cancer preventive properties of ginger: A brief review. Food Chem Toxicol 2007;45:683-90.
38. Gaire BP, Moon SK, Kim H. Herbal medicine in ischemic stroke: Risks or benefits. J Pharmacopuncture 2015;18:5-15.
39. Grzanna R, Lindmark L, Frondoza CG. Ginger - an herbal medicinal product with broad anti-inflammatory actions. J Med Food 2005;8:125-32.
40. Habib SH, Makpol S, Abdul Hamid NA, Das S, Ngah WZ, Yusof YA. Ginger extract (*Zingiber officinale*) has anti-cancer and anti-inflammatory effects on ethionine-induced hepatoma rats. Clinics (Sao Paulo) 2008;63:807-13.
41. Ibironke GF, Ajiboye KI. Studies on the anti-inflammatory and analgesic properties of *Chenopodium ambrosioides* leaf extract in rats. Afr J Biomed Res 1997;10:165-9.
42. Imanishi N, Tuji Y, Katada Y, Maruhashi M, Minami S, Yazaki K, *et al*. Additional inhibitory effect of tea extract on the growth of influenza A and B viruses in MDCK cells. Microbiol Immunol 2002;46:491-4.
43. Islam MS, Bhattacharjee C, Akhter S. Thrombolytic and membrane stabilizing activities of some selected medicinal plants of Bangladesh. Int J Pharm Sci Res 2014;5:1058-62.
44. Theilade I. Revision of *Zingiber* (Zingiberaceae) in Peninsular Malaysia and Singapore. Nord J Bot 1999;19:257-78.
45. USDA Plants Database. *Zingiber officinale* Roscoe - Ginger. Washington, DC, United States: Department of Agriculture Natural Resources Conservation Service; 2023. Available from: https://plants.usda.gov [Last accessed on 2026 Apr 23].
46. Wohlmuth H, Leach DN, Smith MK, Myers SP. Gingerol content of diploid and tetraploid clones of ginger (*Zingiber officinale* Roscoe). J Agric Food Chem 2005;53:5772-8.
47. Zahra A, Aini AN, Norhasnida Z, Nordin MM, Aisyah MN. Red ginger (*Zingiber officinale* var. *rubrum*): Chemical composition, medical uses and functional properties. Int Food Res J 2018;25:549-56.
48. Abdulrazaq NB, Cho MM, Win NN, Zaman R, Rahman MT. Beneficial effects of ginger (*Zingiber officinale*) on carbohydrate metabolism in streptozotocin-induced diabetic rats. Br J Nutr 2012;108:1194-201.
49. Sukmagautama C, Reviono R, Putranto W, Pamungkasari EP, Hartono H, Cilmiaty R, *et al*. Potential of *Zingiber officinale* var. *rubrum* extract in inhibiting *Helicobacter pylori* in chronic gastritis patients: A pilot study in human focusing on inflammation, oxidative stress, and quality of life. Trends Sci 2026;23:12656-6.
50. Altman RD, Marcussen KC. Effects of a ginger extract on knee pain in patients with osteoarthritis. Arthritis Rheum 2001;44:2531-8.
51. Bhagavathula AS, Abutaleb N, Al-Khatib HA, Elnour AA, Shehab A. Ginger and its active ingredients in the management of diabetes. Curr Pharm Des 2016;22:3001-12.
52. Chang JS, Wang KC, Yeh CF, Shieh DE, Chiang LC. Fresh ginger (*Zingiber officinale*) has anti-viral activity against human respiratory syncytial virus in human respiratory tract cell lines. J Ethnopharmacol 2013;145:146-51.

53. Dewi VK, Barkinah T, Kirana R, Rizki MI. The analgesic effect and toxicity of red and white ginger on mus musculus with the acetate writhing test. Med Lab Technol J 2024;10:95-105.
54. Christianty F. Antihyperalgesia potency of *Zingiber officinale var. rubrum* in inflammatory and neuropathy-induced chronic pain condition in mice. Pak J Pharm Sci 2019;32:1663-9.
