Product Data Sheet

Product Name: BMY 7378
Cat. No.: GC10848

Chemical Properties

Cas. No.	21102-95-4		
Chemical Name	8-[2-[4-(2-methoxyphenyl)piperazin-1-yl]ethyl]-8-azaspiro[4.5]decane-7,9-dione;dihydrochloride		
SMILES	COC1=CC=CC=C1N2CCN(CC2)CCN3C(=O)CC4(CCCC4)CC3=O.Cl.Cl		
Formula	$C_{22}H_{31}N_3O_3.2HCl$	M.Wt	458.42
Solubility	DMF: 10 mg/ml,DMSO: 25 mg/ml,Ethanol: 0.2 mg/ml,PBS (pH 7.2): 0.5 mg/ml	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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	BMY 7378		

Protocol

Animal experiment [1]:

Animal models	Spontaneously hypertensive rats (SHR)

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Preparation Method	Thirty-week-old spontaneously hypertensive rats (SHR) were treated for 4 weeks with BMY 7378 (10mg/kg per day, p.o.), or captopril (angiotensin-converting enzyme inhibitor, 40mg/kg per day, p.o.) (as a positive control). Blood pressure and cardiac function were measured in vivo, cardiac hypertrophy by histology, and α_{1D}-AR protein expression by immunofluorescence.
Dosage form	10mg/kg/day; 4 weeks; p.o.
Applications	BMY 7378 and captopril decreased blood pressure and improved hemodynamic parameters and cardiac function in treated SHR vs. untreated SHR. Histology showed increased cardiomyocyte size, fibrosis, and left ventricular hypertrophy in SHR hearts. BMY 7378 ameliorated fibrosis and cardiac hypertrophy, but had no effect on cardiomyocyte size in SHR. Effects of BMY 7378 were associated with increased α_{1D}-AR protein expression in SHR.

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References:
[1]Rodríguez J E, Saucedo-Campos A D, Vega A V, et al. The ?1D-adrenoreceptor antagonist BMY 7378 reverses cardiac hypertrophy in spontaneously hypertensive rats[J]. Journal of Hypertension, 2020, 38(8): 1496-1503.

Background

BMY 7378 is a selective antagonist of α_{1D}-adrenergic receptor (α_{1D}-AR) with a pki value of 8.89. It is also a mixed agonist and antagonist of serotonin 1A receptor (5-HT_{1A} R)[1, 2]. BMY 7378 can inhibit angiotensin converting enzyme and has antihypertensive activity[3].

In vitro, BMY 7378 (10nM, 10μM) treatment of AC01 cells significantly inhibited norepinephrine (NA)-induced inositol [1,4,5] triphosphate (IP_3) production[4].

In vivo, oral treatment of spontaneously hypertensive rats (SHR) with BMY 7378 (10mg/kg/day) for 4 weeks significantly reduced the blood pressure of the treated rats, improved cardiac myocyte fibrosis and cardiac hypertrophy, and increased the expression of α_{1D}-AR protein[5]. BMY 7378 (5mg/kg) was administered to adult male hamsters via surgically implanted osmotic minipumps for 28 days, which upregulated the mRNA of 5-HT_{1A} and 5-HT_{1B} receptors in the hamster hypothalamus, downregulated the mRNA of 5-HT_{1A} and monoamine oxidase-A in the brainstem, and altered the behavioral circadian rhythm of the hamsters[6].

References:
[1] Chen J. Characterisation of novel alpha1-adrenoceptor ligands[D]. UNSW Sydney,

2014.
[2] Jeffers R. The Involvement of the Intergeniculate Leaflet in the Potentiation of Photic Phase Shifts by the 5-HT1A Mixed Agonist/Antagonist BMY 7378[J]. 2013.
[3] Rodríguez J E, Andrade-Jorge E, Barquet-Nieto A, et al. BMY 7378, a selective α1D-adrenoceptor antagonist, is a new angiotensin converting enzyme inhibitor: In silico, in vitro and in vivo approach[J]. Biochimica et Biophysica Acta (BBA)-General Subjects, 2025, 1869(1): 130732.
[4] Ohmi K, Shinoura H, Nakayama Y, et al. Characterization of α1-adrenoceptors expressed in a novel vascular smooth muscle cell line cloned from p53 knockout mice, P53LMAC01 (AC01) cells[J]. British journal of pharmacology, 1999, 127(3): 756-762.
[5] Rodríguez J E, Saucedo-Campos A D, Vega A V, et al. The α1D-adrenoreceptor antagonist BMY 7378 reverses cardiac hypertrophy in spontaneously hypertensive rats[J]. Journal of Hypertension, 2020, 38(8): 1496-1503.
[6] Vijaya Shankara J, Orr A, Mychasiuk R, et al. Chronic BMY 7378 treatment alters behavioral circadian rhythms[J]. European Journal of Neuroscience, 2017, 46(11): 2782-2790.