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Bioactivities from Baicalein Compound: A short Review

Khaled Rashed*

Department of Pharmacognosy, National Research Centre, 33 El-Bohouthst-Dokki, Giza, P.O.12622, Egypt

Abstract

Baicalein compound is a natural flavonoidal compound. It is a flavone, a type of polyphenolic flavonoid. It is isolated from the root of *Scutellaria baicalensis* Georgi with broad bioactivities. It has several biological activities, such as antioxidant, anti-thrombotic, and anti-inflammatory activities. Furthermore, in regards to neuroprotection, where it has been reported to reduce the production of inflammatory cytokines and it –stimulated apoptosis in the rat cerebral cortex.
Keywords: Baicalein, Plant, bioactivities.

***Correspondence Info:**
Dr. Khaled Rashed
Department of Pharmacognosy,
National Research Centre,
33 El-Bohouthst.-Dokki, Giza, P.O.12622, Egypt

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1. Introduction

Extensive attention worldwide has been directed at flavonoids, a large class of phytochemicals with variable phenolic structures, owning to their considerable health benefits[1,2]. The medicinal plant *Scutellaria baicalensis* Georgi has been used widely in traditional Chinese medicine for anti-inflammation, anticancer, antiviral and antibacterial infections, reducing the total cholesterol level and decreasing blood pressures. Baicalein and baicalin are two major flavonoid of *Scutellaria baicalensis* Georgi, exhibit various bioactivities. Baicalein, a dietary flavonoid, is the major constituent of Oroxylum indicum and *Scutellaria baicalensis* which are consumed as teas or dietary supplements in Asia, European, and the United States. Baicalein is a flavonoid originally isolated from the roots of *Scutellaria baicalensis* Georgi, a plant widely usedin China. Baicalein has been demonstrated to possess potent antioxidant and anti-inflammatory properties [3, 4], and has a wide range of pharmacological effects, including antiviral, anti-tumour, neuroprotective and nephroprotective activity etc[5-8].

Besides, baicalein is liver-protective and alleviates hepa-totoxin-induced liver injury [9, 10]. It isreported that baicalein increases the cytotoxicity of cisplatin [11]. Ithas also been demonstrated that baicalein prevents cisplatin-induced renal damage in mice [12]. Baicalein improved insulin-resistance and systemic inflammation in diabetic rats. It reduced lung inflammation by inhibiting Th17 cells in the lungs. It modulated gut microbiota composition and enhanced gut barrier function. This review gave the medicinal uses of Baicalein.

2. Biological activities

2.1 Anti-Alzheimer'sdisease(AD)

Baicalein exhibited strong BACE1 and AChE inhibitory properties (IC_{50} 23.71µ1.91µM and 45.95 µ 3.44 µM, respectively) and reacted in non-competitive and competitive manners with substrates, respectively. In Silico docking analysis was in full agreement with the in vitro results, demonstrating that the compound exhibited powerful binding interaction with target enzymes. Particularly, three continuous hydroxyl groups on the A ring demonstrated strong H-bond binding properties. It is also noteworthy that baicalein complied with all requirements of Lipinski's rule of five by its optimal physicochemical properties for both oral bioavailability and blood–brain barrier permeability. Overall, the present study strongly demonstrated the possibility of baicalein having *in vivo* pharmacological efficacy for specific targets µin the prevention and/or treatment of AD[13].

2.2 Anti-diabetic effects

In the present work, 4-week treatment of baicalein significantly decreased the levels of blood glucose and circulating lipopolysaccharide (LPS) and improved insulin resistance, inflammation, and lipid profile in diabetic rats induced by STZ and high-fat-high-sugar-diet.

These anti-diabetic effects were attributed to the increased SCFAs content and the increased thickness of gut mucus layer, and were associated with the modulation of gut microbiota. Among the key phylotypes, Bacteroides and Bacteroidales S24-7 had the highest relative abundance in the rats receiving high- dose baicalein and showed positive correlation with the phenotypes related to the improvement of type 2 diabetes (T2DM). Our study supports the use of baicalein as a dietary supplement and a potential prebiotic for its ability to modify gut microbiota and to improve T2DM-related biochemical abnormalities [14].

