Isosilybin

Cat. No.: HY-N0779

CAS No.: 72581-71-6

Molecular Formula: $C_{25}H_{22}O_{10}$

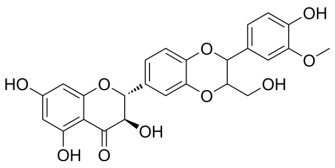
Molecular Weight: 482.44

Target: Cytochrome P450

Pathway: Metabolic Enzyme/Protease

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (207.28 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0728 mL	10.3640 mL	20.7280 mL
	5 mM	0.4146 mL	2.0728 mL	4.1456 mL
	10 mM	0.2073 mL	1.0364 mL	2.0728 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.18 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.18 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.18 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Isosilybin (Isosilybinin) is a flavonoid from Silybum marianum; inhibits CYP3A4 induction with an IC_{50} of 74 μM.

IC_{50} & Target

CYP3

In Vitro

The reporter gene assay shows that milk thistle's components silybin and isosilybin are responsible for the inhibition of PXR-mediated CYP3A4 induction by milk thistle. Compared with silybin, its isomer isosilybin is a stronger inhibitor of PXR-mediated CYP3A4 induction. A solution of 89, 133, and 200 μM isosilybin significantly inhibits CYP3A4 induction by 64, 82,

and 88%, respectively. Isosilybin inhibits CYP3A4 induction with an IC_{50} of 74 μM[1]. Isosilybin B and isosilybin A, two diastereoisomers isolated from silymarin, have anti-prostate cancer (PCA) activity that is mediated via cell cycle arrest and apoptosis induction. Isosilybin B and isosilybin A treatment results in growth inhibition and cell death together with a strong G(1) arrest and apoptosis in human prostate cancer LNCaP and 22Rv1 cells[2]. Isosilybin B causes increased phosphorylation of Akt (Ser-473 and Thr-308) and Mdm2 (Ser-166), which is linked with androgen receptor degradation as pretreatment with PI3K inhibitor (LY294002)-restored androgen receptor level. Isosilybin B treatment enhances the formation of complex between Akt, Mdm2 and AR, which promotes phosphorylation-dependent AR ubiquitination and its degradation by proteasome[3]. Isosilybin A is able to significantly activate PPARγ at a concentration of 30 μM (2.08±0.48 fold, $p<0.01$). Isosilybin A causes transactivation of a PPARγ-dependent luciferase reporter in a concentration-dependent manner. In silico docking studies suggests a binding mode for 3 distinct from that of the inactive silymarin constituents, with one additional hydrogen bond to Ser342 in the entrance region of the ligand-binding domain of the receptor[4].

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

PROTOCOL

Cell Assay [2]

LNCaP cells and 22Rv1 cells are plated and treated at 40–50% confluency with different doses of isosilybin B and isosilybin A (10–90 μM in medium) dissolved originally in Dimethyl sulfoxide (DMSO) for the desired time periods (24–48 h) in serum condition. An equal amount of DMSO (vehicle) is present in each treatment, including control; DMSO concentration did not exceed 0.1% (v/v) in any treatment. At the end of desired treatments, total cell number is determined by counting each sample in duplicate using a hemocytometer under an inverted microscope. Cell viability is determined using trypan blue exclusion method[2].

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

REFERENCES

[1]. Mooiman KD, et al. Milk thistle's active components silybin and isosilybin: novel inhibitors of PXR-mediated CYP3A4 induction. Drug Metab Dispos. 2013 Aug;41(8):1494-504.

[2]. Deep G, et al. Isosilybin B and isosilybin A inhibit growth, induce G1 arrest and cause apoptosis in human prostate cancer LNCaP and 22Rv1 cells. Carcinogenesis. 2007 Jul;28(7):1533-42.

[3]. Deep G, et al. Isosilybin B causes androgen receptor degradation in human prostate carcinoma cells via PI3K-Akt-Mdm2-mediated pathway. Oncogene. 2008 Jun 26;27(28):3986-98.

[4]. Pferschy-Wenzig EM, et al. Identification of isosilybin a from milk thistle seeds as an agonist of peroxisome proliferator-activated receptor gamma. J Nat Prod. 2014 Apr 25;77(4):842-7.

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