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Letter to the editor:

RECENT INSIGHTS INTO THE BIOLOGICAL FUNCTIONS OF BAICALIN

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Flavonoids are molecules possessing a 15-carbon skeleton structure consisting of two aromatic ring systems (A and B rings) and a heterocyclic ring (C). This carbon backbone can be shortened to C6-C3-C6 (Kumar and Pandey, 2013). Flavonoids can be sorted into different subgroups, based on the degree of unsaturation and substitution patterns, consisting of anthocyanins, catechins, chalcone flavanols, flavanones, flavones, flavanonols, flavonols, and isoflavonoids (Santos-Buelga and Feliciano, 2017).

Flavones (from the Latin term *flavus* meaning "yellow") belong to the group of flavonoids that share a 2-phenylchromen-4-one (2-phenyl-1-benzopyran-4-one) backbone, and are secondary metabolites commonly present in plants and fungi, and are naturally yellow-colored (Panche et al., 2016; Kumar and Pandey, 2013).

Baicalin, a flavone glycoside, is one of the most important bioactive compounds in *Scutellaria radix* (the dry raw root of *Scutellaria baicalensis*), which is among the 50 essential herbs used in traditional Chinese medicine (Liang et al., 2017). Baicalin is a 7-*O*-glucuronide derivative of baicalein, and its synthesis is catalyzed by baicalein 7-*O*-glucuronosyltransferase in *S. baicalensis* (Nagashima et al., 2000).

It has been reported effective in exerting several pharmacological activities, namely antibacterial, antiviral, anticancer, anticonvulsant, anti-inflammatory, antioxidant, hepatoprotective, and neuroprotective effects (Cui et al., 2022; Wang et al., 2022; Li et al., 2021; Pan et al., 2021). The pharmacological properties of baicalin are attributed to its ability to scavenge reactive oxygen species (ROS) and interact with several signaling molecules related to apoptosis, autophagy, cell cycle, cytoprotection, inflammation, and mitochondrial dynamics (Hu et al., 2022). The therapeutic potential of baicalin warrants further studies as a natural treatment for

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various human diseases. Here, we report current findings on baicalin's biological properties and pharmacological activities (Table 1).

Table 1: Recent studies on the biological and pharmacological activities of baicalin

Key findings	Reference
Baicalin might be useful in treating senile dementia, especially Alzheimer's disease (AD), as it may regulate neuronal cell cycle progression and apoptosis in amyloid-beta (Aβ) 1-42-treated SH-SY5Y cells through inhibition of the Ras-ERK signaling pathway.	Song et al., 2022
Baicalin may be a potential therapeutic drug to ameliorate diet-induced MetS (metabolic syndrome) by exerting metabolic protection on the gut microbiome.	Lin et al., 2022
Baicalin can prevent the secretion of inflammatory factors by inhibiting the TLR4 (toll-like receptor-4)/MyD88 (myeloid differentiation factor 88)/NF-κB (nuclear factor-kappa B)/NLRP3 (nod-like receptor pyrin containing 3) pathway and the MAPK (mitogen-activated protein kinase) signaling pathway. As a result, it has been shown to effectively reduce the lung bronchial epithelial layer, alveolar damage, and pulmonary edema. Hence, baicalin could be a candidate preventive and therapeutic therapy for ALI (acute lung injury).	Changle et al., 2022
Baicalin has the potential to become a novel treatment for aGVHD (acute graft-versus-host disease), as it regulates autophagy by affecting altered inflammatory cytokine levels as well as mucosal barrier injury.	Sun et al., 2022
Baicalin has proved effective as a hepatoprotective agent in ALD (alcohol-associated liver disease) through miR-205-mediated importinα5 inhibition that represses NF-κB signaling pathway activation. As such, baicalin can be considered a potential therapeutic target for treating ALD.	Fang et al., 2022
Baicalin could be a potential drug for alleviating CS (cytokine storm), a systemic inflammatory syndrome, and a relevant cause of multi-organ failure and even death in patients affected by COVID-19. Baicalin's main pharmacological mechanisms in the treatment of CS were revealed by studying potential targets and baicalin's pathways.	You et al., 2022
To understand baicalin's effects and potential mechanisms on the treatment of chronic gastritis, baicalin-affected proteins and several signaling pathways were studied through proteomic technology, providing relevant insights into the discovery of possible target proteins for chronic gastritis treatment.	Ji et al., 2022
Baicalin may be effective in improving degenerating ovarian function and delaying ovarian aging as it shows potential in increasing the viability of ovarian granulosa cells and the secretion of steroid hormones.	Fan et al., 2022
Baicalin induces myelin production and regeneration through activation of the PPARγ (peroxisome proliferator-activated receptor γ) signal pathway and has proved to be a valid natural product for treating demyelinating diseases.	Ai et al., 2022
The efficacy of baicalin on memory improvement could result from increased synaptic plasticity, mitochondrial fragmentation, and recovery of dysfunction through the inhibition of PDE4 (phosphodiestease4), which is responsible for the activation of pDrp1S637 (phosphorylated Ser637 site of mitochondrial dynamin-related protein 1) in the AβO (amyloid-β oligomer)-induced model.	Yu et al., 2022
Baicalin may promote inflammatory resolution by incrementing efferocytosis by its antioxidant activity via a RhoA (Ras homolog family member A)-dependent pathway and by regulating macrophage polarization.	Cai et al., 2022
Baicalin alleviates ATO (acute arsenic trioxide)-induced hepatic damage in mice, by inhibiting oxidative stress and thus reducing inflammation and apoptosis. This protective mechanism may be associated with the JAK2 (Janus kinase 2)/STAT3 (signal transducer and activator of transcription 3) signaling pathway.	He et al., 2022
Baicalin aid periodontal tissue regeneration by increasing OPG (osteoprotegerin) expression in HCEM (human cementoblast cell line) cells through the Wnt/beta-catenin signaling pathway.	Kunimatsu et al., 2022

