

Product Data Sheet

Product Name: TLK117 (TER117)

Cat. No.: GC30647

Chemical Properties

Cas. No. 152684-53-2

SMILES O=C(O)[C@@H](C1=CC=CC=C1)NC([C@@H](NC(CC[C@H](N)C(O)=O)=O)CSCC2=CC=CC=C2)=O

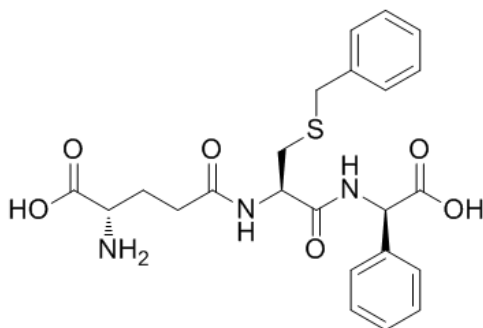
Formula $C_{23}H_{27}N_3O_6S$ M.Wt 473.54

Solubility DMSO : 150 mg/mL (316.76 mM) Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure



Protocol

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Kinase experiment: 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 μ M 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 μ M, 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].

Animal experiment: Mice[1]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 AdTGF β models

References:

- [1]. The human glutathione transferase P1-1 specific inhibitor TER 117 designed for overcoming cytostatic-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.

Background

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

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 μ M)[1]. TER 117 is developed as a GST P1-1 isoenzyme inhibitor 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

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

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].

Oropharyngeal administration of the GSTP inhibitor, TLK117, at a time when fibrosis is already apparent, attenuated bleomycin- and AdTGF β -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].

[1]. The human glutathione transferase P1-1 specific inhibitor TER 117 designed for overcoming cytostatic-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.

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA