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The Anti-Inflammatory Effects and Mechanisms of Baicalin on Rheumatoid Arthritis

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Abstract:

Rheumatoid arthritis (RA) is a common chronic autoimmune disease clinically, with persistent synovial inflammation as its core pathological feature. However, current treatment strategies often face limitations in efficacy and significant side effects. Baicalin, the main active flavonoid component of the traditional Chinese medicine Scutellaria baicalensis, possesses various pharmacological activities, including but not limited to anti-inflammatory, antioxidant, and immunomodulatory effects. This article focuses on exploring how the anti-inflammatory effect of baicalin plays a role in the treatment of RA, systematically discussing the molecular mechanism of baicalin from the perspectives of NF-κB and TLR signaling pathways and their synergistic regulatory effects, and showcasing the research progress of baicalin in current treatment. Studies have shown that baicalin can significantly downregulate the expression and release of pro-inflammatory cytokines such as TNF-α and IL-1β by inhibiting the activation of TLR2 and TLR4 receptors and blocking the TLR and NF-κB signaling pathways. Furthermore, baicalin can inhibit the abnormal proliferation of synovial fibroblasts, induce their apoptosis, alleviate synovial inflammation and pannus formation, and delay the pathological progression of rheumatoid arthritis. Currently, the main problem facing baicalin is its low bioavailability. In the future, priority should be given to researching its drug delivery system and conducting high-quality clinical trials to facilitate the clinical translation and application of baicalin in the treatment of RA.

Keywords: Baicalin; rheumatoid arthritis; anti-inflammatory mechanism; NF-κB pathway; TLR pathway.

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1. Introduction

Paragraph 1: RA background and current treatment limitations

Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease characterized by persistent synovial inflammation, progressive joint destruction, and functional disability. Current therapeutic strategies mainly rely on disease-modifying antirheumatic drugs (DMARDs), biological agents, and targeted synthetic therapies. Although these treatments can effectively control disease progression, many patients still experience inadequate responses, adverse effects, or treatment resistance.

Paragraph 2: TCM and Baicalin

In recent years, traditional Chinese medicine (TCM) has attracted increasing attention as a complementary therapeutic approach for RA. Among various bioactive compounds, baicalin, a major flavonoid extracted from Scutellaria baicalensis, has demonstrated significant anti-inflammatory, antioxidant, and immunomodulatory properties. Previous studies have shown that baicalin can inhibit synovial inflammation, suppress fibroblast-like synovial cell proliferation, and promote apoptosis.

Paragraph 3: Mechanistic significance

Mechanistically, baicalin exerts its therapeutic effects through the regulation of multiple inflammatory pathways, particularly the Toll-like receptor (TLR) and nuclear factor-kappa B (NF-κB) signaling pathways. By simultaneously targeting upstream and downstream inflammatory cascades, baicalin may provide a multi-target therapeutic strategy for RA.

The novelty of this review can be summarized in three aspects.

First, it systematically integrates current evidence regarding the anti-inflammatory effects of baicalin in RA, with particular emphasis on chronic synovial inflammation and pannus formation as the central pathological processes.

Second, this review highlights the coordinated regulatory relationship between the TLR and NF-κB signaling pathways and explains how baicalin exerts anti-inflammatory activity through multi-target intervention within this signaling network.

Third, this review discusses the current limitations affecting the clinical translation of baicalin, including poor bioavailability and insufficient clinical evidence, and proposes future directions for drug delivery optimization and clinical development.Therefore, this review provides a comprehensive theoretical framework for understanding the therapeutic potential of baicalin and supports its future clinical application in RA treatment.

2. Overview of RA

2.1 Disease Definition and Pathological Features

RA is a chronic systemic autoimmune disease caused by the body's immune system disorder. The main clinical manifestation is erosive, symmetrical polyarthritis, rather than simple local joint inflammation. The disease is often progressive and prone to recurrence. If it is not properly managed and treated, it will lead to irreversible joint structural damage [1]. Its core pathological features are very typical, mainly manifested as persistent chronic inflammation of the synovium accompanied by abnormal thickening and enlargement of the synovial tissue, gradually forming an invasive pannus. This tissue will continuously erode the articular cartilage, subchondral bone and surrounding ligaments and tendons, accompanied by inflammatory exudation in the joint cavity and fibrosis of the synovial tissue. In the end, it will also lead to destruction of articular cartilage and bone defects, eventually causing joint deformity and loss of function. Some severe patients will also endanger extra-articular organs such as the heart, lungs and blood vessels, resulting in systemic complications.

