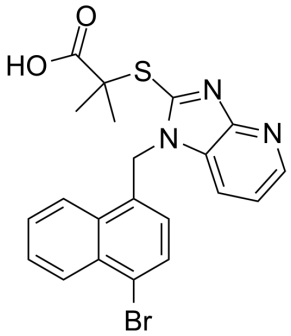
URAT1 inhibitor 2

Cat. No.:	HY-143906
CAS No.:	2803951-18-8
Molecular Formula:	$C_{21}H_{18}BrN_3O_2S$
Molecular Weight:	456.36
Target:	URAT1
Pathway:	Membrane Transporter/Ion Channel
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

URAT1 inhibitor 2 is an orally active and potent URAT1 and CYP isozyme inhibitor, with IC_{50} values of 1.36 μM, 16.97 μM, 5.22 μM for URAT1-mediated ^{14}C-UA uptake, CYP1A2 and CYP2C9, respectively. URAT1 inhibitor 2 is a promising agent candidate in the study of hyperuricemia and gout[1].

IC_{50} & Target

IC_{50}: 1.36 μM (URAT1-mediated ^{14}C-UA uptake), 16.97 μM (CYP1A2), 5.22 μM (CYP2C9), >20 μM (CYP2C19), >20 μM (CYP2D6), and >20 μM (CYP3A4M)[1].

In Vitro

URAT1 inhibitor 2 (compound 23) (0-50 μM, 3-20 min) inhibits URAT1-mediated ^{14}C-UA uptake (IC_{50} = 1.36 μM) and CYP cells activity[1].

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

Cell Viability Assay

Cell Line:	Human URAT1, CYP cells[1]
Concentration:	0, 0.05, 0.15, 0.5, 1.5, 5.0, 15, and 50 μM
Incubation Time:	3-20 min
Result:	Inhibited URAT1-mediated 14C-UA uptake and CYP cells activity.

In Vivo

URAT1 inhibitor 2 (Intravenous at 2 mg/kg or orally at 10 mg/kg) has excellent pharmacokinetic properties with the oral bioavailability of 59.3%[1].

URAT1 inhibitor 2 (4, 2, 1, 0.5, and 0.25 mg/kg; Orally) shows orally active and outstanding SUA-lowering activity with a dose-dependent manner in acute hyperuricemia mice[1].

URAT1 inhibitor 2 (1000 mg/kg, intragastric administration, once) shows favorable safety profiles and no obvious acute toxicity[1].

Pharmacokinetic Parameters of URAT1 inhibitor 2 in male Sprague-Dawley rats[1].

parameter	unit	p.o.	i.v.
$compound_{max}$ (h)		23	23

AUC (0-t)	ng/mL·h	48754.6	16344.8
AUC (0-∞)	ng/mL·h	48781.5	16448.8
MRT (0-∞)	h	3.3	1.0
$t_{1/2}$	h	2.2	1.8
T_{max}	h	0.3	
C_{max}	ng/mL	19185.0	
CL	mL/min/kg		2.2
F	%	59.3	

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

Animal Model:	Male Sprague-Dawley rats (n=10)[1]
Dosage:	2 mg/kg (intravenous) or 10 mg/kg (oral administration)
Administration:	Intravenous or oral administration
Result:	Achieved excellent pharmacokinetic properties with the oral bioavailability of 59.3%.

Animal Model:	Acute hyperuricemia mice[1]
Dosage:	4, 2, 1, 0.5, and 0.25 mg/kg
Administration:	Orally, once
Result:	Showed outstanding SUA-lowering activity.

Animal Model:	Kunming mice[1]
Dosage:	1000 mg/kg
Administration:	Itragastric administration, once
Result:	Showed favorable safety profiles and no obvious acute toxicity.

REFERENCES

[1]. Tong Zhao, et al. Discovery of Novel Bicyclic Imidazolopyridine-Containing Human Urate Transporter 1 Inhibitors as Hypouricemic Drug Candidates with Improved Efficacy and Favorable Druggability. J. Med. Chem. 2022, 65, 5, 4218–4237.

Caution: Product has not been fully validated for medical applications. For research use only.

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