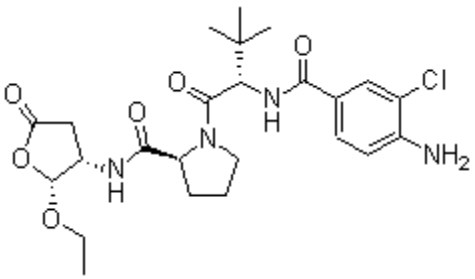
Product Introduction

VX-765

VX-765 is a potent and selective inhibitor of caspase-1 **with** K_i **of 0.8 nM.**

Technical Data:

Molecular Weight (MW):	509	
Formula:	$C_{24}H_{33}ClN_4O_6$	
Solubility (25 ℃) * <1 mg/ml means slightly soluble or insoluble:	DMSO 100 mg/mL	
	Water <1 mg/mL	
	Ethanol 100 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	273404-37-8	

Biological Activity

VX-765 is an orally absorbed prodrug of VRT-043198, which exhibits potent inhibition against ICE/caspase-1 and caspase-4 with Ki of 0.8 nM and less than 0.6 nM, respectively. And VRT-043198 also inhibits IL-1β release from both PBMCs and whole blood with IC50 of 0.67 μM and 1.9 μM, respectively. [1] In collagen-induced arthritis mouse model, VX-765 (200 mg/kg) inhibits LPS-induced IL-1β production by about 60%, and results in a dose-dependent, statistically significant reduction in the inflammation scores and effective protection from joint changes. [1] In vivo, VX-765 blocks kindling epileptogenesis in rats by preventing IL-1β increase in forebrain astrocytes without significant effect on afterdischarge duration. [2] In the mouse model of acute seizures, VX-765 (50 mg/kg-200 mg/kg) produces the anticonvulsant effect by delaying the time to onset of the first seizure and decreasing the number of

seizures as well as their total duration by average 50% and 64%.[3] In adult rats with genetic absence epilepsy (GAERS), VX-765, after the 3rd drug injection, significantly reduces the cumulative duration and number of spike-and-wave discharges (SWDs) by 55% on average by selectively blocking IL-1β biosynthesis. [4]

A potent and selective inhibitor of interleukin-converting enzyme/caspase-1.

References

[1] Wannamaker W, et al. J Pharmacol Exp Ther. 2007, 321(2), 509-516.

[2] Ravizza T, et al. Neurobiol Dis. 2008, 31(3), 327-333.

[3] Maroso M, et al. Neurotherapeutics. 2011, 8(2), 304-315.

[4] Akin D, et al. Neurobiol Dis. 2011, 44(3), 259-269.

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