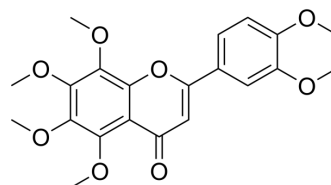


## Nobiletin

<b>Cat. No.:</b>	HY-N0155
<b>CAS No.:</b>	478-01-3
<b>Molecular Formula:</b>	C <sub>21</sub> H <sub>22</sub> O <sub>8</sub>
<b>Molecular Weight:</b>	402.39
<b>Target:</b>	Autophagy; ROR; Reactive Oxygen Species; Apoptosis
<b>Pathway:</b>	Autophagy; Metabolic Enzyme/Protease; Vitamin D Related/Nuclear Receptor; Immunology/Inflammation; NF-κB; Apoptosis
<b>Storage:</b>	Powder    -20°C    3 years 4°C        2 years In solvent   -80°C    1 year -20°C    6 months



### SOLVENT & SOLUBILITY

<b>In Vitro</b>	DMSO : 50 mg/mL (124.26 mM; Need ultrasonic)				
		Solvent Concentration	Mass 1 mg	5 mg	10 mg
	<b>Preparing Stock Solutions</b>	1 mM	2.4852 mL	12.4258 mL	24.8515 mL
		5 mM	0.4970 mL	2.4852 mL	4.9703 mL
10 mM		0.2485 mL	1.2426 mL	2.4852 mL	
Please refer to the solubility information to select the appropriate solvent.					
<b>In Vivo</b>	<ol style="list-style-type: none"> <li>Add each solvent one by one: 10% DMSO &gt;&gt; 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (6.21 mM); Clear solution</li> <li>Add each solvent one by one: 10% DMSO &gt;&gt; 40% PEG300 &gt;&gt; 5% Tween-80 &gt;&gt; 45% saline Solubility: ≥ 2.08 mg/mL (5.17 mM); Clear solution</li> <li>Add each solvent one by one: 10% DMSO &gt;&gt; 90% corn oil Solubility: ≥ 2.08 mg/mL (5.17 mM); Clear solution</li> </ol>				

### BIOLOGICAL ACTIVITY

<b>Description</b>	Nobiletin is a poly-methoxylated flavone from the citrus peel that improves memory loss. Nobiletin is a retinoid acid receptor-related orphan receptors (RORs) agonist. Nobiletin can reduce reactive oxygen species (ROS) levels in differentiated C2C12 myotubes and has anti-inflammation and anti-cancer properties, including anti-angiogenesis, anti-proliferation, anti-metastasis and induced apoptosis <sup>[1][2][3][4]</sup> .
<b>IC<sub>50</sub> &amp; Target</b>	Retinoid acid receptor-related orphan receptors (RORs) <sup>[1]</sup> ; reactive oxygen species (ROS) <sup>[1]</sup> ; apoptosis <sup>[2]</sup>

## In Vitro

Nobiletin (0-100  $\mu$ M; 24 hours; U2OS and HOS cells) treatment progressively reduces protein expressions of MMP-2 and MMP-9. In U2OS and HOS cells, Nobiletin considerably reduces the phosphorylation of p-IKK $\alpha$ / $\beta$  and p-I $\kappa$ B $\alpha$ , and protein expression of NF- $\kappa$ B in the cell nuclear fraction with the concomitant increase of the NF- $\kappa$ B expression in the cytosolic fraction. Nobiletin down-regulates the p-CREB and the SP-1 expressions in the nuclear fraction, whereas Nobiletin does not affect c-Jun and c-Fos expressions<sup>[1]</sup>.

Nobiletin (0-100  $\mu$ M; 24 hours; U2OS and HOS cells) treatment significantly reduces mRNA expressions of MMP-2 and MMP-9 dose-dependently in U2OS and HOS cells<sup>[1]</sup>.

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

### Western Blot Analysis<sup>[1]</sup>

Cell Line:	U2OS and HOS cells
Concentration:	0 $\mu$ M, 25 $\mu$ M, 50 $\mu$ M, 75 $\mu$ M, 100 $\mu$ M
Incubation Time:	24 hours
Result:	Progressively reduced protein expressions of MMP-2 and MMP-9. Considerably reduced the phosphorylation of p-IKK $\alpha$ / $\beta$ and p-I $\kappa$ B $\alpha$ , and protein expression of NF- $\kappa$ B in the cell nuclear fraction with the concomitant increase of the NF- $\kappa$ B expression in the cytosolic fraction. Down-regulated the p-CREB and the SP-1 expressions in the nuclear fraction in U2OS and HOS cells.

### RT-PCR<sup>[1]</sup>

Cell Line:	U2OS and HOS cells
Concentration:	0 $\mu$ M, 25 $\mu$ M, 50 $\mu$ M, 75 $\mu$ M, 100 $\mu$ M
Incubation Time:	24 hours
Result:	Significantly reduced mRNA expressions of MMP-2 and MMP-9 dose-dependently in U2OS and HOS cells.

## In Vivo

Nobiletin (0.1% of regular diet; oral administration; daily; for 20 weeks; male C57BL/6 mice) treatment restores glucose homeostasis and promotes energy expenditure and circadian activity in aged mice<sup>[2]</sup>.

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

Animal Model:	20- to 22-month-old male C57BL/6 mice <sup>[2]</sup>
Dosage:	0.1% of regular diet
Administration:	Oral administration; daily; for 20 weeks
Result:	Fully restored glucose tolerance in aged mice, and increased basal body temperature and cold tolerance in aged mice. Led to a twofold increase in distance run/day on voluntary wheels compared with aged regular diet-fed mice during the active phase.

## CUSTOMER VALIDATION

- Acta Pharm Sin B. 2021 Jan;11(1):143-155.
- Int J Biol Sci. 2022 Sep 11;18(15):5698-5712.
- Food Funct. 2023 Jul 19.

- J Agric Food Chem. 2022 Feb 9;70(5):1536-1546.
- Nutrients. 2023 May 8, 15(9), 2228.

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## REFERENCES

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- [1]. Cheng HL, et al. Nobiletin inhibits human osteosarcoma cells metastasis by blocking ERK and JNK-mediated MMPs expression. *Oncotarget*. 2016 Jun 7;7(23):35208-23.
- [2]. Nohara K, et al. Nobiletin fortifies mitochondrial respiration in skeletal muscle to promote healthy aging against metabolic challenge. *Nat Commun*. 2019 Aug 28;10(1):3923.
- [3]. He B, et al. The Small Molecule Nobiletin Targets the Molecular Oscillator to Enhance Circadian Rhythms and Protect against Metabolic Syndrome. *Cell Metab*. 2016 Apr 12;23(4):610-21.
- [4]. Takito J, et al. Nerve growth factor enhances the CRE-dependent transcriptional activity activated by nobiletin in PC12 cells. *Can J Physiol Pharmacol*. 2016 Jul;94(7):728-33.
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**Caution: Product has not been fully validated for medical applications. For research use only.**

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