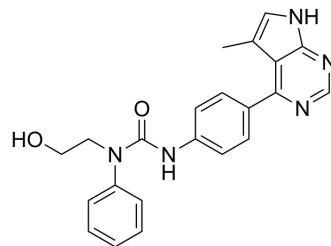


SR7826

| | | | |
|--------------------|---|-------|----------|
| Cat. No.: | HY-19353 | | |
| CAS No.: | 1219728-20-7 | | |
| Molecular Formula: | C ₂₂ H ₂₁ N ₅ O ₂ | | |
| Molecular Weight: | 387.43 | | |
| Target: | LIM Kinase (LIMK) | | |
| Pathway: | Cell Cycle/DNA Damage | | |
| Storage: | Powder | -20°C | 3 years |
| | | 4°C | 2 years |
| | In solvent | -80°C | 6 months |
| | | -20°C | 1 month |



SOLVENT & SOLUBILITY

| | | | | |
|----------|--|--------------------------|-----------|------------|
| In Vitro | DMSO : 100 mg/mL (258.11 mM; Need ultrasonic) | | | |
| | | Solvent Concentration | Mass | |
| | | | 1 mg | 5 mg |
| | | | 10 mg | |
| | Preparing Stock Solutions | 1 mM | 2.5811 mL | 12.9056 mL |
| | 5 mM | 0.5162 mL | 2.5811 mL | |
| | 10 mM | 0.2581 mL | 1.2906 mL | |
| | Please refer to the solubility information to select the appropriate solvent. | | | |
| In Vivo | 1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline) Solubility: 2.5 mg/mL (6.45 mM); Suspended solution; Need ultrasonic | | | |
| | 2. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.5 mg/mL (6.45 mM); Clear solution | | | |

BIOLOGICAL ACTIVITY

| | | | |
|---------------------------|--|--------------------------------------|---------------------------------------|
| Description | SR7826 is a class of bis-aryl urea derived potent, selective and orally active LIM kinase (LIMK) inhibitor with an IC ₅₀ of 43 nM for LIMK1. SR7826 is >100-fold more selective for LIMK1 than ROCK and JNK kinases ^[1] . | | |
| IC ₅₀ & Target | LIMK1 43 nM (IC ₅₀) | ROCKI 5536 nM (IC ₅₀) | ROCKII 6565 nM (IC ₅₀) |
| In Vitro | In the profiling against a panel of 61 kinases, SR7826 (compound 18b) at 1 μM inhibits only Limk1 and STK16 with ≥80% inhibition. SR7826 is highly efficient in inhibiting cell-invasion/migration in PC-3 cells. SR7826 (compound 18b) inhibits cofilin phosphorylation in A7r5 (IC ₅₀ = 470 nM) and PC-3 cells (IC ₅₀ < 1 μM) ^[1] . SR7826 (1 μM) inhibits contractions of prostate strips, which were induced by electrical field stimulation and inhibits cofilin | | |

phosphorylation in prostate tissues and cultured stromal cells (WPMY-1). In WPMY-1 cells, SR7826 causes breakdown of actin filaments and reduced viability^[3].

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

In Vivo

SR7826 (10 mg/kg; oral gavage; once daily; for 11 days; hAPPJ20 mice) treatment significantly reduces the phosphorylation of cofilin at Ser3. SR7826 also increases both apical and basal thin spine density significantly in hAPPJ20 mice over mock-treated animals^[2].

The plasma pharmacokinetics studies on rats are investigated. After intravenous injection, the PK properties of SR7826 (compound 18b; 1mg/kg) with a Cl of 5.2 mL/min/kg, a $T_{1/2}$ of 2.2h, an AUC of 8.4 $\mu\text{M}\cdot\text{h}$ and a C_{max} of 7.7 μM , and has 36% oral bioavailability in rats (oral administration; 2mg/kg)^[1].

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

| | |
|-----------------|--|
| Animal Model: | hAPPJ20 mice (6-month-old) ^[2] |
| Dosage: | 10 mg/kg |
| Administration: | Oral gavage; once daily; for 11 days |
| Result: | Significantly reduced the phosphorylation of cofilin at Ser3, a LIMK1 substrate. |

REFERENCES

[1]. Yan Yin, et al. Bis-aryl urea derivatives as potent and selective LIM kinase (Limk) inhibitors. J Med Chem. 2015 Feb 26;58(4):1846-61.

[2]. Benjamin W Henderson, et al. Pharmacologic inhibition of LIMK1 provides dendritic spine resilience against β -amyloid. Sci Signal. 2019 Jun 25;12(587):eaaw9318.

[3]. Qingfeng Yu, et al. Inhibition of human prostate smooth muscle contraction by the LIM kinase inhibitors, SR7826 and LIMKi3. Br J Pharmacol. 2018 Jun;175(11):2077-2096.

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

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