Key findings	Reference
Baicalin has been shown to effectively improve the developmental ability and quality of heat-stressed mouse embryos through a mechanism by which mitochondrial quality is increased by activation of the ERK1/2 (extracellular regulated kinase 1/2) signaling pathway and promotion of anti-cellular apoptosis.	Li et al., 2022
Baicalin may be an interesting preventive or adjuvant therapeutic agent in breast cancer treatment in combination with 5-FU (5-Fluorouracil), primarily acting via cooperative inhibition of angiogenesis, inflammation, and triggering of apoptotic cell death.	Shehatta et al., 2022
Baicalin might be valuable in treating rhinosinusitis, as it effectively decreases sinonasal inflammation in a mouse model by restoring the immunological balance of Treg (regulatory T cell)/Th17 (T-helper 17) responses.	Yang et al., 2022
Baicalin acts as an anticancer agent by inducing FTH1 (ferritin heavy chain 1)-dependent ferroptosis. Therefore it may be a candidate drug for the treatment of bladder cancer.	Kong et al., 2021
Baicalin effectively prevents EMT (epithelial-mesenchymal transition) by suppressing the PDK1 (phosphatidylinositide-dependent protein kinase 1) and AKT (protein kinase B) pathway in human NSCLC (non-small cell lung cancer) and therefore may be a valuable alternative compound for carcinoma treatment and a new candidate antimetastasis medication.	Chen et al., 2021
Baicalin inhibited APEC (avian pathogenic Escherichia coli) lung infection by remodeling gut microbiota dysbiosis and incrementing SCFA (short-chain fatty acid) production. Therefore, baicalin may become an alternative antibiotic and a new therapy for preventing or treating APEC infection.	Peng et al., 2021
Baicalin may be a valid candidate for preventing inflammation generated by MG (Mycoplasma gallisepticum) infection in macrophages, as it protected HD11 cells from MG-induced oxidative stress and inflammation by opposite modulation of TLR-2-NF-κB-mediated NLRP3-inflammasome pathway and autophagy.	Ishfaq et al., 2021
Baicalin prompts chondrocyte viability and cell-matrix synthesis via the TGF-β (Transforming Growth Factor-β)/Smad3 (Suppressor of Mothers Against Decapentaplegic 2) pathway in the IL-1β (Interleukin-1β)-treated chondrocytes and DMM (destabilization of the medial meniscus)-treated mice. As a result, baicalin may be a possible novel therapy for osteoarthritis.	Wang et al., 2021
Baicalin can prevent HFD (high-fat diet)-induced obesity in mice mainly by inducing adipocyte thermogenesis, and therefore it may be an interesting compound for treating human obesity and related metabolic disorders.	Li and Tang, 2021
Baicalin may mitigate ATO-induced cardiac toxicity by limiting oxidative stress, apoptosis, and inflammation, and its mechanism is connected to the inhibition of the TLR4/NF-κB signaling pathway.	Sun et al., 2021
Baicalin is effective in ameliorating DN (diabetic nephropathy) by lessening oxidative stress and inflammation via the activation of the Nrf2 (nuclear erythroid 2-related factor 2)-mediated antioxidant signaling pathway and the inhibition of the MAPK-mediated inflammatory signaling pathway.	Ma et al., 2021
Baicalin showed a protective effect against oxidative stress by decreasing the caerulein-induced death of AR42J acinar cells and lessening the caerulein-induced damage in pancreatic acinar cells. The mechanism may be related to the reduced expression of Mir-136-5p and the increased expression of the SOD1 (superoxide dismutase1) gene and protein.	Zhao et al., 2021
Baicalin is an interesting potential drug for treating NS (nephrotic syndrome), as it has proved effective in attenuating adriamycin-induced NS by suppressing fibrosis-related genes and preventing inflammatory reactions. These genes may represent potential therapeutic targets.	Tan et al., 2021
Baicalin has the ability to ameliorate COPD (chronic obstructive pulmonary disease) via upregulation of HSP72 (Heat shock protein 72) expression, which results in the inhibition of JNK (c-Jun N-terminal kinase) signaling activation.	Hao et al., 2021