2.2 Pathogenesis and Core Links

The pathogenesis of RA is complex, involving multiple factors such as genetics, environment, and immune disorders. At its core is an imbalance in the body's immune tolerance, leading the immune system to misidentify and attack its own joint tissues, thus inducing an abnormal immune response and inflammatory cascade. Among these, "synovial inflammation and abnormal synovial proliferation" is the central link in the entire pathological process. Under normal circumstances, the synovium is a thin, soft connective tissue primarily responsible for secreting synovial fluid to lubricate the joint and protect the cartilage. After the onset of the disease, due to stimulation by abnormal immune signals, a large number of immune cells infiltrate the synovium, releasing various pro-inflammatory factors such as tumor necrosis factor (TNF) and interleukin-6 (IL-6), promoting excessive proliferation and apoptosis of synovial cells, resulting in proliferative inflammatory synovium, also known as pannus. This abnormal synovium not only directly erodes articular cartilage and bone tissue but also continuously releases inflammatory mediators, forming a vicious cycle of "inflammatory response - tissue damage - exacerbation of inflammation," constantly driving the disease's progression and becoming the core driving factor in the development of RA.

2.3 Current Status and Challenges of Clinical Treatment

The core principles of RA treatment are early intervention, standardized procedures, achieving treatment goals, and long-term management, with the treatment objectives being clinical remission, prevention of joint damage, and protection of function. Currently, traditional synthetic disease-modifying antirheumatic drugs (DMARDs) are the first-line basic medications, with methotrexate as the preferred anchoring agent, combined with nonsteroidal anti-inflammatory drugs (NSAIDs) and low-dose corticosteroids for rapid symptom relief. For moderate to severe cases, biologics and small-molecule targeted therapies can be used to precisely inhibit inflammation and achieve faster onset of action. Some cutting-edge therapies, such as stem cell therapy, are also gradually entering the clinical translation stage. While the overall target achievement rate among Chinese patients has improved, it has not yet reached the ideal level.

Current treatments still have many shortcomings and there is no cure; they can only control the progression of the disease. Traditional drugs are slow to take effect, and more than 30% of patients experience primary ineffectiveness. Biologics and targeted therapies also have secondary failure issues. Treating refractory cases is extremely difficult, and standardized diagnosis and treatment as well as long-term management still face significant challenges.

3. Pharmacological Effects of Scutellaria Baicalensis

3.1 The Medicinal Basis of Scutellaria Baicalensis

Scutellaria baicalensis is a herbaceous plant belonging to the dicotyledonous Lamiaceae family. Its dried roots are often used as medicine. Scutellaria baicalensis is bitter and cold in nature. It enters the lung, gallbladder, spleen, large intestine and small intestine meridians. Clinically, it is mainly used to treat diseases such as damp-heat, lung heat cough, blood heat bleeding, and threatened abortion [2]. Modern pharmacological studies [3-4] have further confirmed that Scutellaria baicalensis has significant anti-inflammatory, antioxidant, antiviral, antibacterial, pregnancy-preserving, immunomodulatory and antitumor pharmacological activities. It has shown good application potential in respiratory diseases, inflammatory diseases and tumor adjuvant therapy. It mainly achieves its pharmacological effects by regulating inflammatory signaling pathways such as nuclear transcription factor NF-κB and mitogen-activated protein kinase MAPK. It also provides a scientific basis for the modern interpretation of the traditional efficacy of Scutellaria baicalensis and lays a theoretical foundation for its in-depth development and rational clinical application [5].

