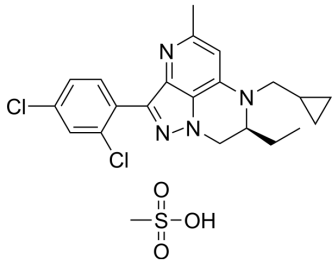
NBI 35965 methanesulfonate

Cat. No.:	HY-103378
CAS No.:	603151-83-3
Molecular Formula:	$C_{22}H_{26}Cl_2N_4O_3S$
Molecular Weight:	497.44
Target:	CRFR
Pathway:	GPCR/G Protein
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	NBI 35965 methanesulfonate is a selective, orally active and brain-penetrant corticotropin-releasing factor receptor 1 (CRF1) antagonist with a K_i value of 4 nM and a pK_i value of 8.5. NBI 35965 methanesulfonate does not inhibit CRF2. NBI 35965 methanesulfonate reduces CRF or stress-induced adrenocorticotropic hormone (ACTH) production in vivo with pIC_{50} values of 7.1 and 6.9, respectively. NBI 35965 methanesulfonate shows anxiolytic effects[1][2].

IC_{50} & Target		
	CRFR1 4 nM (Ki)	CRFR1 8.5 (pKi)

In Vitro

NBI 35965 methanesulfonate displays a high affinity for CRF1 while having no binding affinity to CRF2. NBI 35965 methanesulfonate also inhibits the stimulation of cAMP induced by Sauvagine in CRF1 transfected cells[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

NBI 35965 methanesulfonate (20 mg/kg; oral gavage; once) reduces stress induced ACTH production in mice[1].

In rats, NBI 35965 methanesulfonate (Compound 12a; 10mg/kg) has a volume of distribution 17.8 L/kg, a plasma clearance of 17 mL/min/kg, and a half-life of 12 h. The estimated oral bioavailability is 34% with a mean maximal plasma concentration at 1 h of 560 ng/mL. NBI 35965 methanesulfonate also penetrated the blood-brain barrier, resulting in a mean maximal brain concentration of 700 ng/g[1].

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Animal Model:	Male CD-1 mice (24-26 g) bearing restraint stress[1]
Dosage:	20 mg/kg (10 mL/kg 5% mannitol-d (w/v) in water)
Administration:	Oral gavage; 60 min prior to the initiation of the stressor
Result:	Reduced stress induced ACTH production in vivo.

REFERENCES

[1]. Gross RS, et al. Design and synthesis of tricyclic corticotropin-releasing factor-1 antagonists. J Med Chem. 2005 Sep 8;48(18):5780-93.

[2]. Mulugeta Million, et al. A novel water-soluble selective CRF1 receptor antagonist, NBI 35965, blunts stress-induced visceral hyperalgesia and colonic motor function in rats. Brain Res. 2003 Sep 19;985(1):32-42.

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