

## Product Data Sheet

Product Name: SAR7334

Cat. No.: GC33424

### Chemical Properties

Cas. No. 1333210-07-3

SMILES N[C@@H](C1)CCCN1[C@@H]2CC3=CC=CC=C3[C@H]2OC4=C(Cl)C=C(C#N)C=C4

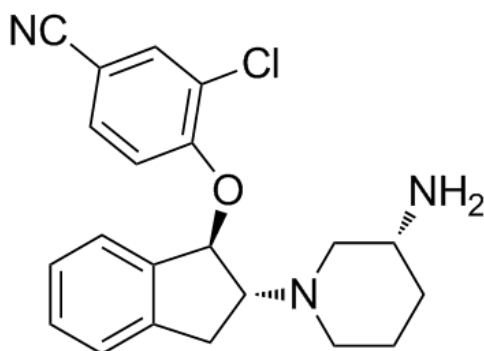
Formula  $C_{21}H_{22}ClN_3O$  M.Wt 367.87

Solubility DMSO :  $\geq 370$  mg/mL (1005.79 mM) Storage Store at  $-20^{\circ}\text{C}$

General tips For obtaining a higher solubility, please warm the tube at  $37^{\circ}\text{C}$  and shake it in the ultrasonic bath for a while. Stock solution can be stored below  $-20^{\circ}\text{C}$  for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT, or blue ice upon request.

### Structure



### Protocol

#### Cell experiment [1]:

Cell lines Immortalized mouse MPC5 podocytes

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

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|-------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Preparation Method            | MPC5 podocytes were cultured and matured in RPMI 1640 medium supplemented with 10% fetal bovine serum at 37°C with 5% CO <sub>2</sub> . Cells pretreated with SAR7334 (1μM) for 30 minutes, followed by stimulation with Angiotensin II (AngII; 1μM) for 24 hours.                                                           |
| Reaction Conditions           | 1μM; 30min pretreatment.                                                                                                                                                                                                                                                                                                     |
| Applications                  | SAR7334 significantly inhibited the AngII-induced overexpression of TRPC6, AT1R, and Caspase-3 proteins. SAR7334 also attenuated the degradation of podocyte structural proteins Nephhrin and Podocin. SAR7334 inhibited the fluorescence intensity of intracellular calcium (Ca <sup>2+</sup> ) and reduced cell apoptosis. |
| <b>Animal experiment [2]:</b> |                                                                                                                                                                                                                                                                                                                              |
| Animal models                 | Male C57BL/6J mice with cisplatin-induced chemotherapy-induced peripheral neuropathy (CIPN)                                                                                                                                                                                                                                  |
| Preparation Method            | A CIPN mouse model was established by administering cisplatin. SAR7334 (10mg/kg) was intraperitoneally injected beginning one day before the second cycle of cisplatin administration and continued for 7 days.                                                                                                              |
| Dosage form                   | 10mg/kg; i.p.; once daily for 7 days.                                                                                                                                                                                                                                                                                        |

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### Applications

SAR7334 alleviated cisplatin-induced CIPN, indicated by an increased paw withdrawal threshold and a shortened response time to an adhesive stimulus. SAR7334 also blocked the loss of intra-epidermal nerve fibers (IENFs) and Merkel cells in the plantar skin. Furthermore, SAR7334 improved anxiety-like behaviors in CIPN mice, increasing activity in the central area of the open field and in the open arms of the elevated plus maze. SAR7334 inhibited the activation of TRPC6 and PKC, and downregulated the excitability markers p-CAMKII and c-Fos in the paraventricular thalamic nucleus (PVT).

### References:

- [1] Feng Y, Li M, Wang Y, et al. Activation of TRPC6 by AngII Induces Podocyte Injury and Participates in Proteinuria of Nephrotic Syndrome. *Front Pharmacol.* 2022 Aug 3;13:915153.
- [2] Jiang YY, Li X, Hu FX, et al. Electroacupuncture alleviates chemotherapy-induced peripheral neuropathy and anxiety by reducing TRPC6/PKC-dependent activation of glutamatergic neurons in the paraventricular thalamic nucleus. *Neuroscience.* 2026 Jan 9;592:97-110.