Key findings	Reference
Baicalin and baicalein may be potential drugs acting on HN (hyperuricemic nephropathy) as they inhibit XO (xanthine oxidase) activity, thus decreasing inflammation and cell apoptosis by down-regulation of the TLRs/NLRP3/NF-κB, MAPK, PI3K/AKT/NF-κB pathways.	Xiang et al., 2021
Baicalin proved to be an effective anti-tumor compound in CRC (colorectal cancer cells) partly via down-regulation of circMYH9 (circRNA myosin heavy chain 9) and HDGF (hepatoma-derived growth factor) and up-regulation of miR-761.	Zhang et al., 2021
Baicalin may exert antidepressant activity by promoting hippocampal neurogenesis by regulating the Wnt/β-catenin signaling pathway.	Xiao et al., 2021
Baicalin shows cardioprotective effects against myocardial ischemia/reperfusion injury by suppressing ACSL4 (acyl-CoA synthetase long-chain family member 4)-controlled ferroptosis, revealing a new target for preventing myocardial ischemia/reperfusion damage.	Fan et al., 2021
Baicalin shows protective effects against DHAV-1 (Duck hepatitis A virus type 1)-induced oxidative stress in hepatic mitochondria inducing activation of the Nrf2/ARE (antioxidant responsive element) signaling pathway.	Su et al., 2021
Baicalin can regulate NF-κB activation in intestinal epithelial cells and modulate autophagic and inflammatory processes, thereby leading to improved paracellular permeability. Therefore, baicalin's anti-inflammatory activity may be linked to the regulation of autophagic flux.	Rizzo et al., 2021
Baicalin offers cardioprotection against ischemic myocardial injury after CA (cardiac arrest) as it suppresses Drp1-mediated mitochondrial fission. Therefore, baicalin shows the potential to become a novel therapy for the treatment of post-CA myocardial injury.	Wu et al., 2021
Baicalin exerted its antitumor activity on lung cancer cells primarily by prompting Akt-dependent cell cycle arrest and apoptosis, demonstrating high potential for developing a new drug targeting lung cancer.	Sui et al., 2021
Baicalin may exert protective effects on endothelial cells against As_2O_3 (arsenic trioxide, an environmental pollutant)-induced oxidative damage and apoptosis.	Tsai et al., 2021
Baicalin possesses therapeutic activity towards AP (acute pancreatitis), implemented by augmenting miR-15a levels and inhibiting CDC42/MAP3K1, thus acting as a brake on AP by targeting MAP2K4 and inhibiting the JNK signaling pathway.	Zhen et al., 2021
Mycoplasma gallisepticum (MG) provokes severe inflammation of the lungs and damages cells through the activation of TLR signaling, NF-κB pathway, and pro-inflammatory cytokine gene expression. Baicalin has shown protective activity against MG-induced chicken lung inflammation, by suppressing TLR6-mediated NF-κB signaling.	Zou et al., 2021
Baicalin dietary supplementation might increase feed efficiency, improve the antioxidative ability, and provide protection against oxidative stress-related hepatotoxicity in tilapia.	Jia et al., 2021
Baicalin may be a valuable alternative therapeutic option to resolve type 2 inflammatory diseases, such as ECRS (eosinophilic chronic rhinosinusitis) and comorbid asthma, as it can interfere with the interaction between mast cells and airway epithelial cells.	Yoshida et al., 2021
Baicalin showed protective activity on bacterial-induced endometritis in rabbits by suppressing NF-κB and JNK signaling pathways and pro-inflammatory cytokines.	Miao et al., 2021
Baicalin may induce ECM (extracellular matrix) synthesis and marker gene expression in chondrocytes by activating HIF-1α (hypoxia-inducible-factor-1α), thus representing a possible novel clinical drug for the treatment of osteoarthritis.	Wang et al., 2020
Baicalin may alleviate diabetes-induced renal injury due to a partial modulation of the Klotho promoter methylation, providing new insights into the treatment of diabetic nephropathy.	Zhang et al., 2020