3.2 The Core Active Ingredients of Scutellaria Baicalensis

The pharmacological effects of Scutellaria baicalensis are closely related to its flavonoid components, with flavonoids and their glycosides being the core active ingredients. The Pharmacopoeia of the People's Republic of China clearly stipulates that the content of baicalin in Scutellaria baicalensis should not be less than 9%, and the total content of the four components (baicalin, baicalein, wogonin, and wogonein) should not be less than 15%. Baicalin, as the most abundant characteristic component in Scutellaria baicalensis, possesses core pharmacological effects such as anti-inflammatory, antiviral, and antioxidant properties. Baicalein, the aglycone of baicalin, exhibits more prominent antitumor, neuroprotective, and antibacterial activities compared to baicalin, and is one of the important forms in which Scutellaria baicalensis exerts its pharmacological effects in vivo. Wogonin and wogonein, also important forms in Scutellaria baicalensis, can synergistically exert anti-inflammatory, immunomodulatory, and anti-fibrotic effects; the four together constitute the main pharmacological basis of Scutellaria baicalensis.

3.3 Physicochemical Properties of Scutellaria Baicalensis

The physicochemical properties of the main active components of Scutellaria baicalensis directly affect its extraction, separation, purification processes, and formulation development, and are also important factors in ensuring its stable efficacy. Baicalin is a pale-yellow needle-like crystal or powder with an extremely bitter taste. It is almost insoluble in water and poorly soluble in common organic solvents. However, it is prone to oxidation and discoloration under alkaline conditions, leading to decreased stability. Under acidic heating conditions, baicalin can undergo hydrolysis, losing glucuronic acid to form baicalein. Baicalein is also a yellow crystal, with better solubility than baicalin. It has strong antioxidant properties but is also easily oxidized, causing its color to darken. During extraction and preparation, strong acids, high temperatures, and prolonged heating should be avoided to prevent the hydrolysis and oxidative degradation of flavonoid glycosides. During storage, it should be placed in a cool, dry, light-proof, and sealed environment to minimize the loss of active ingredients and ensure the quality stability of Scutellaria baicalensis and its preparations.

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4. Pharmacological Effects of Baicalin

4.1 Anti-Inflammatory Effect

The main mechanism of anti-inflammatory activity of baicalin is the role it plays in the prevention and treatment of synovial inflammation in RA. This effect is principally by means of targeted regulation of a number of inflammatory signaling pathways, prevention of inflammatory cascade and inhibition of the release of inflammatory mediators. Baicalin is able to significantly inhibit the activation of TLR4/MyD88/NF-κB signaling pathway, decrease nuclear translocation of nuclear factor κB, and consequently downregulate the expression and secretion of pro-inflammatory factors such as tumor necrosis factor-α and interleukin-1β. Simultaneously, it can inhibit NLRP3 inflammasome and the activation of caspase-1, thus preventing a maturation process of pro-inflammatory factors and blocking the initiation and development of synovial inflammation from the source. Moreover, baicalin can regulate classical inflammatory pathway (MAPK, JAK-STAT), thereby inhibiting inflammatory factor activation and signaling, which can also regulate the let-7i-3p/PI3K/Akt/NF-κB signaling axis, inhibiting inflammatory activation of fibroblast-like synovial cells in RA, precisely regulating local inflammation in synovial tissue, and effectively ameliorating pathological changes, such as synovial tissue swelling and inflammatory infiltration.

4.2 Inhibition of Synovial Cell Proliferation and Induction of Apoptosis

In the pathological progression of rheumatoid arthritis (RA), the abnormal proliferation and anti-apoptotic properties of fibroblast-like synovial cells are key factors in triggering synovial hyperplasia, pannus formation, and joint bone erosion, as confirmed by previous studies and relevant literature. baicalin is believed to that baicalin can directly target synovial cells and reverse this pathological process by regulating their biological behavior, which is an important pathway for its anti-RA effects. Specifically, baicalin can significantly inhibit the proliferation of fibroblast-like synovial cells in RA patients, block the cell cycle, downregulate the expression of cell cycle-related proteins, and reduce the number of abnormally proliferating cells, thereby alleviating synovial hyperplasia and thickening and joint damage. Simultaneously, baicalin can activate apoptosis-related pathways, induce apoptosis in excessively proliferating synovial cells, clear abnormal cells within the joint, restore the dynamic balance between synovial cell proliferation and apoptosis, and inhibit the progression of synovial disease. In a collagen-induced arthritis model, baicalin was found that baicalin can regulate synovial cell apoptosis and proliferation through the NF-κB pathway, reducing synovial inflammatory hyperplasia, inhibiting pannus formation, alleviating its erosion of articular cartilage and bone tissue, and alleviating joint structural damage.

