
Product Data Sheet

Product Name: Isosilybin

Cat. No.: GN10568

Chemical Properties

Cas. No. 72581-71-6

Chemical Name (3R)-3,5,7-trihydroxy-2-[2-(4-hydroxy-3-methoxyphenyl)-3-(hydroxymethyl)-2,3-dihydro-1,4-benzodioxin-6-yl]-2,3-dihydrochromen-4-one

SMILES COC1=C(C=CC(=C1)C2C(OC3=C(O2)C=CC(=C3)C4C(C(=O)C5=C(C=C(C=C5O4)O)O)O)CO)OFormula C₂₅H₂₂O₁₀

M.Wt 482.44

Solubility DMF: 20 mg/ml, DMF:PBS (pH 7.2) (1:9): 0.5 mg/ml, DMSO: 10 mg/ml, Ethanol: 0.1 mg/ml

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:**

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].

References:

[1]. Mooiman KD, et al.
Milk thistle's active components silybin and isosilybin: novel inhibitors of PXR-mediated CYP3A4 induction. Drug Metab

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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
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Background

Isosilybin (Isosilybinin) is a flavonoid from milk thistle; inhibits CYP3A4 induction with an IC₅₀ of 74 μ M.

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 μ M isosilybin significantly inhibits CYP3A4 induction by 64, 82, and 88%, respectively. Isosilybin inhibits CYP3A4 induction with an IC₅₀ of 74 μ M[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

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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 PPAR γ at a concentration of 30 μ M (2.08 ± 0.48 fold, $p < 0.01$). Isosilybin A causes transactivation of a PPAR γ -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].

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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