

# Research Progress on the Pharmacological Effects and Molecular Mechanisms of Garcinol

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**Abstract** Garcinol is a naturally occurring polyisoprenylated benzophenone compound extracted from plants of the genus *Garcinia*. It exhibits various pharmacological effects, including anti-tumor, anti-inflammatory, neuroprotective, metabolic regulatory, and antibacterial properties. Garcinol exhibits anti-tumor effects by inducing apoptosis, inhibiting angiogenesis, arresting the cell cycle, and suppressing proteasome activity. Regarding its anti-inflammatory properties, garcinol modulates signaling pathways such as NF- $\kappa$ B, MAPK, and PI3K/AKT, while also inhibiting the production of pro-inflammatory factors. In terms of neuroprotection, garcinol helps repair nerve damage through its antioxidant and anti-inflammatory actions, as well as by regulating related enzyme activities. In addition, garcinol can regulate glucose and lipid metabolism, protect pancreatic  $\beta$  cells, and inhibit pathogenic bacteria. While garcinol exhibits multi-target properties, its direct targets, pharmacokinetics, and clinical applications require further investigation.

**Key words** Garcinol, Anti-tumor, Anti-inflammatory, Neuroprotection, Metabolic regulation, Antibacterial

## 1 Introduction

Garcinol, also referred to as camboginol, is a naturally occurring polyisoprenylated benzophenone compound predominantly found in the peels and leaves of plants belonging to the genus *Garcinia*, including *Garcinia indica* and *Garcinia cambogia*<sup>[1–2]</sup>. Its chemical structure is characterized by the presence of phenolic hydroxyl groups and  $\beta$ -diketone moieties, which bear resemblance to those found in curcumin. At room temperature, garcinol appears as a yellow crystalline powder. Notably, garcinol exhibits pronounced anti-tumor and anti-inflammatory properties<sup>[3]</sup>. In traditional medicine, garcinol and the plants from which it is derived have been extensively utilized to treat gastrointestinal disorders, inflammatory conditions, and various dermatological diseases<sup>[4]</sup>. Recent *in vitro* and *in vivo* studies have demonstrated the therapeutic potential of garcinol across multiple disease models. The underlying mechanisms of action include the inhibition of histone acetyltransferase and the modulation of several signaling pathways, such as nuclear factor- $\kappa$ B (NF- $\kappa$ B), signal transducer and activator of transcription 3 (STAT3), and phosphatidylinositol 3-kinase (PI3K)/protein kinase B (AKT)<sup>[5–7]</sup>. This article presents a systematic review of the pharmacological effects and molecular mechanisms associated with garcinol.

## 2 Anti-cancer mechanisms

Malignant tumors represent a significant threat to global public

health, with incidence and mortality rates continuously increasing worldwide. Cancers such as lung, liver, pancreatic, oral, and breast cancer pose substantial challenges in clinical treatment due to difficulties in early diagnosis, high rates of recurrence and metastasis, and the development of drug resistance. Consequently, the identification of highly effective and low-toxicity anti-tumor agents, along with elucidation of their mechanisms of action, holds considerable clinical importance. Garcinol, a natural compound exhibiting multi-targeted anti-tumor activities, exerts its effects through mechanisms including the induction of tumor cell apoptosis, inhibition of angiogenesis, cell cycle arrest, and reversal of epithelial-mesenchymal transition<sup>[8–9]</sup>.