Key findings	Reference
Baicalin proved effective in inhibiting the inflammation caused by a joint infection of Mycoplasma gallisepticum and E. coli in chicken, also providing scientific ground for future dose-response and drug-target interaction studies.	Wu et al., 2020
Baicalin might exert its anti-inflammatory activity in Propionibacterium-induced acne through inhibition of the NF-κB/MAPK signaling pathways and subsequent suppression of the activation of the NLRP3 inflammasome both *in vivo* and *in vitro*.	Fang et al., 2020
Baicalin may reduce the symptoms of pregnancy-induced hypertension, as it alleviates vascular endothelial cell damage in pregnant hypertensive rats through the promotion of VEGF (vascular endothelial growth factor), PGI-2 (plasma epoprostenol), eNOS (endothelial nitric oxide synthase), and estrogen expression.	Liu et al., 2020
Baicalin proved effective in decreasing microglia-related neuroinflammation and ameliorating acute neurocognitive deficits in lipopolysaccharide-induced mice via SIRT1 (silent information regulator 1)-dependent downregulation of HMGB1 (high-mobility group box 1), thus being a potential new therapeutic approach in treating acute neurobehavioral deficits including delayed neurocognitive recovery after anesthesia and surgery.	Li et al., 2020
Baicalin could be a new therapeutic approach in treating MDV (Marek's disease virus), as it inhibits viral mRNA, protein levels, and general plaque formation in a time-dependent manner, conjointly inhibiting the virus' replication and directly lowering its infectivity.	Yang et al., 2020
Baicalin showed neuroprotective ability by lessening microglia and astrocyte activation by modulating the inflammatory response by inhibiting the NF-κB expression in the hippocampus with LPS (lipopolysaccharide)-induced neuroinflammation.	Shah et al., 2020
Baicalin proved to be a potent biological compound for restoring the function of EC (endothelial cell) and VSMC (vascular smooth muscle cell) altered by their corresponding microparticles, in addition to inhibiting the release of inflammation markers from activated macrophages.	Paudel and Kim, 2020
Baicalin can inhibit orthodontically-induced inflammatory root resorption by enhancing Runx-2 expression and reducing TNF-α expression, while not affecting tooth movement distance.	Lin et al., 2020
Baicalin might protect piglets from Glaesserella parasuis by improving the inflammatory reaction caused by the bacteria, by decreasing HMGB1 release, diminishing cell apoptosis, and inhibiting MAPK signaling activation. Therefore, baicalin could be used as a novel treatment against G. parasuis infection.	Fu et al., 2020
Intrathecal injection of baicalin has proved effective in producing an antiallodynic effect in spinal nerve ligation-induced neuropathic pain model in rats. The regulation of α2-AR (α2-adrenoceptors) expression might be involved in the mechanism of action.	Huang et al., 2020
Baicalin effectively stimulates liver regeneration in mice after acetaminophen-induced acute liver damage by prompting Nrf2 accumulation in the cytoplasm, which leads to NLRP3 inflammasome activation, and a subsequent increase in the expression of IL-18 (interleukin-18), which stimulates the proliferation of hepatocytes.	Shi et al., 2020
Baicalin ameliorates post-ischemia/reperfusion myocardial injury and lessens inflammation via the JAK/STAT pathway. Therefore, baicalin might be a novel approach for treating myocardial ischaemic complications.	Xu et al., 2020
Baicalin could be an effective treatment for BC (breast cancer) since results show it strongly triggered apoptosis, inhibited metastasis, and enhanced the chemosensitivity of BC.	Zeng et al., 2020
Baicalin can be considered as a possible novel renoprotective agent against podocyte EMT in FSGS (focal segmental glomerular sclerosis) due to its promotion of negative regulation of the Notch1-Snail axis.	Dou et al., 2020

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Conflict of interest

The authors declare no conflict of interest.

