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Research Progress on Pharmacological Effects and Mechanisms of Curcumin

Yuxing Liu, Qingmei Liu *

Guilin Municipal Hospital of Traditional Chinese Medicine, No. 2 Lingui Road, Xiangshan District, Guilin, Guangxi, 541001, China

* Corresponding author: Qingmei Liu (Email: zhuyuanlqm0612@qq.com)

Abstract

Curcumin belongs to a class of polyphenol compounds, and its source is the rhizome of turmeric (belonging to Zingiberaceae). This substance is the main component of turmeric releasing its own pharmacological activity. Pharmacological experiments have confirmed that It has anti-tumor, antioxidant and anti-inflammatory effects, accompanied by high efficiency and low toxicity. It also has high clinical promotion value. This paper reviews the pharmacological research progress of curcumin, hoping to provide new ideas for its clinical application and further research.

Keywords

Curcumin; Pharmacological Action; Dosage Form Development.

1. Introduction

Curcumin, a lipophilic polyphenolic compound extracted from *Curcuma longa L*, has a molecular weight of 368.37 [1]. It exhibits promising development potential for diverse applications. Global research has confirmed its broad pharmacological activities, including antitumor, antifibrotic, antioxidant, anticoagulant, anti-inflammatory, lipid-modulating, and antimicrobial effects [2,3]. It is worth noting that its excellent safety and minimal adverse reactions have emphasized important clinical applications and have attracted increasing attention from the global medical community. However, clinical translation is hindered by intrinsic limitations: poor chemical stability, rapid systemic metabolism and elimination, and low oral bioavailability [4]. This review systematically summarizes recent advances in curcumin research, aiming to provide a valuable reference for further pharmacological studies and clinical applications.

2. Pharmacological Effects of Curcumin

2.1. Antitumor Effects

Studies have shown that curcumin has anti-tumor effects, and its possible mechanisms include regulating the expression of adhesion molecules, inhibiting tumor cell migration, inducing tumor cell apoptosis, inhibiting tumor angiogenesis, regulating tumor cell growth signaling pathways, and enhancing tumor cells' sensitivity to chemotherapy, etc [5-7]. A study has confirmed that curcumin mainly inhibits the formation of tumor microvessels by down-regulating the expression of vascular endothelial growth factor (VEGF), and thereby inhibits the growth of mouse H22 liver cancer xenografts [8]. It has a synergistic effect on chemotherapy drugs. When curcumin is combined with 5-fluorouracil (5-FU), its anti-tumor effect on H22 xenometastasis is significantly higher than that of using any one drug alone ($p < 0.01$), indicating that it has a synergistic effect on chemotherapy drugs. In human colon cancer cells, curcumin can significantly inhibit the proliferation of LoVo colon cancer cells and promote their

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apoptosis. This apoptotic effect is mediated by activating the caspase-3 signaling pathway, resulting in the up-regulation of the pro-apoptotic gene Bax expression and the down-regulation of the anti-apoptotic gene Bcl-2 expression [9]. It can reverse multidrug resistance. Studies have confirmed that curcumin can reverse the resistance of doxorubicin in the HepG2/ADM liver cancer cell line. Its reversal mechanism includes inhibiting the PI3K/Akt/NF-κB pathway, thereby down-regulating the expression of the multidrug resistance gene MDR1[10].

2.2. Anti-inflammatory Effects

Curcumin has relatively good anti-inflammatory activity in clinical practice and can achieve anti-inflammatory effects. After an inflammatory response occurs, it can be used for treatment [11]. The anti-inflammatory effect of curcumin is mainly related to its regulation of inflammatory signaling pathways, inhibition of pro-inflammatory factor production, and antioxidant properties. It can reduce the release of inflammatory mediators by blocking key proinflammatory pathways, and at the same time regulate the activity of immune cells and neutralize free radicals, thereby alleviating inflammatory responses. Studies have shown that curcumin exerts anti-inflammatory effects by inhibiting pro-inflammatory cytokines such as TNF-α, IL-6, IL-1β and IL-10, and also exerts antioxidant effects by inhibiting oxidase and scavenging free radicals, thereby preventing the occurrence and development of arthritis [12-13]. Curcumin exerts its core anti-inflammatory effect by inhibiting the activation of NF-κB (nuclear factor κB). NF-κB is a key transcription factor in the inflammatory response and can trigger the expression of pro-inflammatory cytokines such as TNF-α and IL-6. Curcumin prevents IκB (NF-κB inhibitor protein) from degrading and thus stops NF-κB from entering the cell nucleus to initiate the transcription of inflammatory genes. In addition, it can also inhibit the MAPK (mitogen-activated protein kinase) and JAK-STAT pathways, further reducing the transmission of inflammatory signals[14-16]. Curcumin can significantly reduce the activities of cyclooxygenase-2 (COX-2) and lipoxygenase (LOX), which are key to the synthesis of inflammatory mediators such as prostaglandins and leukotrienes. Experiments show that curcumin can reduce the expression level of COX-2 by 30% to 50%, thereby decreasing the release of prostaglandin E2 (PGE2)[17-18]. At the same time, it can also inhibit the secretion of cytokines such as TNF-α and IL-1β, blocking the inflammatory cascade reaction. The mechanisms of curcumin in treating arthritis include blocking key signaling pathways such as NLRP3, exerting anti-inflammatory and antioxidant activities, increasing integrin protein levels, promoting bone tissue repair, enhancing autophagy ability, increasing the activity of anti-apoptotic proteins, and inhibiting chondrocyte apoptosis, etc [19,20]. Curcumin has a regulatory effect on the activity of immune cells such as macrophages and neutrophils [21,22]. For instance, it can inhibit the excessive production of nitric oxide (NO) and reactive oxygen species (ROS) in macrophages and reduce the migration of macrophages to inflammatory sites. In addition, curcumin can promote the differentiation of regulatory T cells (Tregs), help restore immune balance, and prevent excessive inflammatory responses[23-24].

