

BI-113823: A Chemical Probe for BDKRB1

Version 1.0 (18th June 2024)

Web link for more details: <https://www.sgc-ffm.uni-frankfurt.de/#!specificprobeoverview/BI-113823>

Overview

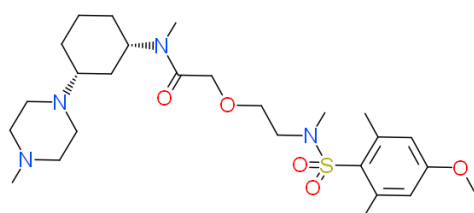
BDKRB1 is a GPCR that has low expression in healthy tissues, however upon injury as well as in inflammatory conditions, higher expression is triggered. By binding to endogenous kinins, the signaling pathway activates phospholipase C that leads to increased intracellular calcium ion concentration leading to inflammatory responses.

Summary

Chemical Probe Name	BI-113823
Negative control compound	BI-5832
Target(s) (synonyms)	BDKRB1 (Bradykinin Receptor B1, B1R)
Recommended <i>in vitro</i> assay concentration	Use at concentration of 100 nM for BI-113823 and BI-5832; use with control for best interpretation of data
Suitability for <i>in vivo</i> use and recommended dose	Tested <i>in vivo</i> in rats and mice with i.v. dose 10 mg/kg, p.o. dose 40 mg/kg (fed male), p.o. dose 10 mg/kg (fasted male)
Publications	PMID: 23236443
<i>In vitro</i> assay(s) used to characterise	Radioligand binding assay (displacement of kallidin)
Cellular assay(s) for target-engagement	Measurement of intracellular calcium in HEK-cells expressing hBDKRB1

Chemical Probe & Negative Control Structures and Use

BI-113823 Chemical Probe



SMILES: Cc1cc(cc(C)c1S(N(C)CCOCC(N(C)[C@H]1CCC[C@H](C1)N1CCN(C)CC1)=O)(=O)=O)OC

InChIKey: BUJJBFHGUQJYSD-XZOQPEGZSA-N

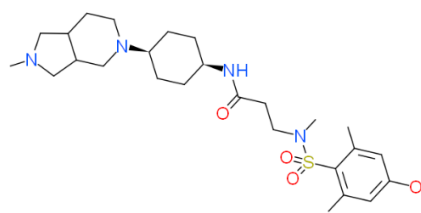
Molecular weight: 524.30 g/mol

Storage: As a dry powder or as DMSO stock solutions (10 mM) at -20 °C.

DMSO stocks beyond 3-6 months or 2 freeze/thaw cycles should be tested for activity before use

Dissolution: Soluble in DMSO up to 10 mM; use only 1 freeze/thaw cycle per aliquot

BI-5832 Negative Control



SMILES: Cc1cc(cc(C)c1S(N(C)CCC(N[C@H]1CC[C@H](CC1)N1CCC2CN(C)CC2C1)=O)(=O)=O)OC

InChIKey: GHZWQLLEBVOHED-ULBZPVTCSA-N

Molecular weight: 520.31 g/mol

Storage: As a dry powder or as DMSO stock solutions (10 mM) at -20 °C.

DMSO stocks beyond 3-6 months or 2 freeze/thaw cycles should be tested for activity before use

Dissolution: Soluble in DMSO up to 10 mM; use only 1 freeze/thaw cycle per aliquot

Chemical Probe Profile

In vitro Potency & Selectivity:

BI-113823 shows potent activity at 10 μM on human BDKRB1 in a radioligand binding assay (displacement of kallidin) with $K_i = 5.3$ nM whereas for human BDKRB2 $K_i > 10$ μM in the same assay. The Eurofins SafetyScreen with 69 targets at 10 μM is clean.

Potency in Cells and Cellular Target Engagement:

In a cellular assay, where the intracellular calcium in HEK-cells expressing hBDKRB1 was measured, BI-113823 has an $IC_{50} = 7$ nM.