**2.1 Mechanism of inducing apoptosis in tumor cells** Induction of apoptosis in tumor cells represents a primary anti-tumor mechanism of garcinol. Aggarwal *et al.*<sup>[10]</sup> investigated the effects of garcinol on oral squamous cell carcinoma (OSCC) cell lines. Their findings demonstrated that garcinol treatment significantly inhibited the growth and proliferation of SCC-4, SCC-9, and SCC-25 cells, while also inducing apoptosis and cell cycle arrest. Western blot analysis revealed that garcinol suppressed the expression of NF- $\kappa$ B and cyclooxygenase-2 (COX-2), concurrently reducing vascular endothelial growth factor (VEGF) levels. These results suggest that garcinol exerts its anti-tumor effects primarily through inhibition of the NF- $\kappa$ B/COX-2 signaling pathway. Cheng *et al.*<sup>[11]</sup> investigated the mechanism by which garcinol induces apoptosis in human liver cancer Hep3B cells. Their findings demonstrated that garcinol treatment resulted in the accumulation of intracellular reactive oxygen species (ROS), upregulation of GADD153 expression, and a reduction in mitochondrial membrane potential. These changes were accompanied by an increased Bax/Bcl-2 ratio, activation of Caspase-8, Caspase-9, and Caspase-3, as well as cleavage of poly (ADP-ribose) polymerase (PARP). These findings indicate that garcinol induces p53-inde-

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pendent apoptosis through both the death receptor and mitochondrial pathways.

In the context of pancreatic cancer, Parasramka *et al.*<sup>[12]</sup> demonstrated that garcinol significantly inhibited the proliferation of BxPC-3 and Panc-1 cell lines, induced apoptosis, and caused cell cycle arrest at the G<sub>0</sub>/G<sub>1</sub> phase. The underlying mechanism involves the downregulation of X-linked inhibitor of apoptosis protein (XIAP) and cellular inhibitor of apoptosis protein (cIAP) expression levels, activation of the cleavage of Caspase-3, Caspase-9, and PARP, concomitant inhibition of NF- $\kappa$ B activation, and reduction in the expression of matrix metalloproteinase-9 (MMP-9), vascular endothelial growth factor (VEGF), interleukin-8 (IL-8), and prostaglandin E2 (PGE2). Furthermore, Ahmad *et al.*<sup>[13]</sup> demonstrated that garcinol inhibited both the phosphorylation and expression levels of STAT3 in breast, prostate, and pancreatic cancer cells. Additionally, garcinol suppressed IL-6-induced STAT3 activation, leading to the downregulation of urokinase-type plasminogen activator (uPA), VEGF, and MMP-9, thereby diminishing the invasive potential of these cells. In a nude mouse xenograft model using MDA-MB-231 breast cancer cells, garcinol significantly inhibited tumor growth and reduced STAT3 expression and activation within tumor tissues.

In glioblastoma, Rizvi *et al.*<sup>[14]</sup> demonstrated that garcinol decreased the viability of rat glioma C6 cells, induced nuclear fragmentation and chromatin condensation, and caused dissipation of mitochondrial membrane potential alongside activation of Caspases in a dose-dependent manner. Further mechanistic investigations revealed that garcinol inhibited NF- $\kappa$ B activity and downregulated the expression of anti-apoptotic proteins, including Bcl-XL, Bcl-2, and Survivin, as well as the proliferation-associated protein Cyclin D1. Molecular docking analysis indicated that garcinol interacted with NF- $\kappa$ B via key amino acid residues (Pro275, Trp258, Glu225, Gly259), suggesting that its pro-apoptotic effects are mediated through inhibition of NF- $\kappa$ B activity. From a target-based perspective, Yu Ying *et al.*<sup>[15]</sup> identified that the non-ATPase regulatory subunit 11 (RPN6) of the 26S proteasome is a direct binding partner of garcinol, as demonstrated using the drug affinity responsive target stability (DARTS) assay. Garcinol inhibits the hydrolase activity of the proteasome and induces the accumulation of ubiquitin. The proteasome inhibitory effect of garcinol is dependent on RPN6. Further investigations reveal that garcinol induces the oligomerization of RPN6 and the formation of nuclear granules, ultimately leading to apoptosis in tumor cells and significantly suppressing the growth of small intestinal adenoma (Apcmin<sup>+</sup>) organoids in mice with APC heterozygous mutations.

