Shikonin

Cat. No.: HY-N0822

CAS No.: 517-89-5

Molecular Formula: $C_{16}H_{16}O_5$

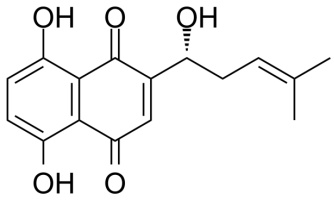
Molecular Weight: 288.3

Target: Chloride Channel; Pyruvate Kinase; NF-κB; TNF Receptor; HIV

Pathway: Membrane Transporter/Ion Channel; Metabolic Enzyme/Protease; NF-κB; Apoptosis; Anti-infection

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (86.72 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	3.4686 mL	17.3430 mL	34.6861 mL
	5 mM	0.6937 mL	3.4686 mL	6.9372 mL
	10 mM	0.3469 mL	1.7343 mL	3.4686 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 0.5% CMC-Na/saline water
   Solubility: 30 mg/mL (104.06 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (7.21 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (7.21 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (7.21 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Shikonin is a major component of a Chinese herbal medicine named zicao. Shikonin is a potent TMEM16A chloride channel inhibitor with an IC_{50} of 6.5 μM[1]. Shikonin is a specific pyruvate kinase M2 (PKM2) inhibitor[2] and can also inhibit TNF-α and NF-κB pathway[3]. Shikonin decreases exosome secretion through the inhibition of glycolysis[4]. Shikonin inhibits AIM2 inflammasome activation[7].

IC_{50} & Target	TMEM16A chloride channel 6.5 μM (IC_{50})	PKM2	NF-κB	TNF-α

In Vitro

Shikonin is an inhibitor of TMEM16A chloride channel with an IC_{50} of 6.5 μM[1]. Shikonin is also a specific inhibitor of PKM2[2] and can also inhibit tumor necrosis factor-α (TNF-α) and prevent activation of nuclear factor-κB (NF-κB) pathway. Shikonin at concentrations higher than 50 μM significantly inhibits ormal human keratinocytes (NHKs) viability, compare with that of control (P<0.05). Pretreatment with Shikonin for 2 h attenuates TNF-α-induced NF-κB p65 nuclear translocation[3]. Treatments of Shikonin at 5 and 7.5 μM significantly inhibit the cell viability starting from 12 h and the inhibitory effects are presented in time-dependent patterns compare with the 0 h group in both cell lines. It is found that 5 μM Shikonin displays greater inhibition compare to 2.5 μM at the time points from 24 to 48 h. The invasiveness of U87 and U251 cells is significantly attenuated when treated with Shikonin at 2.5, 5, and 7.5 μM compare with the control group at 24 and 48 h (p<0.01)[4].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Shikonin significantly inhibits the increase in IL-1β and TNF-α expression levels in the rat model of osteoarthritis, compare with those in the osteoarthritis group (P<0.01). The NF-κB protein expression level is significantly suppressed by Shikonin in the rat model of osteoarthritis, compare with that in the osteoarthritis group (P<0.01). The induction of the iNOS level is suppressed by treatment with Shikonin in the rat model of osteoarthritis, compare with that in the osteoarthritis group (P<0.01). The administration of Shikonin markedly weakens the up-regulation of COX-2 protein expression in the rat model of osteoarthritis, as compare with that in the osteoarthritis group (P<0.01). The elevation of caspase-3 activity is significantly reduced by Shikonin treatment in the rat model of osteoarthritis, compare with that in the osteoarthritis group (P<0.01). The downregulation of Akt phosphorylation is also significantly recovered by treatment with Shikonin in the rat model of osteoarthritis, compare with that in the osteoarthritis group (P<0.01)[5].

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PROTOCOL

Cell Assay [4]

U87 and U251 cells are seeded into 96-well plates at a density of 1×10^4 cells per well in standard DMEM and incubated for 24 h under standard conditions (37°C and 5% CO_2). Then the medium is replaced with either blank, serum-free DMEM or DMEM containing Shikonin at concentrations of 2.5, 5, and 7.5 μM. The total volume in each well is 200 μL. Finally, the plates are shaken softly and the optical density is recorded at 570 nm (OD_{570}) using a plate reader. At least three independent experiments are performed[4].

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Animal Administration [5]

Healthy male Sprague-Dawley rats (n=30; 8 to 10-weeks old, 250 to 300 g) are used in this study. Rats are randomly assigned to three groups: Sham-operated group (n=10), osteoarthritis model group (n=10) and Shikonin-treated group (n=10). In the sham-operated group, the right knee joint of the anesthetized rat is only exposed under sterile conditions, and the rats are treated with 0.1 ml/100 g physiological saline (i.p.). In the osteoarthritis model group, osteoarthritis model rats were treated with 0.1 ml/100 g physiological saline (i.p.). In the Shikonin-treated group, osteoarthritis model rats are treated with 10 mg/kg Shikonin (i.p.) once daily for 4 days after osteoarthritis modeling[5].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Environ Pollut. 15 February 2022, 118708.
- Int J Oncol. November 1, 2021.
- Int J Biochem Cell Biol. 2018 Mar;96:9-19.
- J Cancer. 2021; 12(16):4830-4840.

- Oncol Rep. 2020 Sep;44(3):1049-1063.

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REFERENCES

[1]. Jiang Y et al. Shikonin Inhibits Intestinal Calcium-Activated Chloride Channels and Prevents Rotaviral Diarrhea. Front Pharmacol. 2016 Aug 23;7:270.

[2]. Li W, et al. Shikonin Suppresses Skin Carcinogenesis via Inhibiting Cell Proliferation. PLoS One. 2015 May 11;10(5):e0126459.

[3]. Yan Y, et al. Shikonin Promotes Skin Cell Proliferation and Inhibits Nuclear Factor-κB Translocation via Proteasome Inhibition In Vitro. Chin Med J (Engl). 2015 Aug 20;128(16):2228-33.

[4]. Zhang FY, et al. Shikonin Inhibits the Migration and Invasion of Human Glioblastoma Cells by Targeting Phosphorylated β-Catenin and Phosphorylated PI3K/Akt: A Potential Mechanism for the Anti-Glioma Efficacy of a Traditional Chinese Herbal Medicine. Int J Mol Sci. 2015 Oct 9;16(10):23823-48.

[5]. Fu D, et al. Shikonin inhibits inflammation and chondrocyte apoptosis by regulation of the PI3K/Akt signaling pathway in a rat model of osteoarthritis. Exp Ther Med. 2016 Oct;12(4):2735-2740.

[6]. Kathleen M McAndrews, et al. Mechanisms associated with biogenesis of exosomes in cancer. Mol Cancer. 2019 Mar 30;18(1):52.

[7]. Jernej Zorman, et al. Shikonin Suppresses NLRP3 and AIM2 Inflammasomes by Direct Inhibition of Caspase-1. PLoS One. 2016 Jul 28;11(7):e0159826.

India Contact:
Life Technologies (India) Pvt. Ltd.
306, Aggarwal City Mall, Opposite M2K Pitampura, Delhi – 110034 (INDIA). Ph: +91-11-42208000, 42208111, 42208222, Mobile: +91-9810521400, Fax: +91-11-42208444
Email: customerservice@lifetechindia.com Website: www.lifetechindia.com