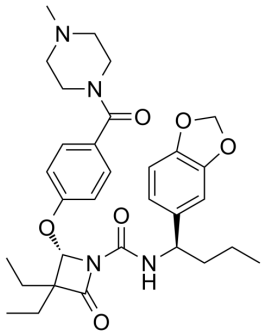
DMP 777

Cat. No.:	HY-75957
CAS No.:	157341-41-8
Molecular Formula:	$C_{31}H_{40}N_4O_6$
Molecular Weight:	564.67
Target:	Elastase
Pathway:	Metabolic Enzyme/Protease
Storage:	-20°C, stored under nitrogen * In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 38.33 mg/mL (67.88 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7709 mL	8.8547 mL	17.7095 mL
	5 mM	0.3542 mL	1.7709 mL	3.5419 mL
	10 mM	0.1771 mL	0.8855 mL	1.7709 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 15% Cremophor EL >> 85% Saline
   Solubility: 35 mg/mL (61.98 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.43 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (4.43 mM); Suspended solution; Need ultrasonic
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.43 mM); Clear solution
5. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.5 mg/mL (4.43 mM); Clear solution
6. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.43 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

DMP 777 is a potent, selective, and orally active human leukocyte elastase (HLE) inhibitor.

IC_{50} & Target	Human leukocyte elastase (HLE)[2]
In Vivo	DMP-777-treated rats show a marked decrease in H/K-ATPase staining parietal cells. DMP-777-induced loss of parietal cells is significantly ameliorated with coadministration of omeprazole. DMP-777-treated animals demonstrates marked foveolar hyperplasia in the fundus with prominent expansion of diastase-resistant, PAS-positive surface mucous cells. When DMP-777 is coadministeredwith omprazole, there is a significant decrease in BrdUpositive S-phase cells compared with rats thatreceive DMP-777 alone[1]. After oral dosing of monkeys at 40 mg/kg with DMP-777 the only stereoisomer detected in the post-dose plasma samples is the starting material DMP-777, and no inversion of the configuration at positions 'a' and 'b' of DMP-777 has occurred in vivo[2]. Mist1-/- mice treated with DMP-777 show fewer chief cell to SPEM transitions. Mist1-/- mice treated with L635 demonstrates significantly fewer proliferative SPEM cells compared to control mice[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Groups 1A and 1B receive control vehicle instead of omeprazole and DMP-777. Group 2A and 2B are dosed with DMP-777 once daily on Study Day 3 or Days 3 and 4, respectively, and receive control vehicle instead of omeprazole. Groups 3A and 3B are treated with omeprazole twice daily on Study Days 1 to 3 or Days 1 to 4, respectively, and receive control vehicle instead of DMP-777. Groups 4A and 4B are dosed with both omeprazole and DMP-777. On Study Days 1 and 2, animals are pretreated with omeprazole twice daily, the dosing intervals separated by approximately 6 hr. On Study Day 3 (Group 4A) or Days 3 and 4 (Group 4B), omeprazole is coadministered with DMP-777. The first dose of omeprazole is administered approximately 1 hr prior to the dose of DMP-777. The second dose is approximately 6 hr after the last dose of DMP-777. Groups 1A, 2A, 3A, and 4A are sacrificed on Day 4. Groups 1B, 2B, 3B, and 4B are sacrificed on Day 5. Bromodeoxyuridine (BrdU) is administered by intraperitoneal injection to all the rats, 2 hr prior to necropsy. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Stem Cell. 2022 May 5;29(5):826-839.e9.
- Cell Rep. 2023 Oct 10;42(10):113236.

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REFERENCES

[1]. Ogawa M, et al. Omeprazole treatment ameliorates oxyntic atrophy induced by DMP-777. Dig Dis Sci. 2006 Mar;51(3):431-9.

[2]. Zagrobelny J, et al. Separation of the four stereoisomers of a potent inhibitor (L-694,458) of human leukocyte elastase and its determination in human plasma using achiral/chiral chromatography with column switching. J Pharm Biomed Anal. 1998 Sep 1;17(6-7

[3]. Weis VG, et al. Maturity and age influence chief cell ability to transdifferentiate into metaplasia. Am J Physiol Gastrointest Liver Physiol. 2016 Nov 23:ajpgi.00326.2016

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