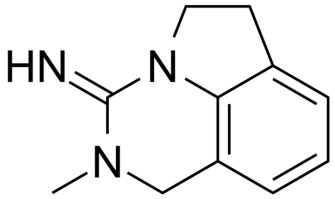
JBSNF-000028 free base

Cat. No.:	HY-151500
CAS No.:	3026599-90-3
Molecular Formula:	$C_{11}H_{13}N_3$
Molecular Weight:	187.24
Target:	Others
Pathway:	Others
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	JBSNF-000028 is an orally active nicotinamide N-methyltransferase (NNMT) inhibitor with IC_{50}s of 0.033 μM, 0.19 μM and 0.21 μM against human NNMT (hNNMT), monkey NNMT (mkNNMT), and mouse NNMT (mNNMT), respectively. JBSNF-000028 can be used for the research of metabolic disorders[1].
IC_{50} & Target	IC_{50}: 0.033 μM (hNNMT), 0.19 μM (mkNNMT), 0.21 μM (mNNMT)[1]
In Vitro	JBSNF-000028 (24 h) inhibits NNMT activity with an EC_{50} of 2.5 μM in U2OS cells[1]. JBSNF-000028 (10-100 μM; 72 h) has no cytotoxicity against HepG2 cells[1]. JBSNF-000028 binds below a hairpin structural motif at the nicotinamide pocket and stacks between Tyr-204 (from Hairpin) and Leu-164 (from central domain)[1]. JBSNF-000028 is inactive against a broad panel of targets related to metabolism and safety[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	JBSNF-000028 (50 mg/kg; p.o.; twice daily for 27 days) improves glucose and lipid handling in mice with diet-induced obesity (DIO)[1]. JBSNF-000028 (50 mg/kg; p.o.; twice daily for 4 weeks) improves glucose tolerance in NNMT knockout mice with diet-induced obesity[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male C57BL6/N mice, diet induced obesity (DIO) model[1]
Dosage:	50 mg/kg
Administration:	Oral administration, b.i.d for 27 days
Result:	Significantly reduced the body weight and fed blood glucose. Reduced 1-methyl-nicotinamide (MNA) levels in visceral WAT and liver. Led to a statistically significant reduction in plasma triglyceride, plasma LDL cholesterol, liver triglyceride and liver total cholesterol.

Animal Model:	Male C57BL6/N mice[1]

Dosage:	1 mg/kg and 10 mg/kg
Administration:	Intravenous and oral administration (Pharmacokinetic Analysis)
Result:	Pharmacokinetic parameters of JBSNF-0000028 in mice following intravenous (1 mg/kg) and oral administration (10 mg/kg)[1].

PK parameters	Intravenous	Oral
Dose (mg/kg)	1	10
AUC_{0-t} (ng h/mL)	446	1369
C_0/C_{max} (ng/mL)	432	452
T_{max} (h)	-	1.00
$T_{1/2}$ (h)	1.77	2.36
T_{last} (h)	8.00	10.0
Cl (mL/min/kg)	36.6	-
Vd (L/kg)	8.69	-
F (%)	-	30

REFERENCES

[1]. Ruf S, et al. Novel tricyclic small molecule inhibitors of Nicotinamide N-methyltransferase for the treatment of metabolic disorders. Sci Rep. 2022 Sep 14;12(1):15440.

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