

---

**Product Data Sheet**

---

Product Name: Sch-42495 racemate

Cat. No.: GC31318

**Chemical Properties**

Cas. No. 145841-10-7

SMILES CSCC[C@@H](C(OCC)=O)NC(C(CSC(C)=O)CC1=CC=CC=C1C)=OFormula C<sub>20</sub>H<sub>29</sub>NO<sub>4</sub>S<sub>2</sub> M.Wt 411.58

Solubility Soluble in DMSO Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°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****Animal experiment:**

Rats[2] Streptozotocin-injected and citrate buffer-injected SHR are randomly allocated to receive by gavage Captopril Captopril (25 mg/kg BID in distilled water), Sch-42495 (30 mg/kg BID in 5% arabic gum), S21402 at 2 different doses (25 mg/kg BID or 50 mg/kg BID in 5% arabic gum), or vehicle for 4 weeks starting on the day of Streptozotocin or buffer injection. The choice of the 2 doses of S21402 is based on previous findings suggesting that sufficient renal NEP inhibition, comparable to 30 mg/kg of Sch-42495, may be obtained with 25 mg/kg of S21402, while 50 mg/kg of S21402 is needed to provide equipotent angiotensin I pressor response inhibitory efficacy compared with 25 mg/kg of Captopril. A group of diabetic SHR is also allocated to receive the combination of Sch-42495 (30 mg/kg BID) and Captopril (25 mg/kg BID) by gavage.

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

---

## Product Data Sheet

---

### References:

[1]. Watkins RW, et al.

Atrial natriuretic factor potentiating and hemodynamic effects of SCH 42495, a new, neutral metalloendopeptidase inhibitor. Am J Hypertens. 1993 May;6(5 Pt 1):357-68.

[2]. Tikkanen T, et al.

Dual inhibition of neutral endopeptidase and angiotensin-converting enzyme in rats with hypertension and diabetes mellitus. Hypertension. 1998 Oct;32(4):778-85.

### Background

Sch-42495 racemate is the racemate of Sch-42495. Sch-42495 is a novel neutral metalloendopeptidase (NEP) inhibitor. Sch-42495 is the orally active ethylester prodrug of SCH 42354.

SCH 42354 selectively inhibits hydrolysis of leu-enkephalin and ANF (IC<sub>50</sub> of 8.3 and 10.0 nM, respectively) in vitro[1].

Plasma levels of exogenous atrial natriuretic factor (ANF) are augmented and ANF clearance from plasma is delayed by oral Sch-42495 (3 to 30 mg/kg) in normotensive

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

---

## Product Data Sheet

---

rats. Plasma ANF levels in volume expanded rats are higher in Sch-42495-treated rats. Diuretic and natriuretic effects of ANF are increased in rats treated with Sch-42495. In Dahl-S hypertensive rats, Sch-42495 (1 to 10 mg/kg orally) produces falls in blood pressure of a magnitude similar to that observed in DOCA-Na hypertensive rats. Significant hypotensive activity is observed 18 h after a single 10 mg/kg oral dose in Dahl-S hypertensive rats. In DOCA-Na hypertensive rats, a single dose of Sch-42495 significantly decreases cardiac output and does not lower systemic vascular resistance, a profile similar to that of ANF[1]. Spontaneously hypertensive rats (SHR) aged 9 to 10 weeks are injected with either Streptozotocin (45 mg/kg) or citrate buffer and randomized to receive either Captopril (25 mg/kg BID), Sch-42495 (30 mg/kg BID), S21402 (25 or 50 mg/kg BID), or vehicle by gavage for 4 weeks. A group of diabetic SHR is also allocated to receive the combination of Sch-42495 (30 mg/kg BID) and Captopril (25 mg/kg BID). The degree of renal NEP inhibition is determined by autoradiography, and plasma renin activity (PRA) is determined by radioimmunoassay. In nondiabetic SHR, S21402 and Captopril are equally effective. Relative heart weight decreases in parallel to the changes in blood pressure. Renal NEP is clearly inhibited (70% to 92%; P

[1]. Watkins RW, et al. Atrial natriuretic factor potentiating and hemodynamic effects of SCH 42495, a new, neutral metalloendopeptidase inhibitor. *Am J Hypertens.* 1993 May;6(5 Pt 1):357-68. [2]. Tikkanen T, et al. Dual inhibition of neutral endopeptidase and angiotensin-converting enzyme in rats with hypertension and diabetes mellitus. *Hypertension.* 1998 Oct;32(4):778-85.

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA