TRV-120027 TFA

Cat. No.: HY-P2141A

Molecular Formula: $C_{45}H_{68}F_3N_{13}O_{12}$

Molecular Weight: 1040.1

Sequence: {Sar}-Arg-Val-Tyr-Ile-His-Pro-Ala

Sequence Shortening: {Sar}-RVYIHPA

Target: Angiotensin Receptor; Arrestin

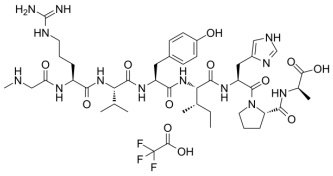
Pathway: GPCR/G Protein

Storage: Sealed storage, away from moisture and light

Powder -80°C 2 years

-20°C 1 year

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (96.14 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	0.9614 mL	4.8072 mL	9.6145 mL
	5 mM	0.1923 mL	0.9614 mL	1.9229 mL
	10 mM	0.0961 mL	0.4807 mL	0.9614 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (2.40 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (2.40 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (2.40 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

TRV120027 TFA, a β-arrestin-1-biased agonist of the angiotensin II receptor type 1 (AT1R), engages ß-arrestins while blocking G-protein signaling[1]. TRV120027 TFA induces acute catecholamine secretion through cation channel subfamily C3 (TRPC3) coupling, promotes the formation of a macromolecular complex composed of AT1R–β-arrestin-1–TRPC3–PLCγ at the plasma membrane. TRV120027 TFA inhibits angiotensin II–mediated vasoconstriction and increases cardiomyocyte contractility. TRV120027 TFA has the potential for the acute decompensated heart failure (ADHF) treatment[2].

IC_{50} & Target	IC50: the angiotensin II receptor type 1 (AT1R)[1]
In Vitro	TRV120027 TFA (100 nM) significantly increases the AT1R and TRPC3 association with the immunoprecipitated β-arrestin-1 in HEK293 cells co-transfected with Flag-AT1R-cherry, HA-β-arrestin-1 and TRPC3-GFP[2]. TRV120027 TFA (100 nM) induces an $[Ca^{2+}]i$ increase in HEK293 cells co-transfected with AT1R, β-arrestin-1, and TRPC3, which are significantly blocked by Pyr3 pre-incubation in HEK293 cells co-transfected with Flag-AT1R-Cherry, HA-β-arrestin-1, and TRPC3-GFP[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	TRV120027 TFA (intravenous injection; 0.3 or 1.5 μg/kg per minute; infusion rate, 0.5 mL/min) when added to furosemide decreases cardiac preload and afterload, systemic and renal vascular resistances, and left ventricular external work while increasing cardiac output and renal blood flow. GFR and renal excretory function are maintained in canines with experimental HF[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male mongrel dogs (weight, 20.5–30 kg)[1]
Dosage:	0.3 or 1.5 μg/kg per minute; infusion rate, 0.5 mL/min
Administration:	Intravenous injection
Result:	Resulted in dose-dependent vasodilation, increased cardiac contractility, and decreased myocardial oxygen consumption in dog.

CUSTOMER VALIDATION

- J Am Heart Assoc. 2022 Feb 15;11(4):e022070.
- University of Medicine Berlin. 2023 Mar.

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REFERENCES

[1]. Boerrigter G, et al. TRV120027, a novel β-arrestin biased ligand at the angiotensin II type I receptor, unloads the heart and maintains renal function when added to furosemide in experimental heart failure.Circ Heart Fail. 2012 Sep 1;5(5):627-34. Epub 2012 Aug 13.

[2]. Liu CH, et al. Arrestin-biased AT1R agonism induces acute catecholamine secretion through TRPC3 coupling.Nat Commun. 2017 Feb 9;8:14335.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA