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The Clinical Landscape of Wogonin: Advancing Targeted Treatments for Chronic Diseases

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Abstract

The traditional Chinese medicinal herb Scutellaria baicalensis Georgi, commonly known as Chinese skullcap or Huang-Qin, has long been used to treat a variety of conditions, including cancer, viral infections, and seizures. Its pharmacological effects are largely attributed to the high concentration of flavones, particularly wogonoside, and its aglycone derivative, wogonin. Among the bioactive compounds found in S. baicalensis, wogonin has garnered the most scientific attention due to its potent therapeutic properties. Extensive preclinical studies have demonstrated that wogonin exerts anti-tumor effects by inducing cell cycle arrest, promoting apoptosis, and inhibiting metastasis. This review provides a comprehensive analysis of published studies highlighting wogonin's chemo-preventive potential and the underlying molecular mechanisms of its anti-cancer activity. It also examines how wogonin can work synergistically to improve the effectiveness of standard chemotherapy treatments. Further research into the chemistry and toxicological profile of wogonin is encouraged to ensure its safety and optimize its therapeutic application, positioning it as a promising candidate for cancer treatment. Scutellaria baicalensis Georgi, a member of the Labiaceae family, is a widely utilized medicinal herb in traditional Chinese medicine (TCM). This herb is rich in various components, primarily flavonoids like baicalin, baicalein, and wogonin. Recent studies have demonstrated that Scutellaria, either on its own or in combination with other herbs, exhibits cytostatic effects on multiple cancer cell lines, both in vitro and in vivo using mouse tumor models.

Keywords: *Scutellaria baicalensis*, wogonin, flavonoids, chemopreventive, anti-tumor

INTRODUCTION

Wogonin is a flavonoid extracted from the traditional Chinese herb *Scutellaria baicalensis*. This compound is recognized for its various therapeutic properties and has been the subject of numerous studies exploring its potential benefits in treating different health conditions. While it has shown significant promise in preclinical studies for its therapeutic effects, including anti-inflammatory, antiviral, anticancer, and neuroprotective properties, it has yet to receive FDA approval for specific medicinal use in the United States [1].

Wogonin has been widely studied for its medicinal properties. It has shown effectiveness in addressing a range of health issues, such as inflammation, viral infections, and specific types of cancer. Notably, wogonin shows anticancer activity by inducing apoptosis in cancer cells, particularly in resistant forms of ovarian and nasopharyngeal carcinomas. Additionally, it has shown neuroprotective and anticonvulsant effects, making it a potential candidate for managing neurological disorders [2].

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Wogonin has also been explored as an anxiolytic, with studies indicating its interaction with benzodiazepine receptors, providing a calming effect. While wogonin is in animal studies, it has been generally well-tolerated; however, possible side effects may include gastrointestinal issues, drowsiness, and allergic reactions. It is essential to study its long-term safety profile before it can be widely recommended [3–5].

An ideal herbal drug, such as wogonin would need to meet specific criteria for FDA approval. These include a clear understanding of its pharmacodynamics, favorable bioavailability, and the absence of severe side effects at therapeutic doses. Furthermore, the drug's mechanism of action must be well understood, particularly in its anti-inflammatory and anticancer properties, to ensure both efficacy and safety in long-term use [6–8].

