Asivatrep

Cat. No.: HY-12777

CAS No.: 1005168-10-4

Molecular Formula: $C_{21}H_{22}F_5N_3O_3S$

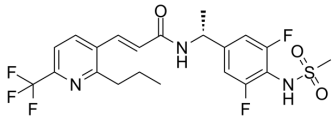
Molecular Weight: 491.47

Target: TRP Channel

Pathway: Membrane Transporter/Ion Channel; Neuronal Signaling

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (101.74 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0347 mL	10.1736 mL	20.3471 mL
	5 mM	0.4069 mL	2.0347 mL	4.0694 mL
	10 mM	0.2035 mL	1.0174 mL	2.0347 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 (5.09 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.09 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Asivatrep (PAC-14028) is a potent and selective transient receptor potential vanilloid type I (TRPV1) antagonist.

In Vitro

Asivatrep (PAC-14028) could prevent barrier damages, accelerate skin barrier recovery and suppress pruritus, showing a potential for the treatment of atopic dermatitis. It could suppress serum IgE increase, epidermal infiltration of inflammatory cells and mast cell degranulation associated with atopic dermatitis[1]. Asivatrep (PAC-14028) shows efficacies against diverse disease models including visceral pain, inflammatory bowel disease, and inflammatory pain[2].

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

In Vivo

Asivatrep (PAC-14028) shows a plasma half-life of 2.1 h in rats while it is extended slightly to 3.8 h in minipigs. Oral bioavailability at 10 mg/kg dose is determined to be 52.7% and 64.2% in rats and minipigs, respectively suggesting that

Asivatrep (PAC-14028) is relatively well-absorbed through oral route[1]. Asivatrep (PAC-14028) could inhibit capsaicin-evoked calcium influx in keratinocytes at sub-micromolar concentrations. This potent TRPV1 antagonistic activity in keratinocytes is manifested in vivo as the blockade of capsaicin-induced blood perfusion increase, and the accelerated barrier recovery from tape-stripping-induced barrier damages in hairless mice[3].

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PROTOCOL

Animal Administration [1]

Rats: 1 mg of Asivatrep (PAC-14028) is dissolved in 10 mL of methanol to obtain a concentration of 100 μg/mL. Male Sprague-Dawley rats/minipigs are given intravenously Asivatrep (PAC-14028) at a single dose of 1 mg/kg, orally PAC-14028 at a single dose of 10 mg/kg as a suspension in 1% methylcellulose and 0.5% Tween80, or topically a single or multiple doses of 10 mg/kg as 1% Asivatrep (PAC-14028) solution (gel form) in 68% PEG400 vehicle. For the topical application, dorsal area is shaved and painted with designated dose of Asivatrep (PAC-14028) formulation. Occlusive dressing is placed on the applied region for 6 h to withhold licking or scratching the area. Blood samples are collected from the retroorbital sinus or jugular vein into heparinized tubes at designated times after drug administration. Blood samples are centrifuged immediately, and the plasma is collected and store for analysis[1].

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

REFERENCES

[1]. Park YH, et al. Oral and topical pharmacokinetic studies of a novel TRPV1 antagonist, PAC-14028 in rats and minipigs using liquid chromatography/tandem mass spectrometric method. J Pharm Biomed Anal. 2012 Mar 5;61:8-14.

[2]. Lim KM, et al. Development of PAC-14028, a novel transient receptor potential vanilloid type 1 (TRPV1) channel antagonist as a new drug for refractory skin diseases. Arch Pharm Res. 2012 Mar;35(3):393-6.

[3]. Yun JW, et al. TRPV1 antagonist can suppress the atopic dermatitis-like symptoms by accelerating skin barrier recovery. J Dermatol Sci. 2011 Apr;62(1):8-15.

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