**2.2 Inhibition of angiogenesis and anti-metastasis mechanism** Tumor angiogenesis plays a critical role in tumor growth and metastasis. Garcinol has been shown to inhibit angiogenesis and tumor metastasis through multiple pathways. Aggarwal *et al.*<sup>[10]</sup> reported that treatment with garcinol significantly reduced the se-

cretion of VEGF, indicating its anti-angiogenic properties. In the context of liver cancer, Sethi *et al.*<sup>[6]</sup> demonstrated that garcinol suppressed both constitutive and IL-6-induced activation of STAT3 in human liver cancer cells. Computer simulation indicate that garcinol binds to the SH2 domain of STAT3, thereby inhibiting its dimerization. As an acetyltransferase inhibitor, garcinol also suppresses the acetylation of STAT3, which reduces its DNA-binding capacity. Treatment with garcinol downregulates the expression levels of multiple proteins involved in proliferation, survival, and angiogenesis, and significantly inhibits tumor growth in a xenograft model of liver cancer in nude mice.

In models of esophageal cancer metastasis, Wang *et al.*<sup>[16]</sup> demonstrated that garcinol inhibited the migration and invasion of human esophageal cancer cell lines KYSE150 and KYSE450 in a dose-dependent manner. Treatment with garcinol decreased the nuclear protein levels of p300/CBP and p-Smad2/3, and suppressed the transforming growth factor- $\beta$ 1 (TGF- $\beta$ 1)-activated Smad and non-Smad signaling pathways. Furthermore, in a mouse model of lung metastasis induced by tail vein injection, intraperitoneal administration of garcinol (20 mg/kg) significantly reduced the number of lung tumor nodules and decreased the expression of Ki-67, p300, and p-Smad2/3 in lung tissue. Furthermore, Ahmad *et al.*<sup>[17]</sup> demonstrated that garcinol effectively reversed the epithelial-mesenchymal transition (EMT) in triple-negative breast cancer cell lines MDA-MB-231 and BT-549. This reversal is characterized by the upregulation of the epithelial marker E-cadherin and the downregulation of the mesenchymal markers vimentin, ZEB1, and ZEB2. Mechanistic studies have demonstrated that garcinol upregulates the expression of microRNAs belonging to the miR-200 and let-7 families and mediates its effects through the inhibition of the NF- $\kappa$ B and Wnt/ $\beta$ -catenin signaling pathways.

**2.3 Cell cycle arrest mechanism** Garcinol has the capacity to arrest tumor cells at various phases of the cell cycle by modulating the expression of proteins associated with cell cycle regulation. Yu *et al.*<sup>[18]</sup> examined the effects of garcinol on lung cancer cell lines H460 (p53 wild-type) and H1299 (p53-null). Their findings demonstrated that garcinol inhibited the proliferation of both cell lines; however, it predominantly induced apoptosis in H460 cells and caused a significant G<sub>1</sub> phase arrest in H1299 cells. Mechanistic investigations have revealed that garcinol suppresses the expression of CDK2, CDK4, Cyclin D1, and Cyclin D3 in H1299 cells, while simultaneously increasing the levels of p21Waf1/Cip1 and p27KIP1. Additionally, garcinol inhibits the activation of the ERK and p38-MAPK signaling pathways. The use of p38-MAPK inhibitors further potentiates garcinol-induced G<sub>1</sub> phase arrest and enhances p21 expression, indicating that garcinol induces G<sub>1</sub> phase arrest through a p53-independent mechanism by inhibiting p38-MAPK signaling and upregulating p21 expression.

In endometrial cancer, Zhang *et al.*<sup>[19]</sup> demonstrated that garcinol inhibited the proliferation of Ishikawa and HEC-1B cells in a dose-dependent manner, inducing cell cycle arrest at the G<sub>1</sub>

and G<sub>2</sub>/M phases, respectively. Treatment with garcinol resulted in increased expression levels of p53 and p21, a progressive reduction in the expression of CDK2, CDK4, Cyclin D1, and Cyclin B1, as well as a significant elevation in phosphorylated c-Jun N-terminal kinase (JNK) and p-c-Jun. In rhabdomyosarcoma, Rangappa<sup>[20]</sup> reported that garcinol suppressed cell proliferation, decreased cell viability, inhibited colony formation, and impaired cell migration. Additionally, garcinol induced apoptosis by causing mitotic arrest at the G<sub>2</sub>/M phase and modulating the expression of pro-apoptotic and anti-apoptotic proteins. Collectively, these findings suggest that garcinol exhibits broad-spectrum anti-proliferative effects across various tumor cell types.

