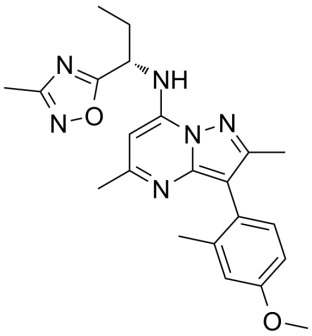
Verucerfont

Cat. No.:	HY-14875
CAS No.:	885220-61-1
Molecular Formula:	$C_{22}H_{26}N_6O_2$
Molecular Weight:	406.48
Target:	CRFR
Pathway:	GPCR/G Protein
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 83.33 mg/mL (205.00 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4601 mL	12.3007 mL	24.6015 mL
	5 mM	0.4920 mL	2.4601 mL	4.9203 mL
	10 mM	0.2460 mL	1.2301 mL	2.4601 mL

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

BIOLOGICAL ACTIVITY

Description

Verucerfont is a corticotropin-releasing factor receptor 1 (CRF1) antagonist with IC_{50}s of ~6.1, >1000 and >1000 nM for CRF1, CRF2, and CRF-BP, respectively.

IC_{50} & Target

IC50: 6.1 nM (CRF1), >1000 nM (CRF2), >1000 nM (CRF-BP)[1]

In Vivo

Post hoc analysis shows that the prototypic non-peptide CRF1 receptor antagonist NBI30775 (R121919) and Verucerfont are both significantly different from vehicle, CP-316 311, and pexacerfont (P<0.001 for all comparisons collapse across time-points); the latter three treatments in turn do not differ from each other. A differential effect of treatments over time is also shown by a significant treatment×time interaction (F[20,140]=6.4, P<0.001). Accordingly, detailed Post hoc analysis shows that both NBI30775 and Verucerfont inhibit ACTH release throughout the following 6 h of measurement (P<0.001 vs vehicle at each time-point, and vs the respective pretreatment baseline)[1].

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

PROTOCOL

Animal Administration [1]

Male Sprague-Dawley rats are received at 175 to 200 g and housed in a 12 to 12 light cycle for 1 week before adrenalectomy. Rats are adrenalectomized at Neurocrine Biosciences, and NaCl is replenished. Adrenalectomy is verified by plasma corticosterone measurements. Seven days after adrenalectomy, rats are implanted with femoral vein catheters. After ~4 days, rats are prepared for blood sampling by attaching their catheters to PE50 tubing and a syringe, and acclimated to individual opaque sampling cages for 1 h. These cages allow sampling to occur without disturbance to the rat. Blood samples (0.3 mL) are taken after acclimation and blood volumes are replaced with 5 U/mL heparinized saline. Blood samples are stored on ice with EDTA. After a baseline blood sample, rats receive oral doses of either vehicle at 5 mL/kg or the respective drug (including Verucerfont) in the same volume of vehicle. In each case, the dose is 10 mg/kg, based on prior pharmacokinetic studies showing that this dose results in adequate and comparable exposure. Blood samples are taken 1, 2, 3, 4, and 6 h later. Plasma is separated by centrifugation at 4°C and stored at -80 °C for subsequent measurement of ACTH by radioimmunoassay[1].

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

REFERENCES

[1]. Schwandt ML, et al. The CRF1 Antagonist Verucerfont in Anxious Alcohol-Dependent Women: Translation of Neuroendocrine, But not of Anti-Craving Effects. Neuropsychopharmacology. 2016 Nov;41(12):2818-2829.

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