(R)-(-)-Gossypol acetic acid

Cat. No.: HY-15464A

CAS No.: 866541-93-7

Molecular Formula: $C_{32}H_{34}O_{10}$

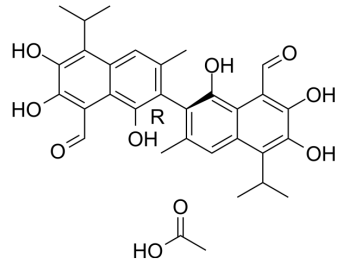
Molecular Weight: 578.61

Target: Bcl-2 Family; Autophagy

Pathway: Apoptosis; Autophagy

Storage: -20°C, protect from light, stored under nitrogen

* The compound is unstable in solutions, freshly prepared is recommended.



SOLVENT & SOLUBILITY

In Vitro

DMSO : 16.67 mg/mL (28.81 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7283 mL	8.6414 mL	17.2828 mL
	5 mM	0.3457 mL	1.7283 mL	3.4566 mL
	10 mM	0.1728 mL	0.8641 mL	1.7283 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: ≥ 1.25 mg/mL (2.16 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 1.25 mg/mL (2.16 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

(R)-(-)-Gossypol acetic acid (AT-101 (acetic acid)) is the levorotatory isomer of a natural product Gossypol. AT-101 is determined to bind to Bcl-2, Mcl-1 and Bcl-xL proteins with K_is of 260±30 nM, 170±10 nM, and 480±40 nM, respectively.

IC_{50} & Target				
	Mcl-1 170 nM (Ki)	Bcl-2 260 nM (Ki)	Bcl-xL 480 nM (Ki)	Autophagy

In Vitro

The natural racemic Gossypol has two enantiomers, namely the (R)-(-)-Gossypol acetic acid (AT-101 (acetic acid)) and (+)-Gossypol enantiomers. (R)-(-)-Gossypol (AT-101) and (+)-Gossypol binds to Bcl-2 or Bcl-xL with similar binding affinities, AT-101 is more potent than (+)-Gossypol in inhibition of cell growth and induction of apoptosis, possibly due to the influence of serum in the cell culture experiments. The racemic form and each of the enantiomers of Gossypol are tested against UM-SCC-6 and UM-SCC-14A in 6-day MTT assays. (R)-(-)-Gossypol (AT-101) exhibits greater growth inhibition relative to (±)-

Gossypol than (+)-Gossypol in both cell lines tested (P<0.001). An intermediate growth inhibitory effect is observed with (±)-Gossypol but this effect is only observed at the higher dose of Gossypol (10 μM, P<0.0001). (R)-(-)-Gossypol (AT-101) binds to the BH3-binding groove of Bcl-xL and Bcl-2 proteins with fairly high affinity, has potent activity against head and neck squamous cell carcinomas (HNSCC) cell lines in vitro. Furthermore, it induces apoptosis with high efficiency in HNSCC tumor cells that express functional p53 and that also kills tumor cells with mutant p53 by a different mechanism. (R)-(-)-Gossypol (AT-101) doses required to inhibit the growth of human fibroblast cell lines by 50% were 2- to 10-fold higher than for HNSCC cell lines. To inhibit human oral keratinocyte growth by 50%, (R)-(-)-Gossypol (AT-101) concentrations are 2-to 3-fold higher than for HNSCC cell lines. (R)-(-)-Gossypol (AT-101) causes dose-dependent inhibition of cell growth in ten UM-SCC cell lines over a range from 0.5 to 10 μM in a 6-day MTT assay. The relative sensitivity of the cell lines vary from a very sensitive group with an IC_{50} of 2-5 μM and a less sensitive group with IC_{50} clusters around 10 μM[1]. (R)-(-)-Gossypol (AT-101) is determined to bind to Bcl-2, Mcl-1 and Bcl-xL proteins with K_i values of 260±30 nM, 170±10 nM, and 480±40 nM, respectively[2].

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

PROTOCOL

Cell Assay [1]

Two representative UM-SCC cell lines, UM-SCC-6 and UM-SCC-14A, are continuously exposed to 0 (vehicle control), 5 or 10 μM (±)-Gossypol, (R)-(-)-Gossypol (AT-101) or (+)-Gossypol in a 6-day MTT cell survival assay[1].

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

CUSTOMER VALIDATION

- Nat Commun. 2023 Jun 10;14(1):3445.
- Cancer Lett. 2019 Oct 1;461:31-43.

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REFERENCES

[1]. Oliver CL, et al. In vitro effects of the BH3 mimetic, (-)-Gossypol, on head and neck squamous cell carcinoma cells. Clin Cancer Res. 2004 Nov 15;10(22):7757-63.

[2]. Sun Y, et al. Apogossypolone, a nonpeptidic small molecule inhibitor targeting Bcl-2 family proteins, effectively inhibits growth of diffuse large cell lymphoma cells in vitro and in vivo. Cancer Biol Ther. 2008 Sep;7(9):1418-26.

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