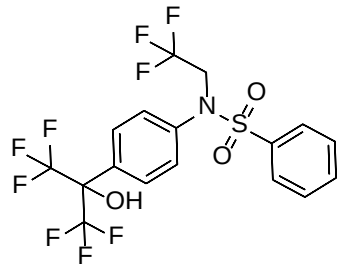
Product data sheet

MedKoo Cat#: 558247 Name: T-0901317 CAS#: 293754-55-9 Chemical Formula: $C_{17}H_{12}F_9NO_3S$ Exact Mass: 481.0394 Molecular Weight: 481.33	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
T-0901317, also known as T-1317; TO-091317; TO 901317, is a liver X receptor (LXR) agonist. T-0901317 inhibits development of atherosclerosis in LDL receptor-deficient mice. T-0901317 significantly reduced the atherosclerotic lesions in LDLR(-/-) mice without affecting plasma total cholesterol levels. T-0901317 increased expression of ATP binding cassette A1 in the lesions in LDLR(-/-) mice as well as in mouse peritoneal macrophages. T-0901317 also significantly induced cholesterol efflux activity in peritoneal macrophages. T-0901317 may be useful therapeutic agents for the treatment of atherosclerosis.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under “QC And Documents” section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	81.38	169.07
Ethanol	72.07	149.73

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.08 mL	10.39 mL	20.78 mL
5 mM	0.42 mL	2.08 mL	4.16 mL
10 mM	0.21 mL	1.04 mL	2.08 mL
50 mM	0.04 mL	0.21 mL	0.42 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of “Calculator”

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Maczewsky J, Sikimic J, Bauer C, Krippeit-Drews P, Wolke C, Lendeckel U, Barthlen W, Drews G. The LXR Ligand T0901317 Acutely Inhibits Insulin Secretion by Affecting Mitochondrial Metabolism. Endocrinology. 2017 Jul 1;158(7):2145-2154. doi: 10.1210/en.2016-1941. PMID: 28449117.
2. Koldamova RP, Lefterov IM, Staufenbiel M, Wolfe D, Huang S, Glorioso JC, Walter M, Roth MG, Lazo JS. The liver X receptor ligand T0901317 decreases amyloid beta production in vitro and in a mouse model of Alzheimer's disease. J Biol Chem. 2005 Feb 11;280(6):4079-88. doi: 10.1074/jbc.M411420200. Epub 2004 Nov 22. PMID: 15557325.

In vivo study

1. Maczewsky J, Sikimic J, Bauer C, Krippeit-Drews P, Wolke C, Lendeckel U, Barthlen W, Drews G. The LXR Ligand T0901317 Acutely Inhibits Insulin Secretion by Affecting Mitochondrial Metabolism. Endocrinology. 2017 Jul 1;158(7):2145-2154. doi: 10.1210/en.2016-1941. PMID: 28449117.

2. Koldamova RP, Lefterov IM, Staufenbiel M, Wolfe D, Huang S, Glorioso JC, Walter M, Roth MG, Lazo JS. The liver X receptor ligand T0901317 decreases amyloid beta production in vitro and in a mouse model of Alzheimer's disease. J Biol Chem. 2005 Feb 11;280(6):4079-88. doi: 10.1074/jbc.M411420200. Epub 2004 Nov 22. PMID: 15557325.

7. Bioactivity

Biological target: T0901317 is an agonist for both LXR and FXR with EC50 of 50 nM and 5 μM, respectively.

In vitro activity

T0901317 strongly and reversibly depolarized ΔΨ. Accordingly, T0901317 decreased the cytosolic ATP concentration. Wash-out of T0901317 led to a drop in [Ca2+]c, which is due to ATP-dependent sarco/endoplasmic reticulum Ca2+-ATPase activation. In patch-clamp experiments, opening of KATP channels by T0901317 is only found in the cell-attached but not in the excised-patch configuration. These data exclude a direct effect of the drug on KATP channels but rather point to an indirect metabolism-mediated effect. In conclusion, the T0901317-induced depolarization of ΔΨ leads to opening of KATP channels due to ATP depletion, which in turn reduces Ca2+ influx and insulin secretion.

Reference: Endocrinology. 2017 Jul 1;158(7):2145-2154. https://academic.oup.com/endo/article/158/7/2145/3754363

In vivo activity

To examine the role of T0901317 on ABCA1 expression in vivo, 11-week-old APP23 mice were treated orally by gastric gavage for 6 days with 50 mg/kg/day T0901317. Control mice received vehicle only. The treatment of APP23 mice resulted in a substantial increase in the expression of ABCA1 (more than 3-fold, $p < 0.001$), whereas the expression of APP was unchanged (Fig. 6, A and B). The effect of T0901317 on Aβ production was also examined. Because at this age Aβ in the brain of APP23 mice is soluble in SDS, Aβ was extracted from the initial brain homogenate by SDS containing RIPA buffer or diethylamine, and the results from the two determinations compared. Fig. 7, A and B show the levels of RIPA-extracted Aβ40 and Aβ42 in APP23 mice were significantly decreased. Similar results were obtained by ELISA determinations of diethylamine-extracted soluble Aβ40 and Aβ42 (not shown), thus confirming that amyloidogenic processing of human APP in APP23 mice was decreased after T0901317 treatment. Because the ratio of secreted sAPPα over sAPPβ was increased in the brain of T0901317-treated mice and Aβ1–40 and Aβ1–42 was decreased, the results suggest that the synthetic LXR ligand increases the non-amyloidogenic processing of APP.

Reference: J Biol Chem. 2005 Feb 11;280(6):4079-88. https://www.jbc.org/article/S0021-9258(20)76044-8/fulltext