Wogonin, a flavonoid derived from the traditional Chinese herb *Scutellaria baicalensis*, has garnered attention for its diverse therapeutic properties, particularly its anticancer effects. Beyond its potential in cancer treatment, wogonin is recognized for its detoxifying capabilities and benefits to cardiovascular health. Research indicates that wogonin influences several critical cells signaling pathways, including the protein kinase B (AKT) pathway and the AMP-activated protein kinase (AMPK) pathway. These pathways play essential roles in cell survival, metabolism, and apoptosis, making them vital targets in cancer therapy. Recent studies have demonstrated that wogonin can effectively induce apoptosis in human hepatoma cells (HepG2) by modulating various apoptotic markers [9–13]. Specifically, wogonin appears to lead to a decrease in mitochondrial membrane potential (MMP) and a depletion of intracellular glutathione levels, which are crucial for maintaining cellular health. This process favors the activation of intrinsic apoptotic pathways, contributing to the selective death of cancerous cells while sparing normal cells. Notably, at lower concentrations, wogonin does not adversely affect embryonic hepatic L02 cells, suggesting a selective action that preferentially targets tumor cells over healthy tissue. However, at higher concentrations (around 200 μM), wogonin does induce some degree of apoptosis, further underscoring the need for careful dosage considerations in therapeutic applications. In addition to its anticancer properties, wogonin has shown promise in protecting renal function during cisplatin-based chemotherapy [14, 15]. Cisplatin is a widely used chemotherapeutic agent known for its effectiveness against various cancers, but it can also lead to significant nephrotoxicity. In experimental models, wogonin has been observed to significantly reduce elevated serum creatinine and blood urea nitrogen (BUN) levels, which are indicators of kidney function. This protective effect positions wogonin as a valuable adjunct in chemotherapy regimens, potentially mitigating one of the most common side effects of cisplatin treatment. Mechanistically, wogonin has been found to inhibit receptor-interacting protein kinase 1 (RIPK1), a key regulator of necroptosis, a form of programmed cell death distinct from apoptosis. By binding to the ATP-binding pocket of RIPK1, wogonin can block its activity, thereby influencing cell death pathways and contributing to its overall anticancer efficacy. This interaction highlights wogonin's potential to not only induce apoptosis but also modulate other forms of cell death that may be relevant in cancer biology. Moreover, wogonin has been shown to enhance the antiproliferative effects of cisplatin on human hepatoma cells. This synergistic effect suggests that combining wogonin with cisplatin could improve therapeutic outcomes, allowing for more effective cancer treatment with potentially reduced side effects [16, 17]. As the search for effective cancer therapies continues, the role of natural compounds like wogonin is increasingly recognized for their ability to enhance conventional treatments. Wogonin stands out as a multifaceted compound with promising applications in cancer therapy. Its ability to selectively induce apoptosis in cancer cells, protect renal function during chemotherapy, and interact with critical signaling pathways makes it a candidate for further research and clinical application. Future studies should focus on elucidating the detailed mechanisms of wogonin's actions, optimizing its dosing strategies, and evaluating its safety profile in clinical settings. As we advance our understanding of wogonin's properties, it may well become an integral component of combination therapies in the fight against cancer (Figure 1) [18, 19].

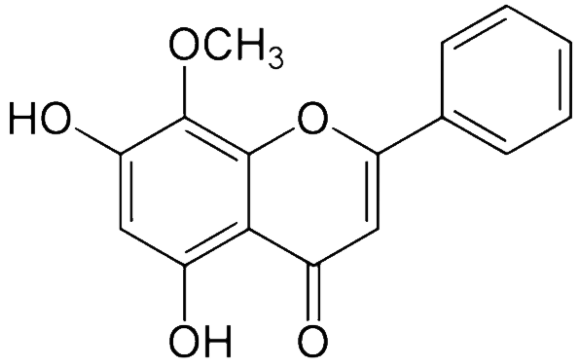

Figure 1. Wogonin [10].

MECHANISM OF ACTION

Wogonin various mechanics for targeting cancerous cells which are as follows:

