TIY-7

Cat. No.: HY-146755

CAS No.: 2846435-83-2

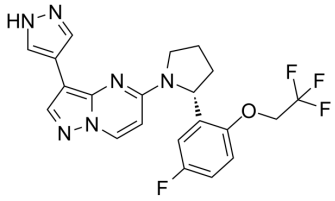
Molecular Formula: $C_{21}H_{18}F_4N_6O$

Molecular Weight: 446.4

Target: Trk Receptor

Pathway: Neuronal Signaling; Protein Tyrosine Kinase/RTK

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

TIY-7 is a selective and orally active tropomyosin receptor kinase (TRK) inhibitor. TIY-7 shows enzyme inhibitory activity with IC_{50}s of 2.9, 1.1, 0.7, 0.8, 0.8, 0.2 nM for TRKA, $TRKA^{G595R}$, $TRKA^{G667C}$, $TRKA^{F589L}$, $TRKC^{G623R}$, $TRKC^{G696A}$, respectively. TIY-7 shows anti-tumor potency in mouse xenograft model[1].

IC_{50} & Target

TrkA	TrkA	TrkC
2.9 nM (IC_{50})		

In Vitro

TIY-7 (compound 12c) shows enzyme inhibitory activity with IC_{50}s of 2.9, 1.1, 0.7, 0.8, 0.8, 0.2 nM for TRKA, $TRKA^{G595R}$, $TRKA^{G667C}$, $TRKA^{F589L}$, $TRKC^{G623R}$, $TRKC^{G696A}$, respectively[1].

TIY-7 (1 μM) shows selectivity with inhibitory rate of 62%, 99%, 11% for ALK, ROS1, and JAK1 kinase[1].

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

In Vivo

TIY-7 (5 mg/kg for p.o.; 1 mg/kg for i.v.) shows good oral bioavailability (F) of 39.8%[1].

TIY-7 (30 mg/kg; P.o.; twice daily for 12-14 consecutive days) inhibits tumor progression in a dose-dependent manner in xenograft model[1].

Pharmacokinetic Parameters of TIY-7 in Male Sprague-Dawley rats[1].

	Dose (mg/kg)	C_{max} (ng/mL)	T_{max} (h)	$T_{1/2}$ (h)	CL (mL/min/kg)	F %	MRT_{0-t} (h)	AUC_{tot} (ng/mL·h)	AUC_{extra} (%)
ip mice	9.103	2078	0.0833	0.8	154	86	0.7	982.3	1.3
iv mice	0.711	322.7	0.0833	1.1	133		0.9	88.8	15.2
iv dog	26.76	272 (μg/mL)	0.0833	3.8	0.69		3.8	654.7 (μg/mL·h)	0.9

Male Sprague-Dawley rats; 5 mg/kg for p.o.; 1 mg/kg for i.v.[1].

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

Animal Model:	Male Sprague-Dawley rats[1]

Dosage:	5 mg/kg for p.o.; 1 mg/kg for i.v.
Administration:	P.o. or i.v.
Result:	Showed good PK properties with an oral bioavailability (F) of 39.8%.

Animal Model:	6-week-old BALB/cA nude mice (BaF3-TMP3-TRKA-WT and BaF3-ETV6-TRKC-G623R xenograft models)[1]
Dosage:	30 mg/kg (dissolved in 70% PEG400 and 30% water)
Administration:	P.o.; twice daily; 12-14 consecutive days
Result:	Dose-dependently inhibited tumor progression with the TGI of 95% and 86% in BaF3-TMP3-TRKA-WT and BaF3-ETV6-TRKC-G623R xenograft model.

REFERENCES

[1]. Mei LC,et al. Conformational adjustment overcomes multiple drug-resistance mutants of tropomyosin receptor kinase. Eur J Med Chem. 2022 Apr 25;237:114406.

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

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