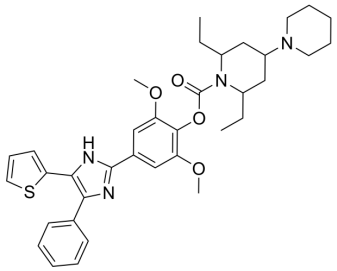
DPTIP-prodrug 18

Cat. No.:	HY-149025
CAS No.:	2881068-33-1
Molecular Formula:	$C_{36}H_{44}N_4O_4S$
Molecular Weight:	628.82
Target:	Phospholipase
Pathway:	Metabolic Enzyme/Protease
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	DPTIP-proagent 18 (P18) is a orally active and brain-penetrable proagent of DPTIP (HY-131002). DPTIP-proagent 18 is a potent nSMase2 inhibitor. DPTIP-proagent 18 significantly inhibits IL-1β-induced EV (extracellular vesicle) release by inhibition of nSMase2 (neutral sphingomyelinase-2) activity. DPTIP-proagent 18 can be used for brain injury research[1].
IC_{50} & Target	nSMase2[1]
In Vitro	DPTIP-prodrug 18 is metabolically stable with >75% intact prodrug remaining after 1 h of incubation at 37 °C[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	DPTIP-prodrug 18 exhibits an excellent PK profile[1]. DPTIP-prodrug 18 shows significant inhibition of nSMase2 activity and IL-1β-induced EV release in mice[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	CES1−/− mice[1]
Dosage:	10 mg/kg DPTIP equivalent
Administration:	Orally, once (Pharmacokinetic Analysis)
Result:	Exhibited >fourfold higher plasma (AUC_{0-t}=1047 pmol·h/mL) and brain exposures (AUC_{0-t} =247 pmol·h/g) versus DPTIP and a significant enhancement of DPTIP half-life (2 h vs ~0.5 h).

Animal Model:	Interleukin-1β-injected mice (a mouse model of brain injury)[1]
Dosage:	0, 3 and 10 mg/kg (DPTIP equivalent)
Administration:	Orally, once
Result:	Significantly inhibited the release of brain-derived GFP+ EVs into the blood at both 3 and 10 mg/kg (DPTIP equivalent dose).

REFERENCES

[1]. Pal A, et al. Discovery of Orally Bioavailable and Brain-Penetrable Prodrugs of the Potent nSMase2 Inhibitor DPTIP. J Med Chem. 2022 Aug 5.

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