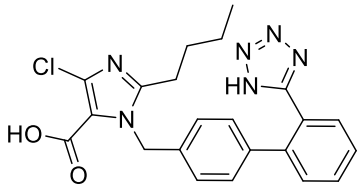
Product data sheet

MedKoo Cat#: 522575 Name: EXP-3174 CAS#: 124750-92-1 Chemical Formula: $C_{22}H_{21}ClN_6O_2$ Exact Mass: 436.1415 Molecular Weight: 436.9	
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:

EXP-3174, also known as Losartan Carboxylic Acid, is a physiologically active metabolite of losartan, produced by cytochrome P450 isoforms in the liver. Like the parent compound, EXP-3174 is a potent AT1 antagonist (Kis = 0.57 and 0.67 nM for rat and human forms, respectively), producing a depressor response and vasodilatation. When administered intravenously, losartan carboxylic acid is more potent and has a longer duration of action than losartan. However, the metabolite has very low oral bioavailability.

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	102.67	235.0
DMF	30.0	68.67
Ethanol	53.56	122.59
Ethanol:PBS (pH 7.2) (1:1)	0.5	1.14

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.29 mL	11.44 mL	22.89 mL
5 mM	0.46 mL	2.29 mL	4.58 mL
10 mM	0.23 mL	1.14 mL	2.29 mL
50 mM	0.05 mL	0.23 mL	0.46 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. Sachinidis A, Ko Y, Weisser P, Meyer zu Brickwedde MK, Düsing R, Christian R, Wieczorek AJ, Vetter H. EXP3174, a metabolite of losartan (MK 954, DuP 753) is more potent than losartan in blocking the angiotensin II-induced responses in vascular smooth muscle cells. J Hypertens. 1993 Feb;11(2):155-62. doi: 10.1097/00004872-199302000-00007. PMID: 8385175.

In vivo study

1. Gromotowicz-Poplawska A, Nazarko-Sadowska J, Chabielska E. Losartan metabolite EXP3174 reduces the weight of formed thrombus in 2K1C hypertensive rats. J Physiol Pharmacol. 2019 Jun;70(3). doi: 10.26402/jpp.2019.3.11. Epub 2019 Sep 27. PMID: 31566190.
2. Lynch JJ Jr, Stump GL, Wallace AA, Painter CA, Thomas JM, Kusma SE, Gould RJ, Grossman W. EXP3174, the AII antagonist human metabolite of losartan, but not losartan nor the angiotensin-converting enzyme inhibitor captopril, prevents the development of

lethal ischemic ventricular arrhythmias in a canine model of recent myocardial infarction. J Am Coll Cardiol. 1999 Sep;34(3):876-84. doi: 10.1016/s0735-1097(99)00253-3. PMID: 10483973.

7. Bioactivity

Biological target:

Losartan Carboxylic Acid (E-3174), an active carboxylic acid metabolite of Losartan, is an angiotensin II receptor type 1 (AT1) antagonist. The Ki values are 0.97, 0.57, 0.67 nM for rat AT1B/AT1A and human AT1, respectively.

In vitro activity

EXP3174 and losartan abolished the angiotensin II-induced formation of inositolphosphates in VSMC. EXP3174 and losartan inhibited the angiotensin II-induced elevation of intracellular cytosolic Ca2+ concentration with an IC50 of 5 X 10(-9) and 5 X 10(-8) mol/l, respectively. EXP3174 was more effective than losartan in blocking the angiotensin II-induced increase in Egr-1 mRNA. EXP3174 and losartan inhibited the angiotensin II-induced cell protein synthesis with an IC50 of 3 X 10(-9) and 4 X 10(-8) mol/l, respectively.

Reference: J Hypertens. 1993 Feb;11(2):155-62. https://pubmed.ncbi.nlm.nih.gov/8385175/

In vivo activity

There were no significant differences between a 7- and 8-hour old thrombus in the control, VEH-treated rats (5.15 ± 1.05 mg versus 7.04 ± 1.02 mg). Administration of EXP3174 resulted in a reduction of the thrombus mass. EXP3174 significantly reduced the weight of formed thrombi to 2.40 ± 0.78 mg and 1.59 ± 0.74 mg for doses 10 and 30 mg/kg, respectively, $P < 0.01$ (Fig. 1). HEP, administered as a positive control, significantly reduced the weight of formed thrombi to 0.38 ± 0.08 mg, $P < 0.001$ (Fig. 1).

Reference: J Physiol Pharmacol. 2019 Jun;70(3). https://pubmed.ncbi.nlm.nih.gov/31566190/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.