

Product Data Sheet

Product Name: Nobiletin
Cat. No.: GN10325

Chemical Properties

Cas. No. 478-01-3

Chemical Name 2-(3,4-dimethoxyphenyl)-5,6,7,8-tetramethoxychromen-4-one

SMILES COC1=C(C=C(C=C1)C2=CC(=O)C3=C(O2)C(=C(C(=C3OC)OC)OC)OC)OC

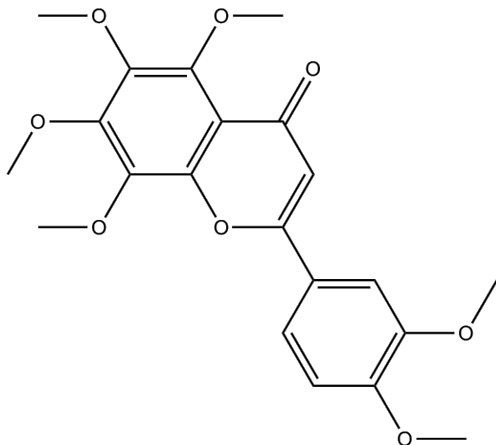
Formula $C_{21}H_{22}O_8$ M.Wt 402.39

Solubility $\geq 40.2\text{mg/mL}$ in DMSO Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines H460 and A549 (human non-small-cell lung cancer cell lines)

Caution: Product has not been fully validated for medical applications. For research use only.

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Preparation Method	Cells were cultured in DMEM supplemented with 10% FBS at 37°C, 5% CO ₂ . Cells were treated with Nobiletin at a concentration of 2.5μM for 24 hours.
Reaction Conditions	2.5μM; 24 hours
Applications	Nobiletin significantly inhibited soft agar colony formation and increased apoptosis in NSCLC cells. Nobiletin also suppressed the invasive and migratory capacities of both A549 and H460 cells. Mechanistically, Nobiletin upregulated negative regulators of WNT/β-catenin signaling (NKD1, AXIN2, WIF1) and inhibited β-catenin and its downstream genes (c-Myc, c-Jun, Cyclin D1). Nobiletin inhibited miR-15-5p expression, which targets NKD1, AXIN2, and WIF1, thereby inactivating the WNT/β-catenin signaling pathway.
Animal experiment [2]:	
Animal models	C57BL/6N wild-type mice
Preparation Method	Mice were subjected to a Lieber-DeCarli alcohol (alcohol-fed, AF) or an isocaloric maltose dextrin control (pair-fed, PF) liquid diet for 8 weeks plus one binge. Half of the mice were supplemented with 100mg/kg/day Nobiletin via intraperitoneal injection for the final four weeks. Tissue collection occurred four hours post-gavage with ethanol (4g/kg) or isocaloric dextrin.
Dosage form	100mg/kg/day; i.p.

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Applications

Nobiletin administration significantly attenuated alcohol-induced hepatic steatosis, endoplasmic reticulum stress, inflammation, and tissue damage in mice. Nobiletin reversed hepatic mitochondrial dysfunction and oxidative stress in both alcohol-fed mice and acetaldehyde-treated hepatocytes. Mechanistically, Nobiletin restored the reduction of hepatic mitochondrial transcription factor A (TFAM) at both mRNA and protein levels.

Reference:

[1] Han SH, Han JH, Chun WJ, et al. Nobiletin Inhibits Non-Small-Cell Lung Cancer by Inactivating WNT/ β -Catenin Signaling through Downregulating miR-15-5p. *Evid Based Complement Alternat Med*. 2021 Dec 30;2021:7782963.

[2] Lu D, Huang A, Tong X, et al. Nobiletin protects against alcohol-induced mitochondrial dysfunction and liver injury by regulating the hepatic NRF1-TFAM signaling pathway. *Redox Rep*. 2024 Dec;29(1):2395779.

