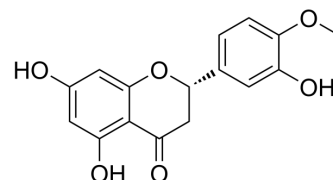


## Hesperetin

<b>Cat. No.:</b>	HY-N0168		
<b>CAS No.:</b>	520-33-2		
<b>Molecular Formula:</b>	C <sub>16</sub> H <sub>14</sub> O <sub>6</sub>		
<b>Molecular Weight:</b>	302.28		
<b>Target:</b>	p38 MAPK; Apoptosis; Autophagy; p38 MAPK		
<b>Pathway:</b>	MAPK/ERK Pathway; Apoptosis; Autophagy		
<b>Storage:</b>	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



### SOLVENT & SOLUBILITY

#### In Vitro

DMSO : 125 mg/mL (413.52 mM; Need ultrasonic)

Concentration	Mass		
	1 mg	5 mg	10 mg
1 mM	3.3082 mL	16.5410 mL	33.0819 mL
5 mM	0.6616 mL	3.3082 mL	6.6164 mL
10 mM	0.3308 mL	1.6541 mL	3.3082 mL

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

#### In Vivo

- Add each solvent one by one: 0.5% CMC/saline water  
Solubility: 20 mg/mL (66.16 mM); Suspended solution; Need ultrasonic
- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline  
Solubility: ≥ 2.5 mg/mL (8.27 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
Solubility: ≥ 2.5 mg/mL (8.27 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil  
Solubility: ≥ 2.5 mg/mL (8.27 mM); Clear solution

### BIOLOGICAL ACTIVITY

#### Description

Hesperetin is a natural flavanone, and acts as a potent and broad-spectrum inhibitor against human UGT activity. Hesperetin regulates apoptosis.

#### In Vitro

Hesperetin has the retention of antioxidant potential in self nano-emulsifying drug delivery system<sup>[1]</sup>. Hesperetin and NGR display broad-spectrum inhibition against human UGTs. Besides, Hesperetin exhibits strong inhibitory effects on UGT1A1,

1A3 and 1A9 (both IC<sub>50</sub> and K<sub>i</sub> values lower than 10 μM) and moderately inhibits UGT1A4, UGT1A7, UGT1A8 (IC<sub>50</sub> values 29.68-63.87 μM)<sup>[2]</sup>. Hesperetin interacts with different types of proteins involving hydrogen bonds, pi-pi effects, pi-cation bonding and pi-sigma interactions with varying binding energies. Hesperetin exhibits drug-like properties which projects its potential as a therapeutic option for CHIKV infection<sup>[3]</sup>. Hesperetin dose-dependently reduces GCDCA-induced caspase-3 activity in cultured primary rat hepatocytes. Hesperetin also dose-dependently reduces CM-induced Nos2 (iNOS) expression in hepatocytes. Interestingly, hesperetin-induced expression of the antioxidant gene haem oxygenase 1 (HO-1) about fourfold compared with cytokine mixture alone<sup>[5]</sup>.

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

#### In Vivo

Preadministration of Hesperetin (40 mg/kg b.w., oral) significantly attenuates the Cd-induced oxidative stress and mitochondrial dysfunction, restores the antioxidant and membrane-bound enzyme activities and decreases apoptosis in the brain of rats<sup>[4]</sup>. Hesperetin (200 mg/kg) attenuates Con A-induced hepatocyte apoptosis and hepatic Nos2 (iNOS) expression in mice. Hesperetin co-treatment also decreases the occurrence of apoptotic bodies, hydropic degeneration, nuclear fragments, autolysis and haemorrhage. The number of leukocytes infiltrated in liver tissue of mice with D-GalN/LPS-induced fulminant hepatitis are significantly decreased by hesperetin in a murine model<sup>[5]</sup>.

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## PROTOCOL

#### Kinase Assay <sup>[4]</sup>

First, 0.5 mL tissue homogenate is diluted with 1 mL water. Then, to this mixture, 2.5 mL ethanol and 1.5 mL chloroform (all reagents chilled) are added and shaken for 1 min at 4°C, then centrifuged. The enzyme activity in the supernatant is determined. The assay mixture contained 1.2 mL sodium pyrophosphate buffer (0.025 M, pH 8.3), 0.1 mL 186 mM phenazine methosulfate (PMS), 0.3 mL 30 mM Nitroblue tetrazolium (NBT), and 0.2 mL of nicotinamide adenine dinucleotide (NADH), and appropriately diluted enzyme preparation and water in a total volume of 3 mL. Reaction is initiated by the addition of NADH. After incubation at 30°C for 90 min, the reaction is stopped by the addition of 1 mL glacial acetic acid. The reaction mixture is stirred vigorously and shaken with 4 mL n-butanol. The intensity of the chromogen in the butanol layer is measured at 560 nm against a butanol blank. A system without enzyme served as control. One unit of enzyme activity is defined as 50% inhibition of NBT reduction in 1 min under the assay conditions.

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

#### Animal Administration <sup>[4]</sup>

After 7 days of adjusting, the animals are randomly divided into 10 experimental groups. Control group (n=8): These animals are treated with the equivalent volume of PBS as used for the administration of Con A and D-GalN/LPS. Control hesperetin group (n=8): The mice are treated with hesperetin 400 mg/kg p.o. in 0.5% sodium carboxymethylcellulose (CMC-Na) solution for 10 days. Con A group (n=15): The animals are treated with the same volume of CMC-Na as used for administration of hesperetin for 10 days and are challenged with Con A (i.v.15 mg/kg). Con A + hesperetin groups: The animals receive various doses of hesperetin (100, 200, 400 mg/kg) p.o. for 10 days before Con A injection (each group n=15). D-GalN/LPS group (n=15): The animals are given CMC-Na for 10 days and injected i.p. with D-GalN (700 mg/kg)/LPS (5 μg/kg). D-GalN/LPS + hesperetin groups: Three doses of hesperetin (100, 200, 400 mg/kg) are given to mice once daily for 10 days. D-GalN (700 mg/kg)/LPS (5 μg/kg) are injected i.p. (each group n=15).

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## CUSTOMER VALIDATION

- Acta Pharm Sin B. 2021 Jan;11(1):143-155.
- Phytother Res. 2024 Jan 17.
- Antioxidants (Basel). 2022, 11(11), 2093.
- Int J Mol Sci. 2022 Sep 7;23(18):10346.
- Infect Dis Ther. 2021 Feb 2;1-12.

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## REFERENCES

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- [3]. Oo A, et al. In silico study on anti-Chikungunya virus activity of hesperetin. *PeerJ*. 2016 Oct 26;4:e2602. eCollection 2016.
- [4]. Shagirtha K, et al. Neuroprotective efficacy of hesperetin against cadmium induced oxidative stress in the brain of rats. *Toxicol Ind Health*. 2016 Nov 1. pii: 0748233716665301
- [5]. Bai X, et al. The protective effect of the natural compound hesperetin against fulminant hepatitis in vivo and in vitro. *Br J Pharmacol*. 2017 Jan;174(1):41-56
- [6]. Li Q, et al. Hesperetin Induces Apoptosis in Human Glioblastoma Cells via p38 MAPK Activation. *Nutr Cancer*. 2019 Jul 11:1-8.
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**Caution: Product has not been fully validated for medical applications. For research use only.**

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