55. Denyer CV. Isolation of antirhinoviral sesquiterpenes from ginger (*Zingiber officinale*). J Nat Prod 1994;57:658-62.
56. Wang D, Jiang Y, Yang X, Wei Q, Wang H. 6-Shogaol reduces progression of experimental endometriosis *in vivo* and *in vitro* via regulation of VGEF and inhibition of COX-2 and PGE2-mediated inflammatory responses. Korean J Physiol Pharmacol 2018;22:627-36.
57. Shirvani MA, Motahari-Tabari N, Alipour A. The effect of mefenamic acid and ginger on pain relief in primary dysmenorrhea: A randomized clinical trial. Arch Gynecol Obstetr 2015;291:1277-81.
58. Rabiei K, Ghobadifar A, Ebrahimzadeh MA, Saeedi M, Mobini M. Effects of ginger and *Elaeagnus angustifolia* extracts in symptomatic knee osteoarthritis. Zahedan J Med Sci 2015:29-33.
59. Minh HB, Diep NT, Duong VB, Van Hien P. Acute and sub-chronic toxicity evaluation of 6 shogaol-enriched dry ginger extract in experimental models. Tạp Chí Nghiên Cứu Y Học 2025;196:307-15.
60. Oryza Oil and Fat Chemical Co., Ltd. Red Ginger Extract: An All-Natural Anti-Arthritic and Anti-Inflammatory Agent for Food and Cosmetics Applications. Ver. 2.3. Ichinomiya, Aichi, JP: Oryza Oil and Fat Chemical Co., Ltd.; 2019.
61. Dewi PS, Ma'ruf MT. Sub-acute toxicity test of red ginger extract (*Zingiber officinale var. rubrum*) on mice (*Mus musculus*). Interdental J Kedokt Gigi. 2023;19(1):1-5
62. March Health. MARCH Health Guideline for Endometriosis. March Health; 2024. Available from: https://march.health/endometriosis-guideline [Last accessed on 2026 Jun 23].
63. Nanjundaiah SM, Annaiah HN, Dharmesh SM. Gastroprotective effect of ginger rhizome (*Zingiber officinale*) extract: Role of gallic acid and cinnamic acid in H2/K+-ATPase/*H. pylori* inhibition and antioxidative mechanism. Evid Based Complement Alternat Med 2011:249487.
64. Prajapati ND, Purohit SS, Sharma AK, Kumar T. A Handbook of Medicinal Plants. 2nd ed. Jodhpur: Agrobios India; 2010.
65. Ozgoli G, Goli M, Moattar F. Comparison of effects of ginger, mefenamic acid, and ibuprofen on pain in women with primary dysmenorrhea. J Altern Complement Med 2009;15:129-32.
66. Prasad S, Tyagi AK, Aggarwal BB. Recent developments in delivery, bioavailability, absorption and metabolism of curcumin: The golden pigment from golden spice. Cancer Res Treat 2014;46:2-18.
67. Yadav AS, Tyagi E, Kumar V, Gupta RK, Kaur S, Singh R. Assessment of ginger (*Zingiber officinale*) rhizome as potential antioxidant and antiulcer agent. Pharmacogn Res 2012;4:107-12.
68. Thomson M, Al-Qattan KK, Al-Sawan SM, Alnaqeeb MA, Khan I, Ali M. The use of ginger (*Zingiber officinale* Rosc.) as a potential anti-inflammatory and antithrombotic agent. Prostaglandins Leukot Essent Fatty Acids 2002;67:475-8.
69. Riyanto S, Winarno H, Hanafi M, Rewindinar. Sub-chronic toxicity study of red ginger (*Zingiber officinale* var. *rubrum* Theilade) rhizome extract in Sprague-Dawley rats. J Appl Pharm Sci 2017;7:109-13.

Source of Support: Nil. **Conflicts of Interest:** None declared.