- *Induction of apoptosis:* Wogonin promotes apoptosis (programmed cell death) in cancer cells by activating caspases and modifying the levels of pro-apoptotic proteins like Bax and anti-apoptotic proteins like Bcl-2, leading to enhanced cell death in tumors [2, 5].
- *Inhibition of cell proliferation:* It disrupts cancer cell proliferation by arresting the cell cycle, particularly at the G1 phase, through the modulation of cyclins and cyclin-dependent kinases (CDKs) [2, 5].
- *Suppression of metastasis:* Wogonin reduces cancer cell migration and invasion by targeting pathways involved in metastasis. It lowers matrix metalloproteinases (MMPs) activity and downregulates markers of epithelial-to-mesenchymal transition (EMT) [3, 5].
- *Modulation of signaling pathways:* Wogonin impacts several crucial signaling pathways, including the PI3K/Akt/mTOR and MAPK/ERK pathways, which are important for cell survival, growth, and differentiation [2, 5].
- *Effect on MCF-7 cells: - W* - Wogonin reduces cell numbers in a dose-dependent manner after 72 hours. Wogonin decreases MCF-7 cell numbers. Pretreating MCF-7 breast cancer cells with wogonin affects their ability to form colonies after radiation exposure. Pre-treatment with wogonin at concentrations of 5-10 μM enhances the resistance of MCF-7 breast cancer cells to radiation therapy. Combining wogonin with radiotherapy requires caution. Cells surviving wogonin treatment show reduced mitotic or apoptotic death after radiation [6].
- *Anti-angiogenic effects:* It inhibits angiogenesis, the process of new blood vessel formation necessary for tumor (Figure 2).

CLINICAL ASPECTS OF WOGONIN IN TARGETED TREATMENT

Anticancer Potential

Recent studies have highlighted wogonin's role in cancer therapy. Clinical investigations suggest that it can inhibit the proliferation of various cancer cell lines, including breast, lung, and prostate cancers. For example, in vitro research has shown that wogonin triggers apoptosis by influencing the levels of apoptosis-related proteins, including Bcl-2 and Bax. This modulation results in an increase in cancer cell death, highlighting wogonin's potential as an effective agent in promoting apoptotic pathways. By altering the balance between pro-apoptotic and anti-apoptotic factors, wogonin facilitates the elimination of malignant cells, thereby contributing to its anticancer properties. These findings suggest that wogonin may play a significant role in developing therapeutic strategies aimed at enhancing apoptosis in cancer treatment. Additionally, wogonin's ability to block cell cycle progression at the G1 phase has been observed, which further contributes to its anticancer efficacy [20].

Several preclinical studies have indicated that wogonin can enhance the effectiveness of conventional chemotherapy agents, such as doxorubicin and cisplatin, by sensitizing cancer cells and reducing drug resistance. This combination approach could potentially improve patient outcomes and minimize the required dosages of traditional chemotherapeutics, thereby reducing associated side effects.

Anti-inflammatory Mechanisms

In the context of inflammatory diseases, wogonin exhibits significant anti-inflammatory properties. Clinical research indicates that it reduces levels of pro-inflammatory cytokines, including TNF-α, IL-6, and IL-1β, which are key players in chronic inflammatory conditions. For example, wogonin has shown promise in managing symptoms of rheumatoid arthritis and inflammatory bowel disease through its inhibition of the NF-kB signaling pathway.

Furthermore, wogonin's antioxidant properties contribute to its anti-inflammatory effects by scavenging free radicals and reducing oxidative stress, which is often a contributing factor in chronic inflammation. Wogonin is positioned as a prospective treatment candidate for a range of inflammatory disorders due to its dual action [21].

Safety and Tolerability

Safety and tolerability are critical considerations in the clinical application of any herbal compound. Preliminary clinical trials indicate that wogonin is well-tolerated, with only a small number of adverse effects reported. The absence of significant toxicity, even at higher doses, supports its potential as a complementary treatment option.

Pharmacokinetics and Bioavailability

Understanding wogonin's pharmacokinetics is essential for optimizing its clinical use. Research indicates that wogonin's low solubility contributes to its low bioavailability.

Recent advances in drug formulation, such as the use of nanoparticles and liposomal delivery systems, aim to enhance its absorption and bioavailability. These strategies are crucial for improving therapeutic efficacy and ensuring that adequate drug levels are achieved in target tissues [22].

