

## Product Data Sheet

Product Name: AR7  
Cat. No.: GC19035

### Chemical Properties

Cas. No. 80306-38-3

SMILES CC1=CC=C(C2=NC3=CC=C(Cl)C=C3OC2)C=C1

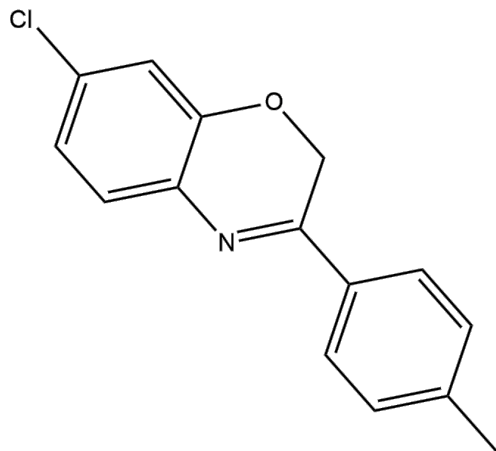
Formula  $C_{15}H_{12}ClNO$  M.Wt 257.71

Solubility DMSO : 25 mg/mL (97.01 mM); Water : < 0.1 mg/mL (insoluble) 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

#### Cell experiment [1]:

Cell lines Primary cortical neurons

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

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To investigate whether AR7 treatment modulates SNCA oligomer levels, mature primary cortical neurons (DIV9) were cultured under normal conditions with or without AR7 (0, 10, or 20 $\mu$ M) for up to 21 days. AR7 dissolved in cell culture-grade DMSO was added to the culture medium at DIV9 and DIV14 at the indicated concentrations. Conditioned medium and total cell lysates were extracted at DIV9, 14, and 21 for Western blotting and SNCA oligomer ELISA analysis.

Reaction Conditions 0-20 $\mu$ M; 21d

Applications AR7 attenuates the progressive accumulation of intracellular and extracellular SNCA oligomers in long-term cultures of cortical neurons.

### Animal experiment [2]:

Animal models C57BL/6 mice

Male C57BL/6 mice (7 weeks old) were housed in an air-conditioned room (24°C) with a 12-hour day/night cycle and allowed free access to water and food for one week. After a one-week acclimation period, the animals were randomly divided into four groups (n=6 mice each): Group 1, vehicle; Group 2, diclofenac; Preparation Method Group 3, AR7; and Group 4, diclofenac + AR7. The vehicle group received an intraperitoneal injection of 0.5% DMSO in saline. The diclofenac group received diclofenac (100mg/kg, intraperitoneally) twice every 12 hours. The AR7 group received AR7 (10mg/kg, intraperitoneally) one hour before diclofenac. The following day, the mice were anesthetized with Zolettiline 50 and sacrificed.

Dosage form 10mg/kg; ip; 6h

Applications AR7 alleviates diclofenac-induced hepatic steatosis in vivo.

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### References:

- [1]. Ho P W L, Leung C T, Liu H, et al. Age-dependent accumulation of oligomeric SNCA/ $\alpha$ -synuclein from impaired degradation in mutant LRRK2 knockin mouse model of Parkinson disease: role for therapeutic activation of chaperone-mediated autophagy (CMA)[J]. Autophagy, 2020, 16(2): 347-370.
- [2]. Lee W, Kim H Y, Choi Y J, et al. SNX10-mediated degradation of LAMP2A by NSAIDs inhibits chaperone-mediated autophagy and induces hepatic lipid accumulation[J]. Theranostics, 2022, 12(5): 2351.

### Background

AR7 is an atypical retinoic acid receptor  $\alpha$  (RAR $\alpha$ ) antagonist [1]. AR7 antagonizes RAR $\alpha$  to relieve its inhibition of CMA, thereby significantly enhancing LAMP2A and CMA activity and promoting the selective degradation of misfolded or aggregated proteins [2-3]. AR7 is commonly used to treat Parkinson's disease [4].

In primary cortical neurons, AR7 (0-20 $\mu$ M; 21d) attenuates the progressive accumulation of intracellular and extracellular SNCA oligomers in long-term cultures of cortical neurons [5]. In SN4741 cells, AR7 (20 $\mu$ M; 24h) reduces lipid droplet accumulation in the Wdr45-deficient model by activating chaperone-mediated autophagy (CMA) and promoting the degradation of the lipid biosynthesis enzyme Fasn [6].

In C57BL/6 mice, AR7 (10mg/kg; ip; 6h) alleviates diclofenac-induced hepatic steatosis [7]. In heterozygous offspring mice, administration of AR7 (10mg/kg; ip; 6 weeks) promotes hepatic SERPINA1<sup>E342K/ATZ</sup> elimination and mitigates hepatic SERPINA1<sup>E342K/ATZ</sup> aggregation pathology [8].

### References:

- [1]. Anguiano J, Garner T P, Mahalingam M, et al. Chemical modulation of chaperone-mediated autophagy by retinoic acid derivatives[J]. Nature chemical biology, 2013, 9(6): 374-382.
- [2]. Bourdenx M, Martín-Segura A, Scrivo A, et al. Chaperone-mediated autophagy prevents collapse of the neuronal metastable proteome[J]. Cell, 2021, 184(10): 2696-2714. e25.

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- [3]. Wang Y T, Lu J H. Chaperone-mediated autophagy in neurodegenerative diseases: molecular mechanisms and pharmacological opportunities[J]. Cells, 2022, 11(14): 2250.
- [4]. Chen J, Mao K, Yu H, et al. p38-TFEB pathways promote microglia activation through inhibiting CMA-mediated NLRP3 degradation in Parkinson's disease[J]. Journal of neuroinflammation, 2021, 18(1): 295.
- [5]. Ho P W L, Leung C T, Liu H, et al. Age-dependent accumulation of oligomeric SNCA/ $\alpha$ -synuclein from impaired degradation in mutant LRRK2 knockin mouse model of Parkinson disease: role for therapeutic activation of chaperone-mediated autophagy (CMA)[J]. Autophagy, 2020, 16(2): 347-370.
- [6]. Xiong Q, Sun H, Wang Y, et al. Lipid droplet accumulation in Wdr45-deficient cells caused by impairment of chaperone-mediated autophagic degradation of Fasn[J]. Lipids in Health and Disease, 2024, 23(1): 91.
- [7]. Lee W, Kim H Y, Choi Y J, et al. SNX10-mediated degradation of LAMP2A by NSAIDs inhibits chaperone-mediated autophagy and induces hepatic lipid accumulation[J]. Theranostics, 2022, 12(5): 2351.
- [8]. Lin J, Wei X, Dai Y, et al. Chaperone-mediated autophagy degrades SERPINA1E342K/ $\alpha$ 1-antitrypsin Z variant and alleviates cell stress[J]. Autophagy, 2025: 1-18.

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