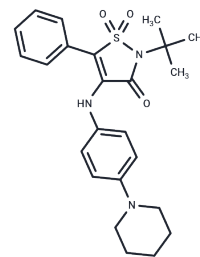


AZ876

## Chemical Properties

CAS No. : 898800-26-5  
 Formula: C<sub>24</sub>H<sub>29</sub>N<sub>3</sub>O<sub>3</sub>S  
 Molecular Weight: 439.57  
 Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year  
 Actual storage temperature shall be subject to the COA.



## Biological Description

Description	AZ876 is a potent, highly selective LXR agonist with Ki/EC50 of 7/6 nM and 11/73 nM for hLXR $\alpha$ and hLXR $\beta$ respectively.
Targets(IC50)	Liver X Receptor
In vitro	AZ876 suppressed up-regulation of hypertrophy- and fibrosis-related genes and further inhibited prohypertrophic and profibrotic TGF $\beta$ -Smad2/3 signaling. In cardiomyocytes, phenylephrine-stimulated cellular hypertrophy was significantly decreased in AZ876-treated cells. In cardiac fibroblasts, AZ876 prevented TGF $\beta$ - and angiotensin II-induced fibroblast collagen synthesis, and inhibited up-regulation of the myofibroblastic marker, $\alpha$ -smooth muscle actin [2].
In vivo	Low-dose AZ876 had no effect on plasma or liver lipids, whereas high-dose AZ876 increased plasma triglycerides and reduced cholesterol compared with controls. Low-dose AZ876 reduced lesion area; and high-dose AZ876 strongly decreased lesion area, lesion number, and severity. In either dose, AZ876 did not affect lesion composition [1]. Cardiac hypertrophy was induced in C57Bl6/J mice via transverse aortic constriction (TAC) for 6 weeks. During this period, mice received chow supplemented or not with AZ876 (20 $\mu$ mol/kg/day). In murine hearts, LXR $\alpha$ protein expression was up-regulated ~7-fold in response to TAC. LXR activation with AZ876 attenuated this increase, and significantly reduced TAC-induced increases in heart weight, myocardial fibrosis, and cardiac dysfunction without affecting blood pressure [2].
Kinase Assay	Binding vectors for His-tagged protein production were prepared by inserting the ligand-binding domain cDNA of human LXR $\alpha$ (amino acids 205-447) in pET28 and the ligand-binding domain cDNA of LXR $\beta$ (amino acids 216-461) in pET24D. Proteins were expressed in Escherichia coli and purified on Ni <sup>+</sup> columns. Binding assays using LXR $\alpha$ and LXR $\beta$ protein were run by adding reagents to Wallac Isoplate 1450-514. Briefly, each 96 plate well contained assay buffer (20 mM Tris pH 7.5, 80 mM NaCl, 2 mM dithiothreitol, 0.125% Chaps and 10% glycerol), 0.1 mg SPA beads (polylysine-coated yttrium silicate beads), LXR $\alpha$ (0.5 $\mu$ g) or LXR $\beta$ (0.25 $\mu$ g), 30 nM 3H-ligand (specific activity of 473 K bq/nmol) and test compound in a 10-point dose-response dilution. The assay mixture was shaken gently for 2 h on a plate shaker after which the beads were allowed to settle for 1 hour before counting. Transactivation vectors were prepared by inserting the ligand-binding domain cDNA sequences of human or mouse LXR $\alpha$ and LXR $\beta$ in frame with the yeast Gal4 transcription factor DNA binding domain and the nuclear

Kinase Assay	localization signal from the T-antigen of polyomavirus in the eucaryotic expression vector pSG5. The ligand-binding domain cDNA of human LXR $\alpha$ and LXR $\beta$ was the same as mentioned previously. The mouse sequence corresponded to amino acids 203-445 for LXR $\alpha$ and amino acids 201-446 for LXR $\beta$ . The vectors were co-transfected with a pGL3 luciferase reporter plasmid containing a minimal SV40 promoter and five copies of the UAS Gal4 recognition site into U2/OS osteosarcoma cells. Ligands were added as 10-point dose-response curves and then luciferase activity was measured after 48 h [1].
Animal Research	Cardiac hypertrophy was induced in male C57Bl6/J mice via transverse aortic constriction (TAC) for 6 weeks. During this period, sham and TAC-operated mice were randomized to receive either regular chow (control) or chow supplemented with AZ876 (20 $\mu$ mol/kg/day). Cardiac function was assessed with echocardiography and invasive haemodynamics. In vitro studies were performed in isolated neonatal rat ventricular myocytes (NRVMs) and adult rat cardiac fibroblasts. Leucine and proline tracer assays were used to measure protein and collagen synthesis, respectively [2].

### Solubility Information

Solubility	DMSO: 55 mg/mL (125.12 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	5% DMSO+40% PEG300+5% Tween 80+50% Saline: 2.5 mg/mL (5.69 mM),Solution. <i>Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.</i>

### Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.275 mL	11.3748 mL	22.7495 mL
5 mM	0.455 mL	2.275 mL	4.5499 mL
10 mM	0.2275 mL	1.1375 mL	2.275 mL
50 mM	0.0455 mL	0.2275 mL	0.455 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

### Reference

- van der Hoorn J et al. Low dose of the liver X receptor agonist, AZ876, reduces atherosclerosis in APOE\*3Leiden mice without affecting liver or plasma triglyceride levels. *Br J Pharmacol.* 2011 Apr;162(7):1553-63.
- Cannon MV et al. The liver X receptor agonist AZ876 protects against pathological cardiac hypertrophy and fibrosis without lipogenic side effects. *Eur J Heart Fail.* 2015 Mar;17(3):273-82.

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