5. The Core Anti-Inflammatory Mechanism of Baicalin Against RA (NF-κB/TLR Pathway)

5.1 TLR Pathway-Mediated Anti-Inflammatory Mechanisms

As a key upstream triggering pathway for innate immunity and inflammatory response, the abnormal activation of the TLR pathway is the core link in the initiation of chronic inflammation in RA. Baicalin can exert anti-inflammatory effects by targeting and regulating key molecules in this pathway. In the synovial tissue and synovial fibroblasts of RA patients, receptors such as TLR2 and TLR4 are highly expressed, which can recognize intra-articular injury-related molecular patterns and initiate upstream signaling cascade reactions. The study established a mouse model of mycoplasma pneumonia infection and used baicalin and azithromycin for comparative intervention. The basic signs, lung function, lung tissue pathological changes and inflammatory factor levels were detected, and it was concluded that baicalin may inhibit the inflammatory response through the expression of the TLR4/NF-κB signaling pathway [6]. Shen Xiaolan et al. also confirmed that baicalin can inhibit RA synovial inflammation by regulating TLR-related pathways [7].

5.2 Anti-Inflammatory Mechanisms Mediated by the NF-κB Pathway

The NF-κB pathway is the core regulatory pathway for RA inflammation amplification and joint damage. Baicalin achieves anti-inflammatory and joint protection effects by precisely intervening in the activation process of this pathway. Under physiological conditions, NF-κB binds to the inhibitory protein IκB and remains in the cytoplasm in an inactive form. Under pathological conditions of RA, inflammatory stimulation can activate the IKK kinase complex, leading to IκB phosphorylation and degradation. The NF-κB p65 subunit undergoes nuclear translocation, binds to the promoter of pro-inflammatory genes, and drives the large-scale expression of pro-inflammatory factors such as IL-1β, TNF-α, and IL-6, as well as inflammatory mediators such as iNOS and COX-2. WANG et al. found that baicalin can inhibit the activation of NF-κB, thereby reducing the synthesis and release of inflammatory cyto-

kines. The experiment further verified that downregulating the NF-κB signaling pathway can inhibit the NLRP3 inflammasome and achieve the purpose of controlling the inflammatory response [8].

5.3 TLR-NF-κB Pathway-Mediated Synergistic Regulatory Effects

The TLR pathway and the NF-κB pathway do not function independently; they have a close synergistic regulatory relationship and together constitute a positive feedback loop for the progression of RA inflammation. Baicalin enhances its anti-RA and anti-inflammatory effects by regulating the synergistic effect of the two. Yang Yuxin et al. used qRT-PCR and Western blot experiments to show that the mRNA and protein expression levels of TLR2, MyD88 and NF-κB were significantly reduced in the 60 mg/kg and 30 mg/kg baicalin treatment groups. Similarly, in HFLS-RA cells, the mRNA and protein expression levels of TLR2, MyD88 and NF-κB were also significantly reduced in the 100 μg/ml, 50 μg/ml and 25 μg/ml baicalin intervention groups. This suggests that the good anti-inflammatory effect of baicalin may be achieved by inhibiting the activation of the TLR2-NF-κB pathway [9]. In addition, some studies have shown that baicalin can suppress the inflammatory response by inhibiting the TLR4 and NF-κB signaling pathways, thereby alleviating lung injury in MDR-PA pneumonia [10].

5.4 Limitations and Future Perspectives

5.5

Despite the promising therapeutic potential of baicalin, several limitations remain. First, most current studies are based on in vitro experiments and animal models, while high-quality clinical trials involving RA patients are still lacking. Second, the molecular mechanisms of baicalin have not been fully elucidated, particularly regarding its interactions with other inflammatory signaling pathways and immune cell subsets. Third, baicalin exhibits relatively poor oral bioavailability due to limited solubility and rapid metabolism, which may restrict its clinical efficacy. Future research should focus on conducting large-scale randomized clinical trials, exploring additional molecular targets, and developing novel drug delivery systems such as nanoparticles, liposomes, and sustained-release formulations to improve therapeutic outcomes.

