

## Product Data Sheet

Product Name: IAA-94  
Cat. No.: GC15308

### Chemical Properties

Cas. No. 54197-31-8

Chemical Name 2-[[[(2R)-6,7-dichloro-2-cyclopentyl-2,3-dihydro-2-methyl-1-oxo-1H-inden-5-yl]oxy]-acetic acid

SMILES ClC1=C(C([C@](C2CCCC2)(C)C3=O)C3=CC(OCC(O)=O)=C1Cl

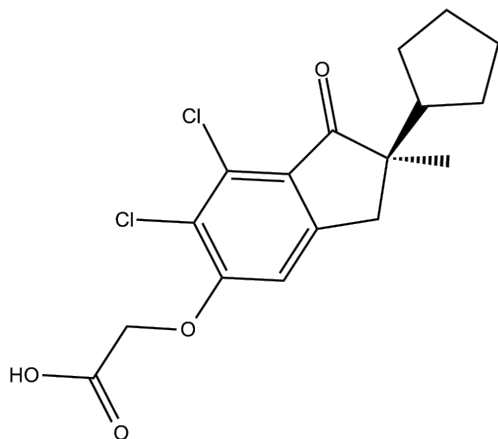
Formula  $C_{17}H_{18}Cl_2O_4$  M.Wt 357.2

Solubility  $\leq 15\text{mg/ml}$  in ethanol;  $15\text{mg/ml}$  in DMSO;  $15\text{mg/ml}$  in dimethyl formamide  
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]:

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Cell lines                      murine microglial cell line BV-2, Primary microglial cell

Preparation Method                      Flow cytometry was used to measure BV-2 cell uptake of fluorescent beads after stimulation with A $\beta$ 25-35, the active fragment of A $\beta$ , and A $\beta$ 35-25, the reverse, inactive form. Cells were treated with aggregated A $\beta$ 25-35 (50  $\mu$ M) for 30 min, 90 min, and 3 hr in the presence or not of the CLIC-1 inhibitor IAA-94 and with A $\beta$ 35-25 (50  $\mu$ M) for 3 hr. Treatments were performed on cells in suspension at 37°C; afterward, cells were washed with medium.

Reaction  
Conditions                      30  $\mu$ M for 3 h

Applications                      Primary microglia showed a phagocytic ability that remained substantially unmodified after A $\beta$  treatment. Treatment with IAA-94 did not modify the phagocytic ability of these cells.

### Animal experiment [2]:

Animal models                      Male CD-1 mice weighing 25-30 g

Preparation Method                      Groups of mice were treated i.t. with a selective  $\delta$ -opioid receptor agonist [D-Ala2]deltorphan II (10  $\mu$ g) in 10% 2-hydroxypropyl- $\beta$ -cyclodextrin/saline solution (5  $\mu$ l), and the antinociception induced by [D-Ala2]deltorphan II was measured for 1 h after the treatment. In order to ascertain the role of Ca<sup>2+</sup>-activated Cl<sup>-</sup> channels in the expression of  $\delta$ -opioid receptor-mediated antinociception, a selective Ca<sup>2+</sup>-activated Cl<sup>-</sup> channel blocker IAA-94 (2% Tween 20/saline solution, 1, 3, 10  $\mu$ g in 5  $\mu$ l) was pretreated i.t. 10 min prior to the [D-Ala2]deltorphan II injection.

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Dosage form 1, 3, 10 µg in 5 µl, i.t.

Applications Mice injected [D-Ala2]deltorphan II showed a marked antinociception (peak effect: 79.5±11.1% MPE). The antinociception induced by [D-Ala2]deltorphan II was attenuated by i.t.-pretreatment with IAA-94 in a dose-dependent manner, and the peak effect was significantly reduced to 44.8±10.0% MPE by 10 µg of IAA-94.

### References:

- [1]: Paradisi S, Matteucci A, Fabrizi C, et al. Blockade of chloride intracellular ion channel 1 stimulates Aβ phagocytosis[J]. Journal of neuroscience research, 2008, 86(11): 2488-2498.  
[2]: Yamazaki M, Mizoguchi H, Ohsawa M, et al. Implications of Ca<sup>2+</sup>-activated Cl<sup>-</sup> channels in the δ-opioid receptor-mediated antinociception in the mouse spinal cord[J]. Neuroscience letters, 2000, 295(3): 113-115.

### Background

IAA-94 (Indanyloxyacetic acid-94) is an intracellular chloride channel blocker [1]. IAA-94 inhibited CLIC-1-dependent chloride permeability with an apparent IC<sub>50</sub> of 8.6 µM [2]. IAA-94 depressed the K<sup>+</sup>-induced force with an IC<sub>50</sub> of 17.0 ± 1.2 µM [3].

In cells treated with IAA-94 (30 µM) with respect to control, the amount of intracellular Aβ<sub>1-42</sub> phagocytosis was remarkably increased after 24 hr of incubation [4]. Inhibition of Cl<sup>-</sup> channels with pan-chloride channel blocker IAA-94 (50 µM) abolished the protection induced by 200 nM CsA pre-treatment in cardiomyocytes [5]. The anion channel blocker IAA-94 (200 µM) significantly blocked glutamate and taurine release against Astrocytes in hypotonic solution [6].

IAA-94 was shown to abrogate cardioprotection mediated by IPC and cyclosporin A (CsA) [7]. Adult male rat hearts were subjected to the left coronary artery occlusion for 45min followed by 3h of reperfusion. A single intravenous bolus of phosphate buffered saline (PBS) (control) or IAA-94

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(20mg/kg body weight) was administered 5min before reperfusion. The infarct size (IS) was significantly higher in the IAA-94-treated group compared to control; the ratio of IS to area at risk was  $58.1 \pm 7\%$  in IAA-94 vs.  $33.5 \pm 6\%$  in control in this rat model [1].

### References:

- [1]. Ponnalagu D, Hussain A T, Thanawala R, et al. Chloride channel blocker IAA-94 increases myocardial infarction by reducing calcium retention capacity of the cardiac mitochondria[J]. Life sciences, 2019, 235: 116841.
- [2]. Tulk B M, Schlesinger P H, Kapadia S A, et al. CLIC-1 functions as a chloride channel when expressed and purified from bacteria[J]. Journal of Biological Chemistry, 2000, 275(35): 26986-26993.
- [3]. Doughty J M, Miller A L, Langton P D. Non-specificity of chloride channel blockers in rat cerebral arteries: block of the L-type calcium channel[J]. The Journal of physiology, 1998, 507(2): 433-439.
- [4]. Paradisi S, Matteucci A, Fabrizi C, et al. Blockade of chloride intracellular ion channel 1 stimulates A $\beta$  phagocytosis[J]. Journal of neuroscience research, 2008, 86(11): 2488-2498.
- [5]. Diaz R J, Fernandes K, Lytvyn Y, et al. Enhanced cell-volume regulation in cyclosporin A cardioprotection[J]. Cardiovascular research, 2013, 98(3): 411-419.
- [6]. Ye Z C, Oberheim N, Kettenmann H, et al. Pharmacological "cross-inhibition" of connexin hemichannels and swelling activated anion channels[J]. Glia, 2009, 57(3): 258-269.
- [7]. Diaz R J, Losito V A, Mao G D, et al. Chloride channel inhibition blocks the protection of ischemic preconditioning and hypo-osmotic stress in rabbit ventricular myocardium[J]. Circulation research, 1999, 84(7): 763-775.

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