FROM PLANTS TO MEDICINE: A COMPREHENSIVE REVIEW OF WOGONIN'S BIOLOGICAL SOURCES, CHEMICAL PROPERTIES, AND PHARMACOLOGICAL EFFECTS

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Abstract

The polyphenolic substances found in fruits, vegetables, and certain medicinal plants are called flavonoids. The bioactive chemicals found in the root of Scutellaria baicalensis, which include Wogonin, Scutellarein, Baicalein, and Baicalin, have long been utilised in traditional Chinese herbal therapy. Wogonin has been shown to have a wide range of biological effects in both laboratory and human settings, including anti-cancer, anti-inflammatory, and anti-bacterial and anti-viral effects. In this article, we will discuss the therapeutic effects of Wogonin, including its antiviral, anti-inflammatory, neuroprotective, anxiolytic, and anticonvulsant properties. Also, the molecular mechanism(s) by which Wogonin modulates cellular signal pathways and immunological responses are reviewed, and the beneficial qualities of Wogonin in a variety of therapeutic contexts are emphasised.

Keywords: wogonin; anti-inflammatory; antioxidant; neuroprotective

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1. Introduction

Wogonin is a naturally occurring flavone compound found in a variety of medicinal plants, including the traditional Chinese herb Scutellaria baicalensis. It has been acknowledged for its therapeutic properties and extensively researched for its pharmacological effects. Wogonin has been shown in studies to have a variety of biological activities, including anti-inflammatory, antioxidant anticancer, and neuroprotective properties. It has been discovered to have a powerful inhibitory effect on cancer cells, including breast cancer, lung cancer, and colon cancer, by inducing apoptosis and inhibiting cell proliferation [1, 2]. Wogonin has been found to have anti-inflammatory properties in addition to anticancer properties, making it a promising candidate for the treatment of inflammatory diseases such as rheumatoid arthritis and inflammatory bowel disease. It has been shown to inhibit the production of pro-inflammatory cytokines and enzymes, both of which are important in the progression of inflammation. Wogonin has also been shown to have neuroprotective properties, protecting neurons from oxidative stress and inflammation-induced damage [3, 4]. It has been shown in animal models of Alzheimer's disease to improve cognitive function and to have a potential therapeutic effect on other neurodegenerative diseases. Wogonin's pharmacological properties make it a promising candidate for the development of new therapeutic agents for a variety of diseases [5, 6]. More research is needed to fully understand the mechanisms of action of this natural compound and its potential clinical applications.

2. Chemistry

Wogonin (5,7-dihydroxy-8-methoxyflavone) is a flavone with the molecular formula C16H12O5 and the molecular weight 284.26 g/mol. It has a yellow crystalline appearance and is soluble in organic solvents such as ethanol and dimethyl sulfoxide but not in water. Wogonin's chemical structure consists of two benzene rings (A and B rings) linked by a heterocyclic pyrone ring (C ring) and a methoxy group at position 8. At positions 5 and 7, the A ring has hydroxyl groups, whereas the B ring is unsubstituted. Wogonin's antioxidant properties are due to its flavone backbone, which allows the compound to scavenge free radicals and prevent oxidative damage to cells [7, 8]. The hydroxyl groups on the A ring are important for its ability to inhibit inflammation by modulating the activity of enzymes involved in the production of pro-inflammatory mediators, such as cyclooxygenase and lipoxygenase. Wogonin's methoxy group at position 8 has been shown to improve its bioavailability and pharmacological effects by increasing its solubility and stability in biological fluids. This group also contributes to its anticancer activity by improving its ability to induce apoptosis and inhibit cancer cell proliferation. Overall, wogonin's chemical structure is important for its pharmacological properties and potential therapeutic applications. Understanding the structure-activity relationships of wogonin and its derivatives is critical for developing new drugs based on this naturally occurring compound [9, 10] (Figure 1).

