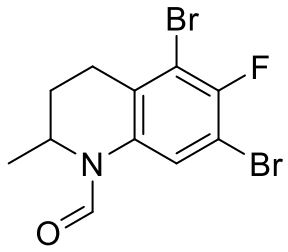
Product data sheet

MedKoo Cat#: 562758 Name: CE3F4 CAS#: 143703-25-7 Chemical Formula: $C_{11}H_{10}Br_2FNO$ Exact Mass: 348.9113 Molecular Weight: 351.01	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
CE3F4 is an inhibitor of human exchange protein directly activated by cyclic AMP isoform 1 (Epac1).

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	50	142.45

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.85 mL	14.24 mL	28.49 mL
5 mM	0.57 mL	2.85 mL	5.70 mL
10 mM	0.28 mL	1.42 mL	2.85 mL
50 mM	0.06 mL	0.28 mL	0.57 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Courilleau D, Bisserier M, Jullian JC, Lucas A, Bouyssou P, Fischmeister R, Blondeau JP, Lezoualc'h F. Identification of a tetrahydroquinoline analog as a pharmacological inhibitor of the cAMP-binding protein Epac. J Biol Chem. 2012 Dec 28;287(53):44192-202. doi: 10.1074/jbc.M112.422956. Epub 2012 Nov 8. PMID: 23139415; PMCID: PMC3531735.

2. Courilleau D, Bouyssou P, Fischmeister R, Lezoualc'h F, Blondeau JP. The (R)-enantiomer of CE3F4 is a preferential inhibitor of human exchange protein directly activated by cyclic AMP isoform 1 (Epac1). Biochem Biophys Res Commun. 2013 Oct 25;440(3):443-8. doi: 10.1016/j.bbrc.2013.09.107. Epub 2013 Oct 4. PMID: 24099776.

In vivo study

1. Prajapati R, Fujita T, Suita K, Nakamura T, Cai W, Hidaka Y, Umemura M, Yokoyama U, Knollmann BC, Okumura S, Ishikawa Y. Usefulness of Exchanged Protein Directly Activated by cAMP (Epac)1-Inhibiting Therapy for Prevention of Atrial and Ventricular Arrhythmias in Mice. Circ J. 2019 Jan 25;83(2):295-303. doi: 10.1253/circj.CJ-18-0743. Epub 2018 Dec 6. PMID: 30518738.

2. Zhang MX, Zheng JK, Wang WW, Kong FQ, Wu XX, Jiang JK, Pan JX. Exchange-protein activated by cAMP (EPAC) regulates L-type calcium channel in atrial fibrillation of heart failure model. Eur Rev Med Pharmacol Sci. 2019 Mar;23(5):2200-2207. doi: 10.26355/eurrev_201903_17267. PMID: 30915767.

7. Bioactivity

Product data sheet

Biological target:

CE3F4 is a selective antagonist of exchange protein directly activated by cAMP (Epac1), with IC50s of 10.7 μM and 66 μM for Epac1 and Epac2(B), respectively.

In vitro activity

CE3F4, a tetrahydroquinoline analog, prevents Epac1 activation in vitro and in living cultured cells by inhibiting the GEF activity of Epac1. However, the activity of the (R)- and (S)-enantiomers of CE3F4, as well as the ability of CE3F4 and its analogs to inhibit Epac2 GEF activity, have not yet been investigated. In this study, it's reported that (R)-CE3F4 is a more potent cAMP antagonist than racemic CE3F4 and (S)-CE3F4, inhibiting the GEF activity of Epac1 with 10-times more efficiency than (S)-CE3F4. Epac2, in contrast to Epac1, is activated more efficiently by cAMP than by 8-(4-chlorophenylthio)-2'-O-methyladenosine-3',5'-cyclic monophosphate (007), an Epac-selective cAMP analog. (R)-CE3F4 displays Epac isoform preference, with 10-fold selectivity for Epac1 over Epac2. Deletion of the N-terminal cyclic nucleotide-binding domain of Epac2 does not affect the characteristics of activation of Epac2 by cAMP and by 007, nor its inhibition by CE3F4. Finally, the evaluation of a series of CE3F4 structural analogs as GEF inhibitors allowed identifying structural features that are important for high Epac1 inhibitory activity of CE3F4. It's concluded that the (R)-enantiomer of CE3F4 is a preferential inhibitor of Epac1 with high potency in the low micromolar range, and it's suggested that this compound may be a useful pharmacological tool for investigating the functional role of Epac1 in cAMP signaling.

Reference: J Biol Chem. 2012 Dec 28;287(53):44192-202. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/23139415/

In vivo activity

The usefulness of CE3F4, an Epac1-selective inhibitor, is examined in the treatment of the arrhythmias in mice. In Epac1 knockout (Epac1-KO) mice, the duration of atrial fibrillation (AF) was shorter than in wild-type mice. In calsequestrin2 knockout mice, Epac1 deficiency resulted in a reduction of ventricular arrhythmia. In both atrial and ventricular myocytes, sarcoplasmic reticulum (SR) Ca2+ leak, a major trigger of arrhythmias, and spontaneous SR Ca2+ release (SCR) were attenuated in Epac1-KO mice. Consistently, CE3F4 treatment significantly prevented AF and ventricular arrhythmia in mice. In addition, the SR Ca2+ leak and SCR were significantly inhibited by CE3F4 treatment in both atrial and ventricular myocytes. Importantly, cardiac function was not significantly affected by a dosage of CE3F4 sufficient to exert anti-arrhythmic effects.

Reference: Circ J. 2019 Jan 25;83(2):295-303. https://dx.doi.org/10.1253/circj.CJ-18-0743

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.