2.3 Baicalein Alleviates Liver Oxidative Stress and Apoptosis

In this study, we investigated the effect of baicalein on protein kinase R-like ER kinase (PERK)/nuclear factor erythroid-2-related factor 2 (Nrf2) pathway for the alleviation of oxidative stress and apoptosis. Human liver HL-7702 cells were stimulated with 60.5 mM of glucose to induce oxidative stress and treated with baicalein.

The apoptosis was determined by fluorescence microscopy and flow cytometry. The regulation of the PERK/Nrf2 pathway by baicalein was determined by immunoblotting in both HL-7702 cells and liver tissues from diabetic mice. We found that baicalein significantly alleviated the oxidative stress and apoptosis in HL-7702 cells stimulated with glucose.

Mechanistic studies showed that baicalein down regulated PERK and up regulated Nrf2, two key proteins involved in endoplasmic reticulum stress, in both HL-7702 cells and liver tissues from diabetic mice receiving baicalein treatment. Furthermore, the subcellular localization of Nrf2 and the regulation of downstream proteins including hemeoxygenase-1 and CCAAT-enhancer-binding protein homologous protein (CHOP) by baicalein were also investigated. Our results suggest that the regulation of the PERK/Nrf2 pathway is one of the mechanisms contributing to the bioactivities of baicalein to improve diabetes-associated complications [15].

2.4 Anti-bacteria activity

The flavonoids of *Scutellaria baicalensis* were tested for antibacterial effect. Nine compounds were isolated and identified as baicalein, wogonin, oroxylin A, 5, 7, 2', 6'-tetrahydroxy flavone, viscidulin III, baicalin, wogonoside, oroxylin A-7-O-beta-D-glucuronide and chrysin-6-C-alpha-L-arabinopyranosyl-8-C-beta-D-glucopyranoside. Baicalein had good anti-bacteria activity, and some compounds showed inhibiting activity against IL-1beta converting enzyme [16].

2.5 Baicalein as novel, natural product inhibitors of SARS-CoV-2 3CL

Human infections with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) cause coronavirus disease 19 (COVID-19) and there is currently no cure. The 3C-like protease (3CLpro), a highly conserved protease indispensable for replication of coronaviruses, is a promising target for development of broad-spectrum antiviral drugs. To advance the speed of drug discovery and development, we investigated the inhibition of SARS-CoV-2 3CLpro by natural products derived from Chinese traditional medicines.

Baicalin and baicalein were identified as the first non-covalent, non-peptidomimetic inhibitors of SARS-CoV-2 3CLpro and exhibited potent antiviral activities in a cell-based system. Remarkably, the binding mode of baicalein with SARS-CoV-2 3CLpro determined by X-ray protein crystallography is distinctly different from those of known inhibitors.

Baicalein is perfectly ensconced in the core of the substrate-binding pocket by interacting with two catalytic residues, the crucial S1/S2 subsites and the oxyanion loop, acting as a “shield” in front of the catalytic dyad to prevent the peptide substrate approaching the active site. The simple chemical structure, unique mode of action, and potent antiviral activities *in vitro*, coupled with the favorable safety data from clinical trials, emphasize that baicalein provides a great opportunity for the development of critically needed anti-coronaviral drugs [17].

2.6 Baicalein decreases uric acid and prevents hyperuricemnephropathy in mice

In this study, molecular docking analysis and Surface Plasmon Resonance revealed a direct interaction between baicalein and xanthine oxidoreductase. Moreover, 50 mg/kg/d baicalein treatment significantly suppressed the viability of xanthine oxidoreductase in hyperuricemia mouse model. The data showed that baicalein remarkably prevented renal dysfunction, ameliorated kidney fibrosis, alleviated epithelial-mesenchymal transition and oxidative stress in hyperuricemia mice. Thus, we concluded that baicalein executed a kidney-protection action in hyperuricemia and therefore may be used as a therapeutic alternative for hyperuricemic nephropathy [18].

3. Conclusion

This review indicated the pharmacological effects of baicalein.

References

[1]. Lv X, Zhao S, Ning Z, *et al*. Citrus fruits as a treasure trove of active natural metabolites that potentially provide benefits for human health. *Chem Cent J.* 2015; 9:68–85.

[2]. Blad E C, Aragon ES G, Arola-Arnal A, *et al*. Proanthocyanidins in health and disease. *Biofactors*. 2016; 42(1):5–12.

[3]. Kang KA, Zhang R, Piao MJ, *et al*. Baicalein inhibits oxidative stress-induced cellular damage via antioxidant effects. *Toxicol Ind Health*. 2012; 28:412–421.