### Background

SAR7334 is a highly potent and specific TRPC6 channel inhibitor ( $IC_{50}=7.9nM$ ). SAR7334 also inhibits TRPC3- and TRPC7-mediated  $Ca^{2+}$  influx into cells<sup>[1-2]</sup>. SAR7334 can be used in research related to fibrotic diseases such as focal segmental glomerulosclerosis, skeletal muscle dysfunction, as well as pulmonary arterial hypertension and pulmonary edema<sup>[3-4]</sup>.

In vitro, hippocampal neurons isolated from young, middle-aged, and aged mice were treated with SAR7334 (0.1  $\mu M$  or 1  $\mu M$ ) for 15 minutes. SAR7334 dose-dependently reduced the resting intracellular calcium ( $[Ca^{2+}]_i$ ) and sodium ( $[Na^+]_i$ ) concentrations in neurons, with a more pronounced reduction observed in middle-aged and aged neurons compared to young ones<sup>[5]</sup>. MPC5 podocytes were pretreated with SAR7334 (1  $\mu M$ ) for 30 minutes, followed by stimulation with AngII (1  $\mu M$ ) for 24 hours. SAR7334 significantly inhibited the expression of TRPC6, AT1R, and Caspase-3 proteins, increased the expression of the podocyte structural proteins Nephron and Podocin, and reduced intracellular  $Ca^{2+}$  fluorescence intensity and cell apoptosis<sup>[6]</sup>.

In vivo, spontaneously hypertensive rats (SHR) were treated with SAR7334 (oral administration;

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10mg/kg) for two days. Compared to the vehicle-treated control group, the SAR7334-treated group showed no significant change in mean arterial pressure (MAP)<sup>[7]</sup>. In establishing a chemotherapy-induced peripheral neuropathy (CIPN) mouse model via cisplatin intervention, SAR7334 (10mg/kg; i.p.) was administered beginning one day before the second cycle of cisplatin treatment and continued for 7 days. SAR7334 significantly alleviated cisplatin-induced CIPN symptoms, including improving the paw withdrawal threshold in mechanical allodynia tests, shortening the response time to an adhesive stimulus, and preventing the loss of intraepidermal nerve fibers and Merkel cells in the plantar skin. Concurrently, SAR7334 ameliorated anxiety-like behaviors in CIPN mice<sup>[8]</sup>.

### References:

- [1] Ilatovskaya DV, Palygin O, Levchenko V, et al. The Role of Angiotensin II in Glomerular Volume Dynamics and Podocyte Calcium Handling. *Sci Rep*. 2017 Mar 22;7(1):299.
- [2] Fang X, Dong S, Wu Y, et al. Ameliorated biomechanical properties of carotid arteries by puerarin in spontaneously hypertensive rats. *BMC Complement Med Ther*. 2021 Jun 22;21(1):173.
- [3] Ducrocq GP, Anselmi L, Stella SL Jr, et al. Inhibition and potentiation of the exercise pressor reflex by pharmacological modulation of TRPC6 in male rats. *J Physiol*. 2025 Sep;603(18):5027-5052.
- [4] Obara K, Takahashi S, Otake M, et al. Pharmacological Characteristics of Extracellular Ca<sup>2+</sup> Influx Pathways Responsible for Platelet-Activating Factor-Induced Contractions in Rat Esophagus Smooth Muscle: Involvement of L-Type, Receptor-Operated, and Store-Operated Ca<sup>2+</sup> Channels. *Biol Pharm Bull*. 2025;48(6):932-940.
- [5] Uryash A, Flores V, Adams JA, et al. Memory and Learning Deficits Are Associated With Ca<sup>2+</sup> Dyshomeostasis in Normal Aging. *Front Aging Neurosci*. 2020 Jul 16;12:224.
- [6] Feng Y, Li M, Wang Y, et al. Activation of TRPC6 by AngII Induces Podocyte Injury and Participates in Proteinuria of Nephrotic Syndrome. *Front Pharmacol*. 2022 Aug 3;13:915153.
- [7] Maier T, Follmann M, Hessler G, et al. Discovery and pharmacological characterization of a novel potent inhibitor of diacylglycerol-sensitive TRPC cation channels. *Br J Pharmacol*. 2015 Jul;172(14):3650-60.
- [8] Jiang YY, Li X, Hu FX, et al. Electroacupuncture alleviates chemotherapy-induced peripheral neuropathy and anxiety by reducing TRPC6/PKC-dependent activation of glutamatergic neurons in the paraventricular thalamic nucleus. *Neuroscience*. 2026 Jan 9;592:97-110.

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