In summary, garcinol demonstrates multifaceted anti-tumor effects, including the induction of tumor cell apoptosis (mitochondrial pathway, death receptor pathway, and endoplasmic reticulum stress pathway), the inhibition of angiogenesis (downregulating the VEGF/STAT3 signaling pathway) and suppressing tumor cell proliferation and migration (regulation of the cell cycle, reversal of EMT, and inhibition of proteasome activity). These findings highlight garcinol's promising potential for the development of anti-tumor therapeutics.

### 3 Anti-inflammatory mechanism

Inflammation constitutes a defensive response of the body to injury or infection, but chronic inflammation is closely associated with the onset and progression of numerous diseases, including arthritis, inflammatory bowel disease, neurodegenerative disorders, metabolic syndrome, and tumors. The NF- $\kappa$ B signaling pathway serves a central regulatory function in the inflammatory response. Garcinol has demonstrated therapeutic potential in various models of inflammatory diseases owing to its pronounced anti-inflammatory properties.

Chantree *et al.*<sup>[21]</sup> examined the anti-inflammatory effects of garcinol in LPS-activated THP-1 and RAW 264.7 macrophage cell lines. Their findings demonstrated that low concentrations of garcinol significantly suppressed both mRNA transcription and protein expression levels of pro-inflammatory cytokines, including TNF- $\alpha$ , IL-8, IL-6, and IL-1 $\beta$ , as well as pro-inflammatory mediators inducible nitric oxide synthase (iNOS) and COX-2, without compromising cell viability. Additionally, garcinol reduced the secretion of PGE2 and nitric oxide (NO). Mechanistic investigations revealed that garcinol downregulated the expression of pIKK $\alpha$ / $\beta$ , pI $\kappa$ B $\alpha$ , and pNF- $\kappa$ B, thereby inhibiting the nuclear translocation of pNF- $\kappa$ B and consequently suppressing the production of inflammatory molecules.

In the context of osteoarthritis research, Zhang *et al.*<sup>[22]</sup> demonstrated that garcinol effectively inhibited IL-1 $\beta$ -induced inflammation in chondrocytes. Treatment with garcinol resulted in decreased expression levels of pro-inflammatory cytokines, including IL-6 and TNF- $\alpha$ , reduced production of iNOS and COX-2, and suppressed the expression of ADAMTS5 and MMPs. Conse-

quently, these effects contributed to the attenuation of extracellular matrix degradation. The underlying mechanism is attributed to garcinol's inhibition of the IL-1 $\beta$ -induced NF- $\kappa$ B signaling pathway.

In the investigation of intervertebral disc degeneration, Zhang Shunli *et al.*<sup>[23]</sup> examined the effects of garcinol on IL-1 $\beta$ -induced inflammation in rat nucleus pulposus cells and the degradation of the extracellular matrix. The findings indicated that garcinol exhibited no cytotoxicity at concentrations ranging from 2.5 to 10  $\mu$ M. Furthermore, garcinol enhanced cell viability under IL-1 $\beta$  stimulation, suppressed the mRNA expression of MMP-3, MMP-9, MMP-13, ADAMTS-4, and ADAMTS-5, and concurrently upregulated the expression levels of collagen II and Aggrecan. Moreover, garcinol inhibited the mRNA transcription of TNF- $\alpha$ , IL-6, IL-8, COX-2, and iNOS. Western blot analysis and immunofluorescence staining demonstrated that garcinol counteracted the IL-1 $\beta$ -induced activation of NF- $\kappa$ B p65, prevented the reduction of I $\kappa$ B $\alpha$  protein levels, and inhibited the nuclear translocation of p65.