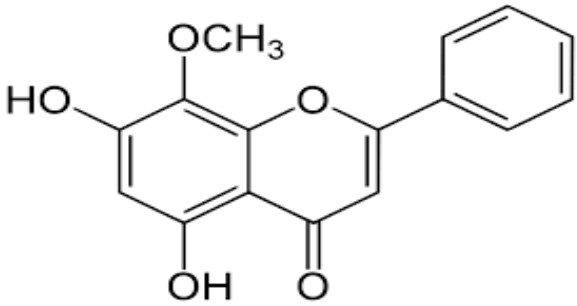

Figure 1: Chemical structure of wogonin

3. Pharmacokinetic studies of wogonin

Wogonin has been the subject of several pharmaco kinetic studies to investigate its absorption, distribution, metabolism, and excretion in the body. These studies' key findings are as follows: Wogonin is poorly soluble in water and has a low bioavailability when taken orally. It can, however, be absorbed through the gastrointestinal tract and quickly metabolised by the liver. Co-administration of wogonin with other compounds, such as piperine, has been shown in studies to improve absorption. Wogonin has a low volume of distribution, indicating that it is mostly found in blood and other fluids rather than tissues [11, 12]. It has been shown to cross the blood-brain barrier and accumulate in the brain, implying that it could be used to treat neurological disorders. Wogonin is metabolised extensively in the liver via phase I and phase II metabolic pathways. Hydroxylation, methylation, glucuronidation, and sulfation are the primary metabolic pathways. Wogonin's main metabolites are 7-O-glucuronide and 7-O-sulfate. Wogonin and its metabolites are primarily excreted in the faeces and urine. Wogonin's elimination half-life in humans has been reported to be 1-2 hours. Wogonin's pharmacokinetic properties indicate that it has low oral bioavailability and rapid metabolism, which may limit its therapeutic applications [13, 14]. However, strategies such as co-administration with absorption enhancers or prodrugs to improve its absorption and stability in

the body may improve its efficacy and pharmacoki netic profile.

4. Toxicity studies of Wogonin

Wogonin toxicity has been studied in both in vitro and in vivo models to determine its safety profile. These studies' key findings are as follows: Wogonin has been shown to have low cytotoxicity in a variety of cell lines, including normal human lung fibroblasts and liver cells, in vitro. At higher concentrations, however, it has been shown to cause cell death and DNA damage in cancer cells. Wogonin has been found to have low acute toxicity in animal studies, with no observed adverse effects at doses up to 2000 mg/kg [15, 16]. However, it has been shown to cause liver and kidney damage at higher doses. Wogonin was administered orally at doses of 50, 100, and 200 mg/kg/day in a 28-day repeated-dose toxicity study in rats. Body weight, food consumption, and haematological and biochemical parameters all showed no significant changes. Major organ histological examination revealed no evidence of toxicity. Wogonin has been shown to have no genotoxic effects in a number of in vitro and in vivo tests, including the Ames test, micronucleus assay, and comet assay [17, 18]. Wogonin has been shown in animal studies to have no significant effects on reproductive and developmental parameters at doses up to 300 mg/kg/day. Overall, the available toxicity studies indicate that wogonin is relatively safe for human consumption at therapeutic doses. More research is needed, however, to fully understand its long-term effects and potential interactions with other drugs [19].

5. Pharmacological effects of Wogonin

5.1 Neuroprotective effect of Wogonin

Wogonin, a flavonoid compound extracted from the roots of Scutellaria baicalensis, has been shown in numerous in vitro and in vivo studies to have neuroprotective properties. Here is a review of the literature on wogonin's neuroprotective role: Neuro inflammation plays an important role in the pathogenesis of many neurodegenerative diseases. Wogonin has been shown in vitro and in vivo to inhibit the production of pro-inflammatory cytokines and chemokines, reduce the activation of microglia and astrocytes, and suppress the expression of inducible nitric oxide synthase and cyclooxygenase-2. Oxidative stress has been linked to the onset of neurodegenerative diseases [20, 21]. Wogonin has been shown to have powerful antioxidant properties by scavenging free radicals, lowering lipid peroxidation, and increasing the activity of antioxidant enzymes like superoxide dismutase and catalase. Wogonin has been shown to inhibit neuronal apoptosis by increasing the expression of anti-apoptotic proteins like Bcl-2 and decreasing the expression of pro-apoptotic proteins like Bax and caspase-3. Excitotoxicity is a pathological process that contributes to the development of numerous neurodegenerative diseases. Wogonin has been shown to reduce glutamate and N-methyl-D-aspartate (NMDA) excitotoxicity in cultured neurons and in vivo. Wogonin has been shown to promote neuronal survival and differentiation via the extracellular signal-regulated kinase (ERK) and phosphoinositide 3-kinase (PI3K)/Akt signalling pathways [22, 23]. Wogonin's neuroprotective properties are due to its anti-inflammatory, antioxidant, anti-apoptotic, anti-excitotoxic, and neurotrophic properties. These findings suggest that wogonin may have therapeutic potential in the treatment of neurodegenerative diseases such as Alzheimer's, Parkinson's, and stroke. However, more research is required to fully comprehend its mechanisms of action and potential clinical applications [24, 25].