2.3. Antioxidant Effects

Curcumin is a plant polyphenol extracted from turmeric and is also the most important active component for turmeric to exert its pharmacological effects. The phenolic hydroxyl groups in the curcumin molecular structure can provide electrons or hydrogen atoms, directly eliminating reactive oxygen free radicals such as superoxide anions (O_2^-) and hydroxyl radicals (-OH), and blocking the oxidation chain reaction they trigger. This ability makes it a powerful electron donor, reducing the oxidative damage of free radicals to cell membranes, proteins and DNA. This component can achieve antioxidant effects, thereby eliminating free radicals in the body and protecting the liver and kidneys [25]. Curcumin can neutralize free radicals in the body, reduce oxidative stress damage, delay cellular aging, and lower the risk of chronic

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diseases. For instance, it enhances the expression of antioxidant enzymes by activating the Nrf2 pathway, protecting cells from oxidative damage [26]. Curcumin also can activate the Keap1-Nrf2 pathway within cells, promoting the entry of the nuclear transcription factor Nrf2 into the cell nucleus, and thereby up-regulating the gene expression of various antioxidant enzymes (such as superoxide dismutase SOD, glutathione peroxidase GPx). These enzymes can systematically eliminate free radicals and enhance the overall antioxidant defense capacity of cells [27]. By inhibiting the activities of pro-oxidases such as NADPH oxidase (NOX) and COX-2, curcumin reduces the source of intracellular reactive oxygen species production and blocks the triggering factors of oxidative stress from the upstream [28,29].

2.4. Anticoagulant Effects

Curcumin has a certain anticoagulant effect, but its efficacy is weaker than that of clinical anticoagulant drugs (such as warfarin), and its mechanism of action is different from that of the drugs. It mainly affects the coagulation process by inhibiting platelet aggregation and regulating the activity of coagulation factors, but the specific effect varies from person to person and cannot replace regular treatment [30]. Curcumin can inhibit platelet aggregation by reducing the production of thromboxane A2 and lowering platelet adhesion, thereby slowing down thrombosis. Curcumin can also prolong coagulation time. Animal experiments have shown that curcumin may prolong prothrombin time (PT) and activated partial thromboplastin time (APTT). It also indirectly protects vascular endothelial function and reduces the risk of abnormal coagulation by alleviating vascular inflammatory responses and oxidative stress [31]. Experimental studies have confirmed that curcumin compounds can significantly prolong plasma recalcemation time and thrombin time, indicating that they directly act on coagulation factors and inhibit the activation process of the endogenous coagulation pathway. In animal models, this effect effectively reduces the risk of thrombosis, and is more effective than traditional anticoagulant drugs such as aspirin, while avoiding obvious side effects[32]. Therefore, curcumin becomes a potential natural therapy for preventing thrombotic events related to cardiovascular diseases.

2.5. Antifibrotic Effects

Curcumin has anti-fibrotic effects, mainly achieved by inhibiting inflammatory responses, antioxidative stress and regulating cellular signaling pathways. Curcumin can inhibit the expression of inflammatory mediators such as COX-2, PGE2 and TNF-α, and reduce the recruitment of inflammatory cells and collagen deposition. For instance, in a pulmonary fibrosis model, it can reduce the expression levels of TNF-α and IL-6 [33]. Curcumin can also block the expression of inflammatory factor genes by inhibiting the activity of NF-κB and AP-1 transcription factors. In the study of renal fibrosis, curcumin reduces collagen production by inhibiting the NF-κB pathway [34].

3. Conclusion

Curcumin has garnered significant attention for its broad-spectrum pharmacological activities—including antitumor, anti-inflammatory, antioxidant, anti-fibrotic and anticoagulant effects. Curcumin is a natural polyphenolic compound, derived from the curcumin in the rhizome of turmeric. Curcumin has been widely applied in fields such as medicine, cosmetics and food. In recent years, research on curcumin has gradually increased, and the research results show that curcumin has a very broad application prospect. Therefore, conducting a feasibility study on curcumin is of great significance application. This paper reviews the pharmacological research progress of curcumin, hoping to provide new ideas for its clinical application and further research.

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