Future Directions and Clinical Trials

Although promising, the clinical translation of wogonin is still in its early stages. Ongoing and future clinical trials are necessary to further evaluate its efficacy and safety in various patient populations. Investigating potential biomarkers for patient selection could also optimize treatment outcomes, ensuring that individuals who are most likely to benefit from wogonin therapy are identified.

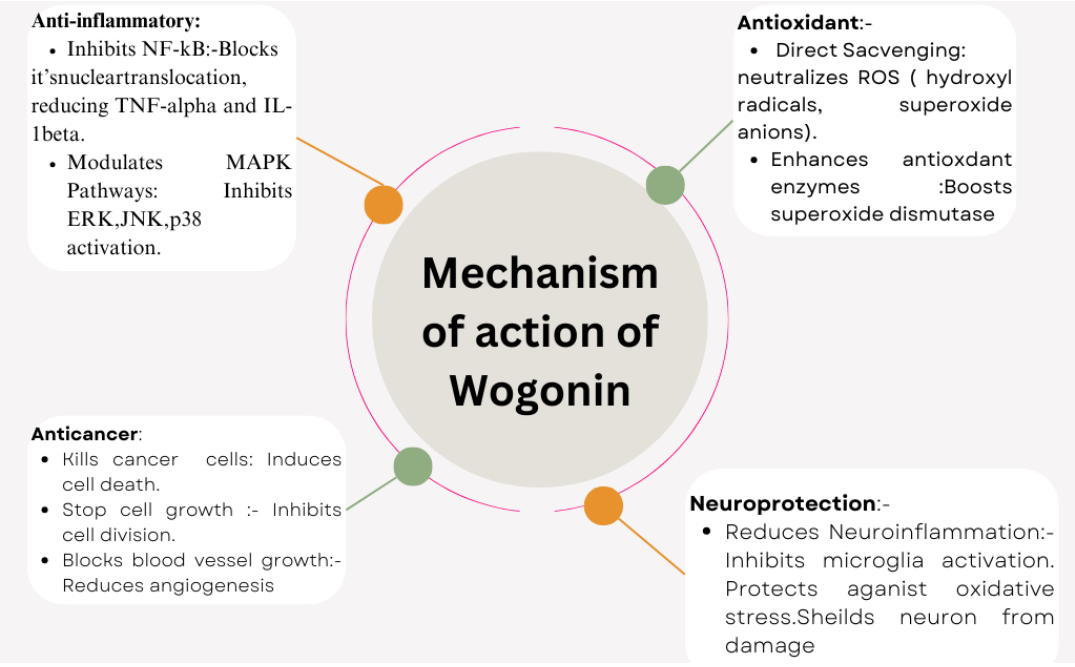

Figure 2. Mechanism of action of wogonin.

Edges of Wogonin

- Wogonin may offer a cost-effective option, especially when compared to more expensive pharmaceutical drugs used for treating inflammation and cancer. Its potential to reduce healthcare costs, particularly when used as part of an integrative medicine approach, makes it an attractive option for patients seeking affordable alternatives.
- Wogonin is considered to have a favorable safety profile, with low toxicity observed in preclinical studies. Even at higher dosages, it has been associated with minimal adverse effects, suggesting it is a promising candidate for therapeutic applications. Nonetheless, additional clinical trials are essential to thoroughly assess the safety of wogonin in human subjects. While initial findings suggest a favorable safety profile, comprehensive studies are needed to evaluate potential long-term effects and to confirm its overall tolerability. These subsequent trials should aim to include a larger and more diverse population, allowing for a better understanding of any risks associated with wogonin. Ensuring its safety in various demographics is crucial before considering broader therapeutic applications, as a complete assessment will help establish confidence in its use as a treatment option.

MANUFACTURING AND EXTRACTION

In India, the regulatory approval process for herbal is overseen by the Ministry of AYUSH, which regulates traditional and herbal medicines. For an herbal drug to be approved of a specific medical use it must undergo rigorous clinical trials and safety assessment, which are then review by regulatory authorities (Figures 3 and 4) [8].

