# TLK117

**Cat. No.:** HY-13634B

**CAS No.:** 152684-53-2

**Molecular Formula:** $C_{23}H_{27}N_3O_6S$

**Molecular Weight:** 473.54

**Target:** Gutathione S-transferase

**Pathway:** Metabolic Enzyme/Protease

**Storage:**

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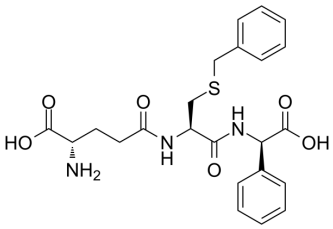
|---|---|---|
| Powder | -20°C | 3 years |
| | 4°C | 2 years |
| In solvent | -80°C | 6 months |
| | -20°C | 1 month |



## SOLVENT & SOLUBILITY

**In Vitro**

DMSO : 150 mg/mL (316.76 mM; Need ultrasonic)

**Preparing Stock Solutions**

| Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|
| 1 mM | 2.1118 mL | 10.5588 mL | 21.1175 mL |
| 5 mM | 0.4224 mL | 2.1118 mL | 4.2235 mL |
| 10 mM | 0.2112 mL | 1.0559 mL | 2.1118 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 (5.28 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.28 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.28 mM); Clear solution

## BIOLOGICAL ACTIVITY

**Description**

TLK117, the active metabolite of TLK199, selective inhibits Glutathione S-transferase P1–1 (GSTP1-1) with a $K_i$ of 0.4 μM for GSTP. TLK117 also competitively inhibits glyoxalase I with a $K_i$ of 0.56 μM.

**$IC_{50}$ & Target**

Ki: 0.4 μM[1], 0.56 μM (glyoxalase I)[2]

**In Vitro**

TLK117 is the most specific GSTP inhibitor to date, with a binding affinity greater than GSH itself and a selectivity for GSTP over 50-fold greater than the GSTM and GSTA classes ($K_i$=0.4 μM)[1]. TER 117 is developed as a GST P1-1 isoenzyme inhibitor

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| | to circumvent the indicated contribution of GST P1-1 to drug resistance of tumor cells. To facilitate the cellular uptake of TER 117, it is delivered as a diethyl ester (TER 117 DEE, also called TER 199). TER 117 is found to be a competitive inhibitor of both GST P1-1 and glyoxalase I[2].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |
| **In Vivo** | Oropharyngeal administration of the GSTP inhibitor, TLK117, at a time when fibrosis is already apparent, attenuated bleomycin- and AdTGFβ-induced remodeling, α-SMA, caspase activation, FAS S-glutathionylation, and total protein S-glutathionylation. Four hours after administration of 50 mg/kg TLK117, GSTP activity is strongly decreased and remains decreased by about 60% for at least 24 hours[2].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

## PROTOCOL

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| **Kinase Assay** [2] | The potency of TER 117 in the inhibition of GST P1-1/Ile-105 and GST P1-1/Val-105 is determined by means of GSH competition experiments using 1 μM TER 117 and three different fixed concentrations of GSH: 0.2, 0.6, and 2.0 mM. The concentration of the second substrate, 1-chloro-2,4-dinitrobenzene (CDNB) ranged between 0.15 and 1.8 mM. In addition, the inhibitor is tested at different concentrations, 0 to 8 μM, at a CDNB concentration of 1 mM and the above GSH concentrations. Initial velocities are determined spectrophotometrically at 30°C. The conjugation reaction between GSH and CDNB is monitored at 340 nm in 1 mL of 0.1 M sodium phosphate, pH 7.0[2].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |
| **Animal Administration** [1] | Mice[1]<br><br>TLK117 is administered oropharyngeally at a dose of 50 mg/kg in a 0.375 M Tris-HCl solution, pH =7.4, with 0.02% DMSO. This Tris-HCl/DMSO solution is used as a vehicle control. Treatments are performed once every 3 days from day 14 to day 26 in both >bleomycin and AdTGFβ models<br><br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

## REFERENCES


[1]. The human glutathione transferase P1-1 specific inhibitor TER 117 designed for overcomingcytostatic-drug resistance is also a strong inhibitor of glyoxalase I. Mol Pharmacol. 2000 Mar;57(3):619-24.

[2]. McMillan DH, et al. Attenuation of lung fibrosis in mice with a clinically relevant inhibitor of glutathione-S-transferase π. JCI Insight. 2016 Jun 2;1(8). pii: e85717.





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