In the investigation of cardiomyocyte inflammation, Hung *et al.*<sup>[24]</sup> demonstrated that garcinol suppressed the production of CRP, IL-1 $\beta$ , IL-6 and TNF- $\alpha$  in nicotine-stimulated human AC16 cardiomyocytes. In addition, garcinol inhibited the phosphorylation of p38 MAPK, AKT, STAT3, NF- $\kappa$  B-P65, IKK $\alpha$ / $\beta$  and I $\kappa$ B $\alpha$  induced by nicotine, as well as the nuclear translocation of NF- $\kappa$ B p65. These anti-inflammatory effects of garcinol are mediated via the inhibition of the p38 MAPK/NF- $\kappa$ B signaling pathway, which is regulated by the  $\alpha$ 7-nicotinic acetylcholine receptor ( $\alpha$ 7-nAChR).

In a spinal cord injury model, Dai *et al.*<sup>[25]</sup> demonstrated that garcinol facilitated functional recovery in mice by modulating microglial polarization. *In vitro* studies revealed that garcinol promoted the polarization of microglia toward an anti-inflammatory phenotype, decreased the production of pro-inflammatory cytokines TNF- $\alpha$  and IL-6, suppressed M1 markers iNOS and CD86, and upregulated M2 markers Arg-1 and CD163. In a mouse model of contusive spinal cord injury, daily intraperitoneal administration of garcinol (20 mg/kg for consecutive 28 d) significantly attenuated microglial activation and neuroinflammation, mitigated secondary tissue damage, and enhanced the recovery of motor and bladder functions. Network pharmacology and mechanistic investigations confirm that these therapeutic effects are mediated through inhibition of the EGFR/PI3K/AKT signaling pathway.

In the investigation of diabetic wound healing, Li *et al.*<sup>[26]</sup> employed network pharmacology in conjunction with cellular experiments to demonstrate that garcinol mitigated dysfunction in human umbilical vein endothelial cells induced by high glucose levels and enhanced their angiogenic capacity. Garcinol was found to downregulate the secretion of inflammatory cytokines by macrophages through inhibition of the PI3K/Akt/NF- $\kappa$ B signaling pathway and to suppress NLRP3 inflammasome-mediated pyroptosis.

Furthermore, in a full-thickness skin wound model of diabetic mice, treatment with garcinol facilitated wound healing, promoted angiogenesis, and attenuated inflammation and pyroptosis.

Kalita *et al.* [27] reported that aquaporins AQP1, AQP3, and AQP4 can function as markers of inflammation. The methanol extract of *Garcinia*, along with garcinol, effectively inhibited the production of pro-inflammatory cytokines in LPS-stimulated RAW264.7 and THP-1 cells and reduced the expression of aquaporins, thereby attenuating the inflammatory response. In summary, garcinol suppresses the production and release of inflammatory mediators and facilitates the polarization toward anti-inflammatory phenotypes by modulating multiple signaling pathways, including NF- $\kappa$ B, MAPK, and PI3K/AKT, demonstrating potent anti-inflammatory effects across various models of inflammatory diseases.

## 4 Neuroprotective effects

**4.1 Mechanism of anti-Alzheimer's disease** Alzheimer's disease (AD) is a neurodegenerative disorder primarily characterized by cognitive impairment. Oxidative stress, inflammation, and apoptosis are critical factors contributing to its pathogenesis. Kandasamy *et al.* [28] examined the neuroprotective effects of garcinol against aluminum chloride-induced AD-like neurodegeneration in *Drosophila melanogaster*. *In vitro* free radical scavenging assays demonstrated that garcinol possessed significant antioxidant activity. Furthermore, computational simulation analyses revealed that garcinol effectively interacted with amyloid- $\beta$  (A $\beta$ ), acetylcholinesterase (AChE), and  $\beta$ -secretase, thereby inhibiting their activities. In a fruit fly model of AD induced by aluminum chloride, pretreatment with garcinol was found to ameliorate behavioral and cognitive impairments, modulate oxidative stress markers, reduce AChE activity, and decrease levels of pro-inflammatory cytokines. Through comprehensive computational simulations and *in vitro* analyses, Mishra *et al.* [29] demonstrated that garcinol exhibited high bioavailability, low toxicity, and a strong binding affinity (greater than 10) for key anti-AD targets. Molecular dynamics simulations further revealed that garcinol can stably bind to the 6IYC binding pocket. *In vitro* DPPH assays confirmed the antioxidant properties of garcinol, while MTT assays indicated its non-toxicity to normal brain cells.

