
Product Data Sheet

Product Name: AR-13324 mesylate

Cat. No.: GC19034

Chemical Properties

Cas. No. 1422144-42-0

SMILES CC1=CC(C)=C(C(OCC2=CC=C([C@@H](CN)C(NC3=CC(C=CN=C4)=C4C=C3)=O)C=C2)=O)C=C1.CS(=O)(O)=O.CS(=O)(O)=O

Formula C₃₀H₃₅N₃O₉S₂ M.Wt 645.74

Solubility DMSO : 100 mg/mL (154.86 mM; Need ultrasonic) 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 [1]:**

Animal models Seven adult female cynomolgus monkeys, each weighing 3 to 5 kg with normotensive IOP

Preparation Method 50 μL (25 μL×2) of 0.04% AR-13324 was topically applied to 1 eye of each monkey. An equal volume of vehicle was applied to the contralateral control eye. IOP was measured before drug administration and 6 hours after dosing with a calibrated neumatonometer in the sitting position. IOP reading was taken 2 times on each eye and the average of 2 values was used to perform statistical analysis.

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

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Dosage form 50 μ L (25 μ L \times 2) of 0.04% AR-13324

Applications Six hours after a single dose of 0.04% AR-13324 to 7 normal monkey eyes, the IOP measured by pneumatonometer in treated eyes was reduced ($P < 0.005$) by 25% when compared with baseline measurements and by 24% when compared with contralateral vehicle-treated eyes

Animal experiment [2]:

Animal models Male DB rabbits (n=11, 2.15-0.09 kg)

Preparation Method The protocol entailed once per day—topical application of 1 drop of 0.04% AR-13324 for 2 days. Then, on the morning of the third day the animals were anesthetized and surgically prepared, and then, measurements were obtained before dosing with AR-13324 or vehicle (baseline measurements) and for 3 h after dosing.

Dosage form 1 drop of 0.04% AR-13324 for 2 days

Applications At 3 h postdosing, the reduction in EVP caused by AR-13324 treatment accounted for 42% of the measured reduction in IOP.

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References:

[1]. Wang RF, et al. Effect of 0.04% AR-13324, a ROCK, and norepinephrine transporter inhibitor, on aqueous humor dynamics in normotensive monkey eyes. J Glaucoma. 2015 Jan;24(1):51-4.

[2]. Kiel JW, Kopczynski CC. Effect of AR-13324 on episcleral venous pressure in Dutch belted rabbits. J Ocul Pharmacol Ther. 2015 Apr;31(3):146-51.

Background

AR-13324 is a potent inhibitor of ROCK I and ROCK II that has been shown to induce morphologic changes in cultured human and porcine TM cells at low concentration. AR-13324, a rho kinase inhibitor, and an inhibitor of the norepinephrine transporter, reduces intraocular pressure (IOP) in normotensive monkey eyes [1]. AR-13324 produces statistically significant lowering of EVP in DB rabbits [2].

The fixed-dose combination of AR-13324 0.02% and latanoprost 0.005% in PG324 Ophthalmic Solution provides clinically and statistically superior ocular hypotensive efficacy relative to its individual active components at the same concentrations [3]. AR-13324 0.02% was less effective than latanoprost by approximately 1 mmHg in patients with unmedicated IOPs in the range of 22 to 35 mmHg [4]

Six hours after a single dose of 0.04% AR-13324 to 7 normal monkey eyes, the IOP measured by pneumatonometer in treated eyes was reduced ($P < 0.005$) by 25% when compared with baseline measurements and by 24% when compared with contralateral

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vehicle-treated eyes [1]. At 3 h postdosing, the reduction in EVP caused by AR-13324 treatment accounted for 42% of the measured reduction in IOP [2].

References:

[1].Wang RF, et al. Effect of 0.04% AR-13324, a ROCK, and norepinephrine transporter inhibitor, on aqueous humor dynamics in normotensive monkey eyes. J Glaucoma. 2015 Jan;24(1):51-4.

[2].Kiel JW, Kopczynski CC. Effect of AR-13324 on episcleral venous pressure in Dutch belted rabbits. J Ocul Pharmacol Ther. 2015 Apr;31(3):146-51.

[3].Lewis RA, Levy B, Ramirez N, et al Fixed-dose combination of AR-13324 and latanoprost: a double-masked, 28-day, randomised, controlled study in patients with open-angle glaucoma or ocular hypertension British Journal of Ophthalmology 2016;100:339-344.

[4].Bacharach J, Dubiner HB, Levy B, Kopczynski CC, Novack GD; AR-13324-CS202 Study Group. Double-masked, randomized, dose-response study of AR-13324 versus latanoprost in patients with elevated intraocular pressure. Ophthalmology. 2015 Feb;122(2):302-7.

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