Tolrestat

Cat. No.: HY-16500

CAS No.: 82964-04-3

Molecular Formula: $C_{16}H_{14}F_3NO_3S$

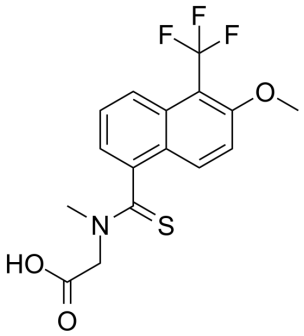
Molecular Weight: 357.35

Target: Aldose Reductase

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 : 50 mg/mL (139.92 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.7984 mL	13.9919 mL	27.9838 mL
	5 mM	0.5597 mL	2.7984 mL	5.5968 mL
	10 mM	0.2798 mL	1.3992 mL	2.7984 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 (7.00 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (7.00 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.00 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Tolrestat is a potent, orally active aldose reductase inhibitor with IC_{50} of 35 nM.

IC_{50} & Target

IC50: 35 nM (Aldose Reductase)

In Vivo

Tolrestat (1.8 mg/kg per day) causes a reversal to normal RBC sorbitol levels diabetic rats[1]. In 21-day diabetic rats, the estimated ID in the sciatic nerve and lenses is 4.8 and about 20 for tolrestat, and 1.7 and 2.2 for (±)sorbinil,respectively[2]. Either tolrestat or sorbinil inhibits tissue AR activity but does not significantly affect plasma lipoprotein levels, or affect the

body weight of the mice or their general health. Accumulation of cholesterol-rich foam cells is significantly increased in aortic roots of tolrestat-fed mice[3].

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

PROTOCOL

Animal Administration [2]

For a period of four days, rats weighing about 70 g are given unlimited access to water and Chow supplemented with 20% (wt/wt) galactose and tolrestat at various dose levels. Rats used as control receive chow containing galactose (20%, wt/wt) or glucose (20%, wt/wt). The rats are killed; the lenses and sciatic nerves are removed and homogenized in 5% trichloroacetic acid; the deproteinized extracts are then analyzed for galactitol by a modification of a method for glycerol determination. The values obtained in the group fed 20% glucose are used for background correction.

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

REFERENCES

[1]. Sestanj K, et al. N-[5-(trifluoromethyl)-6-methoxy-1-naphthalenyl]thioxomethyl]- N-methylglycine (Tolrestat), a potent, orally active aldose reductase inhibitor. J Med Chem. 1984 Mar;27(3):255-6.

[2]. Simard-Duquesne N, et al. The effects of a new aldose reductase inhibitor (tolrestat) in galactosemic and diabetic rats. Metabolism. 1985 Oct;34(10):885-92.

[3]. Srivastava S, et al. Aldose reductase protects against early atherosclerotic lesion formation in apolipoprotein E-null mice. Circ Res. 2009 Oct 9;105(8):793-802.

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