**4.2 Mechanism of anti-parkinson's disease** Neuroinflammation plays a critical role in the degeneration of dopaminergic neurons within the substantia nigra in Parkinson's disease (PD). Chetia Phukan *et al.* [30] examined the effects of garcinol in an MPTP-induced mouse model of PD. Their findings demonstrated that garcinol ameliorated motor deficits (including motor impairment, rigidity, and abnormal posturing) in PD model mice. Furthermore, garcinol significantly prevented the loss of dopaminergic neurons in the substantia nigra and reduced the expression of glial fibrillary acidic protein (GFAP), a marker of inflammation. These results suggest that garcinol confers neuroprotection through its anti-inflammatory properties. Mazumder *et al.* [31] employed

molecular docking techniques to identify garcinol as a potent inhibitor of monoamine oxidase B (MAO-B), with inhibitory efficacy comparable to established MAO-B inhibitors. Moreover, garcinol was found to prevent levodopa-induced hyperhomocysteinemia and enhance levodopa bioavailability by inhibiting catechol-O-methyltransferase (COMT).

**4.3 Other neuroprotective mechanisms** In a neuropathic pain model, Wang *et al.* [32] demonstrated that intrathecal administration of garcinol significantly alleviated nociceptive behaviors in spinal nerve ligation (SNL) rats. This treatment inhibited the activation of spinal microglia and reduced the expression of pro-inflammatory mediators, including IL-1 $\beta$ , IL-6, iNOS/NO, and COX-2/PGE2. Moreover, garcinol decreased the levels of acetylated p65 protein and suppressed the nuclear translocation of NF- $\kappa$ B. In a zebrafish larval neurotoxicity model induced by acrylamide, Sharma *et al.* [33] reported that garcinol ameliorated acrylamide-induced cognitive and neurocranial deficits. The compound also inhibited abnormal processing of amyloid precursor proteins and excessive tau protein phosphorylation mediated by cathepsin B (CAT-B), exerting neuroprotective effects through activation of CREB and BDNF pathways. Algefare *et al.* [34] observed that garcinol mitigated sodium arsenite-induced neurobehavioral abnormalities in mice by modulating acetylcholinesterase activity, GSK-3 $\beta$ , and CREB signaling. It also attenuated oxidative damage by activating the Nrf2/HO-1 pathway, thereby enhancing redox homeostasis.

## 5 Other pharmacological effects and mechanisms

**5.1 Metabolic regulatory effects** Lee *et al.* [35] demonstrated that garcinol mitigated high-fat diet-induced obesity in mice by modulating the gut microbiota composition, inhibiting lipogenesis, and activating the AMPK signaling pathway. Similarly, Majeed *et al.* [36] reported that a 20% concentration of garcinol extract derived from *G. indica* suppressed adipogenesis in 3T3-L1 cells, alleviated endoplasmic reticulum stress, and reduced visceral fat accumulation in mice subjected to a high-fat diet. This effect is attributed to the regulation of the AMPK-endoplasmic reticulum stress axis. In a randomized, double-blind, placebo-controlled clinical trial involving a non-alcoholic steatohepatitis (NASH) model, Majeed *et al.* [37] demonstrated that administration of a combination of garcinol (50 mg), curcumin (250 mg), and piperine (5 mg) twice daily for 90 consecutive days significantly reduced serum levels of AST and ALT in patients with NASH. Additionally, this treatment improved liver stiffness values and CAP scores, decreased body weight, blood lipid levels, hsCRP, and IL-6, while upregulating adiponectin levels. Basumatary *et al.* [38] reported that garcinol administration in C57BL/6 mice fed a high-fat diet resulted in reductions in body weight, serum lipids (triglycerides and total cholesterol), and liver function enzymes (ALP and AST). Furthermore, garcinol modulated lipid metabolism by inhibiting the PCK1/ACC/SREBP1/FASn signaling path-

way. Concurrently, it enhanced the diversity of intestinal microbiota and improved the expression of intestinal tight junction proteins.