REFERENCES

Ai RS, Xing K, Deng X, Han JJ, Hao DX, Qi WH, et al. Baicalin promotes CNS remyelination via PPARγ signal pathway. Neurol Neuroimmunol Neuroinflamm. 2022;9(2):e1142.

Cai X, Shi Y, Dai Y, Wang F, Chen X, Li X. Baicalin clears inflammation by enhancing macrophage efferocytosis via inhibition of RhoA/ROCK signaling pathway and regulating macrophage polarization. Int Immunopharmacol. 2022;105:108532.

Changle Z, Cuiling F, Feng F, Xiaoqin Y, Guishu W, Liangtian S, et al. Baicalin inhibits inflammation of lipopolysaccharide-induced acute lung injury via toll like receptor-4/myeloid differentiation primary response 88/nuclear factor-kappa B signaling pathway. J Tradit Chin Med. 2022;42(2):200.

Chen J, Yuan CB, Yang B, Zhou X. Baicalin inhibits EMT through PDK1/AKT signaling in human non-small cell lung cancer. J Oncol. 2021;2021:4391581.

Cui L, Yuan T, Zeng Z, Liu D, Liu C, Guo J, et al. Mechanistic and therapeutic perspectives of baicalin and baicalein on pulmonary hypertension: A comprehensive review. Biomed Pharmacother. 2022;151: 113191.

Dou Y, Shang Y, Shen Y, Qu J, Liu C, Cao J. Baicalin alleviates adriamycin-induced focal segmental glomerulosclerosis and proteinuria by inhibiting the Notch1-Snail axis mediated podocyte EMT. Life Sci. 2020; 257:118010.

Fan H, He J, Bai Y, He Q, Zhang T, Zhang J, et al. Baicalin improves the functions of granulosa cells and the ovary in aged mice through the mTOR signaling pathway. J Ovarian Res. 2022;15(1):34.

Fan Z, Cai L, Wang S, Wang J, Chen B. Baicalin prevents myocardial ischemia/reperfusion injury through inhibiting ACSL4 mediated ferroptosis. Front Pharmacol. 2021;12:628988.

Fang F, Xie Z, Quan J, Wei X, Wang L, Yang L. Baicalin suppresses Propionibacterium acnes-induced skin inflammation by downregulating the NF-κB/MAPK signaling pathway and inhibiting activation of NLRP3 inflammasome. Braz J Med Biol Res. 2020;53(12): e9949.

Fang L, Wang HF, Chen YM, Bai RX, Du SY. Baicalin confers hepatoprotective effect against alcohol-associated liver disease by upregulating microRNA-205. Int Immunopharmacol. 2022;107:108553.

Fu S, Yin R, Zuo S, Liu J, Zhang Y, Guo L, et al. The effects of baicalin on piglets challenged with Glaesserella parasuis. Vet Res. 2020;51(1):102.

Hao D, Li Y, Shi J, Jiang J. Baicalin alleviates chronic obstructive pulmonary disease through regulation of HSP72-mediated JNK pathway. Mol Med. 2021;27(1): 53.

He Q, Sun X, Zhang M, Chu L, Zhao Y, Wu Y, et al. Protective effect of baicalin against arsenic trioxide-induced acute hepatic injury in mice through JAK2/STAT3 signaling pathway. Int J Immunopathol Pharmacol. 2022;36:20587384211073397.

Hu Z, Guan Y, Hu W, Xu Z, Ishfaq M. An overview of pharmacological activities of baicalin and its aglycone baicalein: New insights into molecular mechanisms and signaling pathways. Iran J Basic Med Sci. 2022;25: 14-26.

Huang LJ, Jia SS, Sun XH, Li XY, Wang FF, Li W, et al. Baicalin relieves neuropathic pain by regulating α2-adrenoceptor levels in rats following spinal nerve injury. Exp Ther Med. 2020;20:2684-90.