Background

Nobiletin is a polymethoxylated flavone extracted from citrus plants^[1]. Nobiletin has a variety of pharmacological effects, including antioxidant, anti-inflammatory, and anti-tumor properties^[2]. Nobiletin can be used to improve metabolic syndrome and regulate lipid and blood glucose levels^[3]. Nobiletin can also induce apoptosis in cancer cells, inhibit the proliferation and metastasis of tumor cells, and has potential applications in cancer therapy^[4].

In vitro, Nobiletin (50–100 μ M) pre-treated RAW 264.7 macrophages for 16 hours, followed by stimulation with LPS (200ng/mL), significantly inhibited the expression of pro-inflammatory factors and promoted the polarization of macrophages towards the M2 phenotype by activating ROR α and increasing Klf4 expression^[5]. Nobiletin (2.5 μ M) pre-treated non-small-cell lung cancer (NSCLC) cell lines H460 and A549 for 24 hours, inhibited cell colony and sphere formation, and induced apoptosis by suppressing the activity of the WNT/ β -catenin signaling pathway^[6].

In vivo, Nobiletin (100mg/kg/day) was orally administered to D-galactose-induced aging C57BL/6J mice for 10 weeks. Nobiletin significantly increased mouse body weight, hindlimb muscle mass, and

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lean body mass, and improved skeletal muscle function. Nobiletin also improved muscle fiber size, increased the main protein components of skeletal muscle, and inhibited the production of inflammatory factors^[7]. Nobiletin (100mg/kg/day) was intraperitoneally injected into C57BL/6N mice with alcohol-induced hepatic steatosis for 4 weeks. Nobiletin significantly attenuated alcohol-induced hepatic steatosis, endoplasmic reticulum stress, inflammation, and tissue damage in mice. Nobiletin reversed alcohol-induced hepatic mitochondrial dysfunction and oxidative stress^[8].

References:

- [1] Mileykovskaya E, Yoo SH, Dowhan W, et al. Nobiletin: Targeting the Circadian Network to Promote Bioenergetics and Healthy Aging. *Biochemistry (Mosc)*. 2020 Dec;85(12):1554-1559.
- [2] Huang J, Chang Z, Lu Q, et al. Nobiletin as an inducer of programmed cell death in cancer: a review. *Apoptosis*. 2022 Jun;27(5-6):297-310.
- [3] Huang Q, Tian L, Zhang Y, et al. Nobiletin alleviates myocardial ischemia-reperfusion injury via ferroptosis in rats with type-2 diabetes mellitus. *Biomed Pharmacother*. 2023 Jul;163:114795.
- [4] Moazamiyanfar R, Rezaei S, AliAshrafzadeh H, et al. Nobiletin in Cancer Therapy; Mechanisms and Therapy Perspectives. *Curr Pharm Des*. 2023;29(22):1713-1728.
- [5] Wang SW, Lan T, Sheng H, et al. Nobiletin Alleviates Non-alcoholic Steatohepatitis in MCD-Induced Mice by Regulating Macrophage Polarization. *Front Physiol*. 2021 May 20;12:687744.
- [6] Han SH, Han JH, Chun WJ, et al. Nobiletin Inhibits Non-Small-Cell Lung Cancer by Inactivating WNT/ β -Catenin Signaling through Downregulating miR-15-5p. *Evid Based Complement Alternat Med*. 2021 Dec 30;2021:7782963.
- [7] Wang HH, Zhang Y, Qu TQ, et al. Nobiletin Improves D-Galactose-Induced Aging Mice Skeletal Muscle Atrophy by Regulating Protein Homeostasis. *Nutrients*. 2023 Apr 7;15(8):1801.
- [8] Lu D, Huang A, Tong X, et al. Nobiletin protects against alcohol-induced mitochondrial dysfunction and liver injury by regulating the hepatic NRF1-TFAM signaling pathway. *Redox Rep*. 2024 Dec;29(1):2395779.

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