[4]. Lee W, Ku SK, Bae JS. Anti-inflammatory effects of baicalin, baicalein, and wogonin *in vitro* and *in vivo*. *Inflammation* 2015; 38:110–125.

[5]. Zandi K, Teoh BT, Sam SS, *et al*. Novel antiviral activity of baicalein against dengue virus. *BMC Complement Altern Med [Internet]*. 2012 24; 12:214.

[6]. Han Z, Zhu S, Han X, *et al*. Baicalein inhibits hepatocellular carcinoma cells through suppressing the expression of CD24. *Int Immunopharmacol.* 2015; 29:416–422.

[7]. Moon JH, Park SY. Baicalein prevents human prion protein-induced neuronal cell death by regulating JNK activa-tion. *Int J Mol Med*. 2015; 35(2):439–445.

[8]. Wang W, Zhou PH, Xu CG, *et al*. Baicalein attenuates renalfibrosis by inhibiting inflammation via down-regulatingNF-kB and MAPK signal pathways. *J Mol Histol.* 2015; 46:283–290.

[9]. Zhang Y, Shan L, Hua Y, *et al*. Baicalein selectively inducesapoptosis in activated lymphocytes and ameliorates concanavalin a-induced hepatitis in mice. *PLoS One* 2013; 24; 8: e69592.

[10]. Wu YL, Lian LH, Wan Y, *et al*. Baicalein inhibits nuclear factor-kB and apoptosis via c- FLIP and MAPK in D-GalN/LPS induced acute liver failure in murine models. *Chem Biol Interact*. 2010; 188:526–534.

[11]. Wang Y, Wang Q, Zhang S, *et al*. Baicalein increases the cytotoxicity of cisplatin by enhancing gap junction intercellular communication. *Mol Med Rep*. 2014; 10: 515–521.

[12]. Sahu BD, Mahesh Kumar J, Sistla R. Baicalein, a bioflavonoid, prevents cisplatin-induced acute kidney injury by up-regulating antioxidant defenses and down-regulating the MAPKs and NF-kB pathways. *PLoS One* 2015; 10:e0134139.

[13]. Jin Han, Yeongseon Ji Kumju Youn, Gyu Tae Lim, Jinhyuk Lee Dong Hyun Kim and Mira Jun. Baicalein as a Potential Inhibitor against BACE1 and AChE: Mechanistic Comprehension through *In Vitro* and Computational Approaches *Nutrients* 2019; 11: 2694.

[14]. Zhang Wenlong S Yua Jin Suna,,LiyanYuc, Yue sheng Dong. Anti-diabetic effect of baicalein is associated with the modulation of gut microbiota in streptozotocin and high- fat-diet induced diabetic rats. *Journal of Functional Foods* 46; 2018: 256-267.

[15]. Yuesheng Dong, Yan Xing, Jin Sun, Wenlong Sun, Yongbin Xu, Chunshan Quan. Baicalein Alleviates Liver Oxidative Stress and Apoptosis Induced by High-Level Glucose through the Activation of the PERK/Nrf2 Signaling Pathway. *Molecules* 2020; 1-30.

[16]. Xi Qin Zhou, Hong Liang, Xin Hua Lu, Shao Qing Cai, Bin Wang, Yu Ying Zhao. Flavonoids from *Scutellaria baicalensis* and their bioactivities. *Beijing* 2009; 41(5):578-84.

[17]. Haixia Su, Sheng Yao, Wenfeng Zhao, Minjun Li, Jia Liu, WeiJuan Shang, Hang Xie, Changqiang Ke, Meina Gao, Kunqian Yu, Hong Liu, Jingshan Shen, Wei Tang, Leike Zhang, Jianping Zuo, Hualiang Jiang, Fang Bai, Yan Wu, Yang Ye, Yechun Xu. Discovery of baicalin and baicalein as novel, natural product inhibitors of SARS-CoV-2 3CL protease *in vitro* doi: https://doi.org/10.1101/2020.04.13.038687.

[18]. Xiaolu Meng, Zhuo Mao, Xin Li, Dandan Zhong, Min Li, Yingli Jia, Jing Wei, Baoxue Yang and Hong Zhou. Baicalein decreases uric acid and prevents hyperuricemic nephropathy in mice. *Oncotarget,* 2017; 8 (25); 40305-40317.