Figure 3. Wogonin extraction.

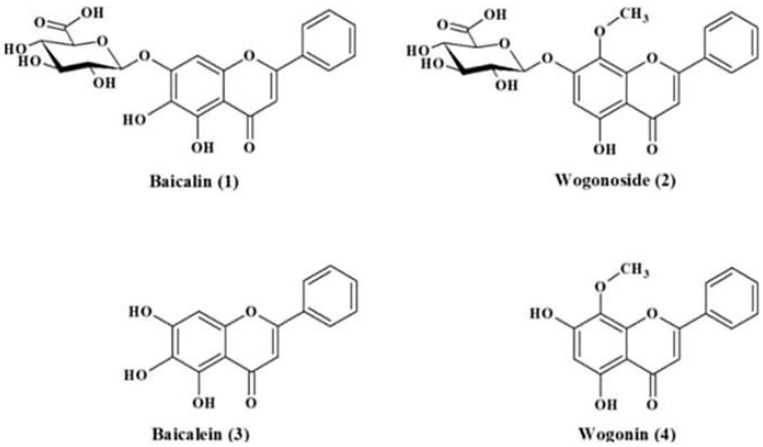

Figure 4. Derivatives of wogonin [7, 9].

CONCLUSIONS

In summary, wogonin shows significant potential as an advanced targeted therapy due to its precise action on specific disease –related pathways. Preliminary research indicates that wogonin effectively targets crucial molecular mechanisms, offering the promise of enhanced treatment efficacy with reduced side effects. Further studies are needed to better understand its mechanisms, refine dosage protocols and confirm its clinical benefits. As personalized medicine progresses, wogonin could play a vital role in developing more effective and targeted treatment options, ultimately improving patient outcomes across diverse health conditions.

REFERENCES

1. Park HG, Yoon SY, Choi JY, Lee GS, Choi JH, Shin CY, et al. Anticonvulsant effect of wogonin isolated from Scutellaria baicalensis. Eur J Pharmacol 2007;574(2–3):112–119. doi:10.1016/j.ejphar.2007.07.011.
2. Cao Z. Wogonin a review of its pharmacological and pharmacokinetic properties. Phytother Res. 2020;34(3):617–629.
3. Sharma N, Singh AK, Sodhi SS, Zhang JJ, Mongre RK, Ghosh M, et al. Anti-tumor activity of wogonin, an extract from Scutellaria baicalensis, through regulating different signaling pathways. Chin J Nat Med. 207;15(1):15–40. doi:10.1016/S1875-5364(17)30005-5.
4. Liu W. Wogonin inhibits tumor growth by targeting multiple signaling pathways. Cancer Lett. 2016;380(0032):297–306.
5. Uemura S, Matsushita H, Li W, Glassford AJ, Asagami T, Lee KH, et al. Diabetes mellitus enhances vascular matrix metalloproteinase activity: role of oxidative stress. Circulation Research. 2001;88(12):1291–1298. doi:10.1161/hh1201.092042.
6. Rouhani M, Dalfard AH. Wogonin from scutellaria baicalensis-induced radioresistance in MCF-7 breast cancer cell line. Eurasian J Med Oncol. 2022;6(4):345–350. doi:10.14744/ejmo.2022.17217.
7. Tronina T, Mrozowska M, Bartmańska A, Popłoński J, Sordon S, Huszcza E. Simple and rapid method for wogonin preparation and its biotransformation. Int J Mol Sci. 2021;22(16):8973. doi:10.3390/ijms22168973.
8. Banik K, Khatoon E, Harsha C, Rana V, Parama D, Thakur KK, et al. Wogonin and its analogs for the prevention and treatment of cancer: A systematic review. Phytother Res. 2022;36(5):1854–1883. doi:10.1002/ptr.7386.
9. Wang Q, Shi R, Dai Y, Li Y, Wang T, Ma Y, et al. Mechanism in the existent difference in form of wogonin/wogonoside between plasma and intestine/liver in rats. RSC Adv. 2018;8(7):3364–3373. doi:10.1039/C7RA08270C.
10. Zhao T, Tang H, Xie L, Zheng Y, Ma Z, Sun Q, et al. Scutellaria baicalensis Georgi. (Lamiaceae): a review of its traditional uses, botany, phytochemistry, pharmacology and toxicology. J Pharm Pharmacol. 2019;71(9):1353–1369. doi:10.1111/jphp.13129.