Ishfaq M, Wu Z, Wang J, Li R, Chen C, Li J. Baicalin alleviates Mycoplasma gallisepticum-induced oxidative stress and inflammation via modulating NLRP3 inflammasome-autophagy pathway. Int Immunopharmacol. 2021;101(Pt B):108250.

Ji W, Huo Y, Zhang Y, Wang X, Zhang Y. Revealing therapeutic targets and mechanism of baicalin for anti-chronic gastritis using proteomic analysis of the gastric tissue. J Chromatogr B Analyt Technol Biomed Life Sci. 2022;1196:123214.

Jia R, Du J, Cao L, Feng W, Xu P, Yin G. Effects of dietary baicalin supplementation on growth performance, antioxidative status and protection against oxidative stress-induced liver injury in GIFT tilapia (Oreochromis niloticus). Comp Biochem Physiol C Toxicol Pharmacol. 2021;240:108914.

Kong N, Chen X, Feng J, Duan T, Liu S, Sun X, et al. Baicalin induces ferroptosis in bladder cancer cells by downregulating FTH1. Acta Pharm Sin B. 2021;11: 4045-54.

Kumar S, Pandey AK. Chemistry and biological activities of flavonoids: an overview. ScientificWorldJournal. 2013;2013:162750.

Kunimatsu R, Kimura A, Sakata S, Tsuka Y, Yoshimi Y, Abe T, et al. Effects of baicalin on the proliferation and expression of OPG and RANKL in human cementoblast-lineage cells. J Dent Sci. 2022;17:162-9.

Li H, Cong X, Sui J, Jiang Z, Fu K, Huan Y, et al. Baicalin enhances the thermotolerance of mouse blastocysts by activating the ERK1/2 signaling pathway and preventing mitochondrial dysfunction. Theriogenology. 2022;178:85-94.

Li H, Tang S. Baicalin attenuates diet-induced obesity partially through promoting thermogenesis in adipose tissue. Obes Res Clin Pract. 2021;15:485-90.

Li K, Liang Y, Cheng A, Wang Q, Li Y, Wei H, et al. Antiviral properties of baicalin: A concise review. Rev Bras Farmacogn. 2021;31:408-19.

Li Y, Liu T, Li Y, Han D, Hong J, Yang N, et al. Baicalin ameliorates cognitive impairment and protects microglia from LPS-induced neuroinflammation via the SIRT1/HMGB1 pathway. Oxid Med Cell Longev. 2020;2020:4751349.

Liang W, Huang X, Chen W. The effects of baicalin and baicalein on cerebral ischemia: a review. Aging Dis. 2017;8:850-67.

Lin P, Guo XX, Wang YL, Wei ZL, Xin HY, Liu TB. Inhibitory effect of baicalin on orthodontically induced inflammatory root resorption in rats. J Int Med Res. 2020;48(9):0300060520955070.

Lin Y, Wang ZY, Wang MJ, Jiang ZM, Qin YQ, Huang TQ, et al. Baicalin attenuate diet-induced metabolic syndrome by improving abnormal metabolism and gut microbiota. Eur J Pharmacol. 2022;925: 174996.

Liu Y, Xiong M, Zhou F, Shi N, Jia Y. Effect of baicalin on gestational hypertension-induced vascular endothelial cell damage. J Int Med Res. 2020;48(10): 0300060520934288.

Ma L, Wu F, Shao Q, Chen G, Xu L, Lu F. Baicalin alleviates oxidative stress and inflammation in diabetic nephropathy via Nrf2 and MAPK signaling pathway. Drug Des Devel Ther. 2021;15:3207-21.

Miao Y, Ishfaq M, Liu Y, Wu Z, Wang J, Li R, et al. Baicalin attenuates endometritis in a rabbit model induced by infection with Escherichia coli and Staphylococcus aureus via NF-κB and JNK signaling pathways. Domest Anim Endocrinol. 2021;74:106508.

Nagashima S, Hirotani M, Yoshikawa T. Purification and characterization of UDP-glucuronate: baicalein 7-O-glucuronosyltransferase from Scutellaria baicalensis Georgi. cell suspension cultures. Phytochemistry. 2000;53:533-8.

Pan L, Cho KS, Yi I, To CH, Chen DF, Do CW. Baicalein, baicalin, and wogonin: protective effects against ischemia-induced neurodegeneration in the brain and retina. Oxid Med Cell Longev. 2021;2021: 8377362.

