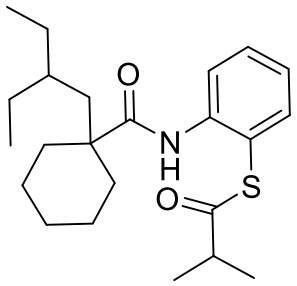
Product data sheet

MedKoo Cat#: 319508 Name: Dalcetrapib CAS#: 211513-37-0 Chemical Formula: $C_{23}H_{35}NO_2S$ Exact Mass: 389.23885 Molecular Weight: 389.598	
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:

Dalcetrapib, aslo known as JTT-705, is a CETP inhibitor. The drug was aimed at raising the blood levels of "good cholesterol" (cholesterol carried in HDL particles, aka HDL-C). Prevailing observations indicate that high HDL levels correlate with better overall cardiovascular health, though it remains unclear whether raising HDL levels consequently leads to an increase in cardiovascular health. Development of this drug was halted on May 7, 2012 “due to a lack of clinically meaningful efficacy.

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	49.0	125.77
Ethanol	54.0	138.60

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.57 mL	12.83 mL	25.67 mL
5 mM	0.51 mL	2.57 mL	5.13 mL
10 mM	0.26 mL	1.28 mL	2.57 mL
50 mM	0.05 mL	0.26 mL	0.51 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. Niesor EJ, Boivin G, Rhéaume E, Shi R, Lavoie V, Goyette N, Picard ME, Perez A, Laghrissi-Thode F, Tardif JC. Inhibition of the 3CL Protease and SARS-CoV-2 Replication by Dalcetrapib. ACS Omega. 2021 Jun 17;6(25):16584-16591. doi: 10.1021/acsomega.1c01797. PMID: 34235330; PMCID: PMC8230949.

In vivo study

1. Mancek-Keber M, Gradisar H, Iñigo Pestaña M, Martinez de Tejada G, Jerala R. Free thiol group of MD-2 as the target for inhibition of the lipopolysaccharide-induced cell activation. J Biol Chem. 2009 Jul 17;284(29):19493-500. doi: 10.1074/jbc.M109.003756. Epub 2009 May 27. PMID: 19473973; PMCID: PMC2740575.

7. Bioactivity

Biological target:

Dalcetrapib (JTT-705; RO-4607381) is a rhCETP inhibitor with IC50 of 0.2 μM that increases the plasma HDL cholesterol.

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In vitro activity

Dalcetrapib exerts its lipid-modulating effect by binding covalently to cysteine 13 of a cholesteryl ester transfer protein. Because 12 free cysteine residues are present in the 3CL protease, the potential of dalcetrapib to inhibit 3CL protease activity and SARS-CoV-2 replication was investigated. Molecular docking investigations suggested that dalcetrapib-thiol binds to the catalytic site of the 3CL protease with a delta G value of -8.5 kcal/mol. Dalcetrapib inhibited both 3CL protease activity in vitro and viral replication in Vero E6 cells with IC50 values of 14.4 ± 3.3 μM and an EC50 of 17.5 ± 3.5 μM (mean ± SD). Near-complete inhibition of protease activity persisted despite 1000-fold dilution after ultrafiltration with a nominal dalcetrapib-thiol concentration of approximately 100 times below the IC50 of 14.4 μM, suggesting stable protease-drug interaction. The inhibitory effect of dalcetrapib on the SARS-CoV-2 3CL protease and viral replication warrants its clinical evaluation for the treatment of COVID-19.

Reference: ACS Omega. 2021 Jun 17;6(25):16584-16591. https://pubmed.ncbi.nlm.nih.gov/34235330/

In vivo activity

Animals were fed JTT-705-containing mouse pellets for 6 days, and each animal received an estimated dose of 0.6 mg of compound/day. As shown in Fig. 8, treatment with JTT-705 completely abrogated LPS-dependent TNFα production and resulted in serum levels of TNFα indistinguishable from those measured in the PMB-treated animals. However, reduction of TNFα did not result in protection against the lethal effects of endotoxic shock, since groups treated with JTT-705 displayed a mortality at 72 h postinoculation similar (90%) to that detected in nontreated animals. Overall, oral intake of JTT-705 significantly inhibited endotoxin-triggered tumor necrosis factor alpha production in mice.

Reference: J Biol Chem. 2009 Jul 17;284(29):19493-500. https://pubmed.ncbi.nlm.nih.gov/19473973/