5.2 Anticonvulsant and anxiolytic effect of wogonin

Anxiety disorders are a common psychiatric condition that can have a significant negative impact on a person's quality of life. Several studies have shown that wogonin has anxiolytic effects in animal anxiety models. For example, researchers discovered that wogonin had anxiolytic effects in mice subjected to a maze test in a study published in the journal Progress in Neuro-Psycho pharmacology & Biological Psychiatry. The researchers discovered that wogonin reduced anxiety-like behaviours in mice by increasing time spent in the maze's open arms [26, 27]. Wogonin has also been shown in animal models of epilepsy to have anticonvulsant properties. Wogonin had anticonvul sant effects in rats exposed to a seizure-inducing agent, according to a study published in the journal Epilepsy Research. Wogonin was found to reduce the number and duration of seizures in rats, according to the researchers. While these findings are encouraging, more research is required to determine the mechanisms by which wogonin exerts its anxiolytic and anticonvulsant effects, as well as to assess its safety and efficacy in humans. As a result, before using wogonin or any other herbal supplement to treat anxiety or epilepsy, it is critical to consult a healthcare professional [28-30].

5.3 Anti inflammatory effect of Wogonin

Wogonin, a flavonoid compound found in the root of the Scutellaria baicalensis plant, has been shown

to inhibit inflammation via multiple signalling pathways. The nuclear factor-kappa B (NF-B) pathway is one important signalling pathway involved in wogonin's anti-inflammatory effects. NF-B is a transcription factor that regulates the expression of genes involved in inflammation. NF-B translocates from the cytoplasm to the nucleus after activation, where it binds to DNA and promotes the expression of pro-inflammatory cytokines and chemokines [31, 32]. Wogonin has been shown to inhibit NF-B activation by preventing the phosphorylation and degradation of IB, an NF-B inhibitor, resulting in the suppression of pro-inflammatory gene expression. The mitogen-activated protein kinase (MAPK) pathway is another signalling pathway involved in wogonin's anti-inflammatory effects. MAPKs are a type of serine/threonine kinase that regulates cellular responses to inflammation. Wogonin has been shown to inhibit the phosphorylation of MAPKs such as p38, JNK, and ERK, all of which play a role in the activation of pro-inflammatory signalling pathways [33,34]. Furthermore, wogonin has been shown to activate the AMP-activated protein kinase (AMPK) pathway, which is important in the regulation of cellular energy homeostasis. AMPK activation has been shown to inhibit NF-B activation and the production of pro-inflammatory cytokines. Wogonin's anti-inflam matory effects are mediated by the inhibition of the NF-B and MAPK signalling pathways, as well as the activation of the AMPK pathway, which results in the inhibition of pro-inflammatory gene expres sion and the reduction of inflammation [35, 36].

5.4 Antioxidant effect of Wogonin

Wogonin, a flavonoid compound found in the root of the Scutellaria baicalensis plant, has been shown to activate multiple signalling pathways. The nuclear factor erythroid 2-related factor 2 (Nrf2) pathway is one important signalling pathway involved in wogonin's antioxidant effect. Nrf2 is a transcription factor that controls the expression of genes involved in antioxidant defence [37-41]. When activated, Nrf2 moves from the cytoplasm to the nucleus, where it binds to antioxidant response elements (AREs) and promotes the expression of antioxidant enzymes like superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx). Wogonin has been shown to activate the Nrf2 pathway by promoting Nrf2 nuclear translocation and the expression of ARE-driven antioxidant genes, resulting in increased antioxidant defences (Figure 2). The phosphoinositide 3-kinase (PI3K)/Akt pathway is another signalling pathway involved in wogonin's antioxidant effect [42-45]. Activation of the PI3K/Akt pathway has been shown to increase the expression and activity of antioxidant enzymes while decreasing the production of reactive oxygen species (ROS). Wogonin has been shown to activate the PI3K/Akt pathway, which leads to an increase in antioxidant enzymes and a decrease in ROS production. Furthermore, wogonin has been shown to inhibit ROS production as well as the activation of the nuclear factor-kappa B (NF-B) pathway, which is involved in the regulation of inflammation and oxidative stress [46-49]. Overall, wogonin's antioxidant effects involve the activation of the Nrf2 and PI3K/Akt signalling pathways, as well as the inhibition of ROS production and NF-B activation, resulting in an increase in antioxidant defences and a reduction in oxidative stress [50, 51].