Panche AN, Diwan AD, Chandra SR. Flavonoids: an overview. J Nutr Sci. 2016;5:e47.

Paudel KR, Kim DW. Microparticles-mediated vascular inflammation and its amelioration by antioxidant activity of baicalin. Antioxidants. 2020;9(9):890.

Peng LY, Shi HT, Tan YR, Shen SY, Yi PF, Shen HQ, et al. Baicalin inhibits APEC-induced lung injury by regulating gut microbiota and SCFA production. Food Funct. 2021;12:12621-33.

Rizzo V, Ferlazzo N, Currò M, Isola G, Matarese M, Bertuccio MP, et al. Baicalin-induced autophagy preserved LPS-stimulated intestinal cells from inflammation and alterations of paracellular permeability. Int J Mol Sci. 2021;22(5):2315.

Santos-Buelga C, Feliciano AS. Flavonoids: from structure to health issues. Molecules. 2017;22(3):477.

Shah MA, Park DJ, Kang JB, Kim MO, Koh PO. Baicalin alleviates lipopolysaccharide-induced neuroglial activation and inflammatory factors activation in hippocampus of adult mice. Lab Anim Res. 2020;36:32.

Shehatta NH, Okda TM, Omran GA, Abd-Alhaseeb MM. Baicalin; a promising chemopreventive agent, enhances the antitumor effect of 5-FU against breast cancer and inhibits tumor growth and angiogenesis in Ehrlich solid tumor. Biomed Pharmacother. 2022;146: 112599.

Shi L, Zhang S, Huang Z, Hu F, Zhang T, Wei M, et al. Baicalin promotes liver regeneration after acetaminophen-induced liver injury by inducing NLRP3 inflammasome activation. Free Radic Biol Med. 2020; 160:163-77.

Song Z, He C, Yu W, Yang M, Li Z, Li P, et al. Baicalin attenuated Aβ1-42-induced apoptosis in SH-SY5Y cells by inhibiting the Ras-ERK signaling pathway. BioMed Res Int. 2022;2022:9491755.

Su L, Wang R, Qiu T, Wang J, Meng J, Zhu J, et al. The protective effect of baicalin on duck hepatitis A virus type 1-induced duck hepatic mitochondria dysfunction by activating nuclear erythroid 2-related factor 2/antioxidant responsive element signaling pathway. Poult Sci. 2021;100(5):101032.

Sui X, Han X, Chen P, Wu Q, Feng J, Duan T, et al. Baicalin induces apoptosis and suppresses the cell cycle progression of lung cancer cells through downregulating Akt/mTOR signaling pathway. Front Mol Biosci. 2021;7:602282.

Sun X, Wang X, He Q, Zhang M, Chu L, Zhao Y, et al. Investigation of the ameliorative effects of baicalin against arsenic trioxide-induced cardiac toxicity in mice. Int Immunopharmacol. 2021;99:108024.

Sun X, Pisano M, Xu L, Sun F, Xu J, Zheng W, et al. Baicalin regulates autophagy to interfere with small intestinal acute graft-versus-host disease. Sci Rep. 2022; 12(1):6551.

Tan N, Sun CX, Zhu HJ, Li DY, Huang SG, He SD. Baicalin attenuates adriamycin-induced nephrotic syndrome by regulating fibrosis procession and inflammatory reaction. Genes Genomics. 2021;43:1011-21.

Tsai CL, Tsai CW, Chang WS, Lin JC, Hsia TC, Bau DT. Protective effects of baicalin on arsenic trioxide-induced oxidative damage and apoptosis in human umbilical vein endothelial cells. In Vivo. 2021;35:155-62.

Wang P, Zhu P, Liu R, Meng Q, Li S. Baicalin promotes extracellular matrix synthesis in chondrocytes via the activation of hypoxia-inducible factor-1α. Exp Ther Med. 2020;20(6):226.

Wang P, Liu J, Zhang S, Zhu P, Xiong X, Yu C, et al. Baicalin promotes chondrocyte viability and the synthesis of extracellular matrix through TGF-β/Smad3 pathway in chondrocytes. Am J Transl Res. 2021;13: 10908-21.

Wang X, Xie L, Long J, Liu K, Lu J, Liang Y, et al. Therapeutic effect of baicalin on inflammatory bowel disease: a review. J Ethnopharmacol. 2022;283: 114749.