**5.2 Anti-diabetic effects** Madhuri *et al.* [39] reported that oral administration of garcinol at doses of 10 and 20 mg/kg for 30 d significantly improved several biochemical parameters in streptozotocin-induced diabetic rats, including fasting blood glucose, glycated hemoglobin, urea, ALT, AST, MDA, total cholesterol, triglycerides, LDL, and VLDL. Additionally, garcinol treatment enhanced plasma insulin levels, HOMA- $\beta$ , glycogen content, HDL, and activities of antioxidant enzymes. Mali *et al.* [40] demonstrated that garcinol administered at 25, 50, and 100 mg/kg significantly decreased blood glucose, glycated hemoglobin, and blood lipid levels in diabetic rats. Histopathological analysis further revealed that garcinol promoted the regeneration of pancreatic  $\beta$  cells.

**5.3 Antibacterial effects** Patra *et al.* [41] reported that garcinol exhibited antibacterial activity against *Staphylococcus aureus* FR1722, with a minimum inhibitory concentration (MIC) of 20  $\mu\text{g/mL}$ , and against *Listeria monocytogenes* Scott A, with an MIC of 50  $\mu\text{g/mL}$ . Besides, garcinol inhibited biofilm formation by up to 80%. Chatterjee *et al.* [42] demonstrated that garcinol exerted a bactericidal effect on *Helicobacter pylori*, achieving complete inhibition at concentrations of 31.5  $\mu\text{g/mL}$  within 6 h and 3.9  $\mu\text{g/mL}$  within 12 h. The efficacy of garcinol was comparable to or exceeded that of clarithromycin. Angela *et al.* [43] found that garcinol inhibited the ribonuclease H (RNase H) activity associated with HIV-1 reverse transcriptase, exhibiting superior activity relative to the known inhibitor RDS1759, while maintaining full efficacy against drug-resistant HIV-1 reverse transcriptase. Molecular docking studies suggest that the enolated  $\beta$ -dione moiety of garcinol participates in the chelation of metal ions.

In conclusion, garcinol exhibits multi-target and multi-pathway pharmacological properties and has demonstrated distinct advantages in areas including anti-tumor activity, anti-inflammatory effects, neuroprotection, and metabolic regulation. With ongoing research elucidating its mechanisms of action and continuous progress in formulation development, garcinol is anticipated to emerge as a lead compound among natural drugs with potential clinical applications.

## 6 Prospects

Garcinol, a natural polyisoprenylated benzophenone compound exhibiting multi-target pharmacological activities, has demonstrated broad potential applications in antitumor, anti-inflammatory, neuroprotective, metabolic regulatory contexts, *etc.* In recent years, considerable progress has been achieved in garcinol research, but several limitations and challenges remain. First, although significant progress has been made in identifying various action targets of garcinol, its direct molecular targets remain insufficiently characterized, and the relationships among targets associated with different pharmacological activities require further investigation. Sec-

ond, *in vivo* pharmacokinetic studies of garcinol are relatively limited. While pharmacokinetic parameters following different administration routes have been reported, garcinol's low oral bioavailability, rapid metabolism, and poor water solubility have constrained its clinical application. Third, clinical research on garcinol is still at an early stage. To date, only a few clinical trials have evaluated the therapeutic effects of garcinol, often in combination with curcumin and other agents, in patients with NASH. The clinical efficacy and safety of garcinol, either as a monotherapy or in combination with other drugs, require validation through large-scale, multicenter clinical trials. In short, garcinol is a natural compound with considerable potential for development and application, and further research is necessary to advance its clinical utility.

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