11. Liu Y, Wang H, Cai X. Optimization of the extraction of total flavonoids from Scutellaria baicalensis Georgi using the response surface methodology. J Food Sci Technol. 2015;52:2336–2343. doi:10.1007/s13197-014-1275-0.
12. Dzięcioł M, Wala K, Wróblewska A, Janda-Milczarek K. The effect of the extraction conditions on the antioxidant activity and bioactive compounds content in ethanolic extracts of Scutellaria baicalensis root. Mol. 2024;29(17):4153. doi:10.3390/molecules29174153.
13. Tzanova M, Atanasov V, Yaneva Z, Ivanova D, Dinev T. Selectivity of current extraction techniques for flavonoids from plant materials. Processes. 2020;8(10):1222. doi:10.3390/pr8101222.
14. Do HT, Nguyen TH, Nghiem TD, Nguyen HT, Choi GJ, Ho CT, et al. Phytochemical constituents and extracts of the roots of Scutellaria baicalensis exhibit in vitro and in vivo control efficacy against various phytopathogenic microorganisms. South Afr J Bot. 2021;142:1–1. doi:10.1016/j.sajb.2021.05.034.
15. Patra A, Abdullah S, Pradhan RC. Review on the extraction of bioactive compounds and characterization of fruit industry by-products. Bioresour Bioprocess. 2022;9(14). doi:10.1186/s40643-022-00498-3.
16. Liu Y, Nie Y, Lu X, Zhang X, He H, Pan F, Zhou L, Liu X, Ji X, Zhang S. Cascade utilization of lignocellulosic biomass to high-value products. Green Chem. 2019;21(13):3499–3535. doi:10.1039/C9GC00473D.
17. Yang MX, Liang YG, Chen HR, Huang YF, Gong HG, Zhang TY, et al. Isolation of flavonoids from wild Aquilaria sinensis leaves by an improved preparative high-speed counter-current chromatography apparatus. J Chromatogr Sci. 2018;56(1):18–24. doi:10.1093/chromsci/bmx076.
18. Yin M, Wang J, Huang H, Huang Q, Fu Z, Lu Y. Analysis of flavonoid compounds by terahertz spectroscopy combined with chemometrics. ACS Omega. 2020;5(29):18134–1841. doi:10.1021/acsomega.0c01706.
19. Tan CX, Schrader KK, Khan IA, Rimando AM. Activities of wogonin analogs and other flavones against Flavobacterium columnare. Chem Biodivers. 2015;12(2):259–272. doi:10.1002/cbdv.201400181.
20. Shi LK, Zheng L, Liu RJ, Chang M, Jin QZ, Wang XG. Chemical characterization, oxidative stability, and in vitro antioxidant capacity of sesame oils extracted by supercritical and subcritical techniques and conventional methods: a comparative study using chemometrics. Eur J Lipid Sci Technol. 2018;120(2):1700326. doi:10.1002/ejlt.201700326.
21. Li, HB, Jiang, Y, Chen, F. Li HB, Jiang Y, Chen F. Separation methods used for Scutellaria baicalensis active components. J Chromatogr B Analyt Technol Biomed Life Sci. 2004;812(1–2):277–290. doi:10.1016/j.jchromb.2004.06.045.
22. Rawat S, Gupta G, Pathak S, Singh SK, Singh H, Mishra A, et al. Current biological and pharmacological updates on wogonin. EXCLI. 2020;19:635–40.