Wu J, Chen H, Qin J, Chen N, Lu S, Jin J, et al. Baicalin improves cardiac outcome and survival by suppressing Drp1-mediated mitochondrial fission after cardiac arrest-induced myocardial damage. Oxid Med Cell Longev. 2021;2021:8865762.

Wu Z, Fan Q, Miao Y, Tian E, Ishfaq M, Li J. Baicalin inhibits inflammation caused by coinfection of Mycoplasma gallisepticum and Escherichia coli involving IL-17 signaling pathway. Poult Sci. 2020;99:5472-80.

Xiang H, Lei H, Liu Z, Liu Y, Li Y, Qiu Y, et al. Network pharmacology and molecular docking analysis on molecular targets: Mechanisms of baicalin and baicalein against hyperuricemic nephropathy. Toxicol Appl Pharmacol. 2021;424:115594.

Xiao Z, Cao Z, Yang J, Jia Z, Du Y, Sun G, et al. Baicalin promotes hippocampal neurogenesis via the Wnt/β-catenin pathway in a chronic unpredictable mild stress-induced mouse model of depression. Biochem Pharmacol. 2021;190:114594.

Xu M, Li X, Song L. Baicalin regulates macrophages polarization and alleviates myocardial ischaemia/reperfusion injury via inhibiting JAK/STAT pathway. Pharm Biol. 2020;58:655-63.

Yang F, Feng C, Yao Y, Qin A, Shao H, Qian K. Antiviral effect of baicalin on Marek's disease virus in CEF cells. BMC Vet Res. 2020;16(1):371.

Yang M, Zhu X, Fu F, Guo Q, Zhu X, Xu Y, et al. Baicalin ameliorates inflammatory response in a mouse model of rhinosinusitis via regulating the Treg/Th17 balance. Ear Nose Throat J. 2022;101(2S):8S-16S.

Yoshida K, Takabayashi T, Kaneko A, Takiyama M, Sakashita M, Imoto Y, et al. Baicalin suppresses type 2 immunity through breaking off the interplay between mast cell and airway epithelial cell. J Ethnopharmacol. 2021;267:113492.

You J, Li H, Fan P, Yang X, Wei Y, Zheng L, et al. Inspiration for COVID-19 treatment: network analysis and experimental validation of baicalin for cytokine storm. Front Pharmacol. 2022;13:853496.

Yu HY, Zhu Y, Zhang XL, Wang L, Zhou YM, Zhang FF, et al. Baicalin attenuates amyloid β oligomers induced memory deficits and mitochondria fragmentation through regulation of PDE-PKA-Drp1 signalling. Psychopharmacology. 2022;239:851-65.

Zeng A, Liang X, Zhu S, Liu C, Luo X, Zhang Q, et al. Baicalin, a potent inhibitor of NF-κB signaling pathway, enhances chemosensitivity of breast cancer cells to docetaxel and inhibits tumor growth and metastasis both in vitro and in vivo. Front Pharmacol. 2020;11: 879.

Zhang W, Liu Q, Luo L, Song J, Han K, Liu R, et al. Use Chou's 5-steps rule to study how Baicalin suppresses the malignant phenotypes and induces the apoptosis of colorectal cancer cells. Arch Biochem Biophys. 2021;705:108919.

Zhang XT, Wang G, Ye LF, Pu Y, Li RT, Liang J, et al. Baicalin reversal of DNA hypermethylation-associated Klotho suppression ameliorates renal injury in type 1 diabetic mouse model. Cell Cycle. 2020;19: 3329-47.

Zhao ZF, Zhang Y, Sun Y, Zhang CH, Liu MW. Protective effects of baicalin on caerulein-induced AR42J pancreatic acinar cells by attenuating oxidative stress through miR-136-5p downregulation. Sci Prog. 2021; 104(2):00368504211026118.

Zhen J, Chen W, Liu Y, Zang X. Baicalin protects against acute pancreatitis involving JNK signaling pathway via regulating miR-15a. Am J Chin Med. 2021;49:147-61.

Zou M, Yang L, Niu L, Zhao Y, Sun Y, Fu Y, et al. Baicalin ameliorates Mycoplasma gallisepticum-induced lung inflammation in chicken by inhibiting TLR6-mediated NF-κB signalling. Br Poult Sci. 2021; 62:199-210.