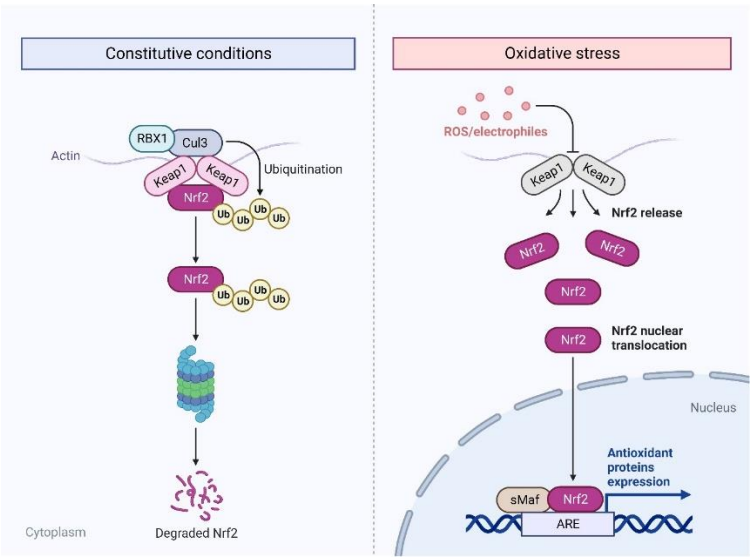

Figure 2: Oxidative stress mechanism and pathway

6. Conclusion and future perspective of wogonin

Wogonin is an anti-inflammatory flavonoid isolated from medicinal plants. It prevents macrophages, lymphocytes, microglia, and endothelial cells from producing inflammatory mediators. Wogonin is also a neuroprotectant, anti-allergy medication, anxiolytic, and anticonvulsant. Wogonin's molecular processes and inhibitory effects have been linked to a number of signalling pathways, including ER stress-mediated apoptosis and autophagy, MAPK, ROS, NF-B, and AP-1 transcription factor repression, and intracellular Ca2+ signalling. Wogonin effectively suppresses and prevents viral infection by inhibiting the virus's connection to the cells and also by reducing viral protein production (such as E6 and E7 protein). Wogonin also promotes anti-inflammatory responses by modulating the NF-kappa B (NF-kB) and AP-1 (Activator Protein 1) signalling pathways, as well as triggering IFN-induced antiviral signalling (STAT1/IRF3 pathway). Wogonin regulates the ROS/MAPK/Nrf2/AP1/NF-B signalling pathways in inflammatory diseases to reduce the production of inflammatory cytokines/ chemokines (IL-6, IL-1, IFN-β, TNF-α, RANTES, eotaxin) and oxidative stress mediators (COX-2, PGE2, NO, iNOS). Wogonin reduces the production of adhesion molecules such as ICAM-1 and matrix metalloproteinases such as MMP1, MMP2, and MMP13, which inhibits inflammatory leukocyte infiltration. Wogonin reduces inflammation by increasing the Treg population and decreasing the effector T cell population, owing to the importance of maintaining the balance between effector T (CD4+ and CD8+) cells and regulatory T (CD25+FOXP3+) cells for immunolo gical homeostasis. Notably, wogonin's actions on convulsion-related activities such as myorelaxation and anticonvulsant are mediated by the GABAergic neuron. When the 5, 7-dihydroxyl groups of wogonin bind to the BZD binding site of GABAA located at the 2 subunit, both the electrophysiological current and the intracellular concentration of Cl ions increase. Finally, wogonin acts as a neuroprotector by decreasing inflammatory mediators (such as tumour necrosis factor-alpha, interleukin-1 beta, interleukin-6, nitric oxide, and inducible nitric oxide synthase) and signalling pathways (such as MAPK/Nrf2/NF-kappaB and intracellular calcium). Wogonin inhibits the neurotransmitter glutamate or the NMDA receptor, reducing brain cell death and protecting hippocampus neurons from ischemic death.

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