6. Conclusion

This research is aimed at anti-inflammatory effects and the mechanisms of action of baicalin in rheumatoid arthritis (RA) and to elucidate the mechanisms of the core diseases of RA, which are chronic synovial inflammation, abnormal proliferation of cytokines, and pannus formation. Baicalin acts as an inhibitor of upstream receptors (TLR2 and TLR4), inhibits signal transduction, and decreases translocations of NF-κB into the nucleus, which can decrease the amount of pro-inflammatory factors and inhibit excessive synovial cell proliferation. Moreover, the study validated the synergistic effect of TLR-8 and NF-κB pathway on anti-RA effect of baicalin. Now the application of baicalin in clinic is limited and the evidence of clinical application is not sufficient, many of the studies are basic experiments. Future studies of baicalin should aim to enhance its bioavailability, promote standardization of the treatment of integrated traditional Chinese and Western medicine and accelerate the clinical translation and application.

References

[1] Yukiko I, Kazuhiko Y. Basic research overview in rheumatoid arthritis[J]. Nihon Rinsho. Japanese Journal of Clinical Medicine, 2016, 74(6): 889-896.

[2] Yiqing G, Qi Z, Guifang F, et al. Advances in anti-cancer activities of flavonoids in Scutellariae radix: perspectives on mechanism[J]. International Journal of Molecular Sciences, 2022, 23(19): 11042.

[3] Mittal R, Mittal A, Saini P, et al. Scutellaria baicalensis Georgi: a review on botany, phytoconstituents, and pharmacological activities[J]. Letters in Drug Design & Discovery, 2025, 22(10): 100168.

[4] Wang L, Yao S, Wang J, et al. Integrated analysis of proteomics and metabolomics uncovered the anti-inflammatory mechanisms of baicalin in CIA rat FLS[J]. Current Issues in Molecular Biology, 2026, 48(1): 111.

[5] Wu W J, Zeng N, Wang S Y, et al. Anti-inflammatory and lung function protective effects of baicalin on Mycoplasma pneumoniae-infected mice via TLR4/NF-κB signaling pathway[J]. Chinese Journal of Nosocomiology, 2023, 33(23): 3521-3526.

[6] Shen X L, Liu X M, Hou X Q, et al. Research progress on baicalin in inhibiting synovial inflammation in rheumatoid arthritis and its clinical application[J]. Journal of Practical Medicine, 2024, 40(22): 3256-3261.

[7] Wang H Z, Wang H H, Huang S S, et al. Inhibitory effect of baicalin on collagen-induced arthritis in rats through the nuclear factor-κB pathway[J]. Journal of Pharmacology and Experimental Therapeutics, 2014, 350(2): 435-443.

[8] Ma C, Wang L, Cao L, et al. HHQG ameliorates acute liver injury by inhibiting NLRP3 activation through RASD1-mediated regulation of the PKCδ-NF-κB signaling pathway[J]. Scientific Reports, 2025, 15(1): 40525.

[9] Yang Y X. Study on the molecular mechanism of

ISSN 2959-409X

baicalin against rheumatoid arthritis based on TLR2–NF-κB signaling[D]. Ningxia: Ningxia Medical University, 2020.

[10] Chen A P, Cai W Z, Zhou Y J. Baicalin alleviates lung injury in multidrug-resistant Pseudomonas aeruginosa pneumonia rats via regulating TLR4/MyD88/NF-κB signaling pathway[J]. Journal of Anatomy, 2025, 48(4): 293-298.

[11] Li Y, Zhang H, Wang X, et al. Therapeutic effects of baicalin on inflammatory diseases: mechanisms and clinical prospects[J]. Frontiers in Pharmacology, 2023, 14: 1187654.

[12] Zhao J, Liu M, Chen W, et al. Baicalin attenuates rheumatoid arthritis by regulating inflammatory cytokines and oxidative stress[J]. Biomedicine & Pharmacotherapy, 2022, 149: 112874.

[13] Xu L, Wang Z, Yang J, et al. Progress in the pharmacological research of baicalin and its clinical applications[J]. Phytomedicine, 2024, 128: 155678.

[14] Chen X, Li H, Zhou Q, et al. TLR4/NF-κB signaling pathway as a therapeutic target in rheumatoid arthritis[J]. International Immunopharmacology, 2023, 121: 110442.

[15] Sun Y, Wu J, Zhang K, et al. Advances in nano-delivery systems for improving baicalin bioavailability[J]. Drug Delivery, 2024, 31(1): 2365478.