Product Data Sheet

Product Name: Guanfacine
Cat. No.: GC14813

Chemical Properties

Cas. No.	29110-47-2		
Chemical Name	N-(diaminomethylidene)-2-(2,6-dichlorophenyl)acetamide		
SMILES	C1=CC(=C(C(=C1)Cl)CC(=O)N=C(N)N)Cl		
Formula	$C_9H_9Cl_2N_3O$	M.Wt	246.09
Solubility	Soluble in DMSO	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	Guanfacine		

Protocol

Cell experiment [1]:

Cell lines	Human mesenchymal stem cells (hMSC) and human osteoblast-like MG63 cells

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Preparation Method	hMSC and MG63 monolayers or 3D spheroids were cultured in DMEM/F12 medium with 10% fetal calf serum. For chondrogenic differentiation, hMSC spheroids were treated with Guanfacine (17.7ng/mL) in chondrogenic differentiation medium for 21 days; for osteogenic differentiation, spheroids were exposed to the same guanfacine concentration in osteogenic differentiation medium for 28 days. Medium and drug were refreshed every 2 days.
Reaction Conditions	17.7ng/mL; 21 days or 28 days
Applications	Guanfacine significantly reduced chondrogenic differentiation, indicated by downregulation of key chondrogenic genes (SOX9, Aggrecan, COL2A1) and decreased proteoglycan synthesis. Guanfacine also inhibited osteogenic differentiation.

Animal experiment [2]:

Animal models	Adult male wild-type (WT) and Nf1+/- mice (3–4 months old, C57BL/6J background)
Preparation Method	Mice were administered Guanfacine (0.1 or 0.3mg/kg, i.p.) daily for 6 days. Behavioral assessments were conducted 30 minutes post-injection using the open field test (OFT), cliff avoidance reaction (CAR) test, and delay discounting task (DDT).
Dosage form	0.1-0.3mg/kg; i.p.; Daily injection for 6 days.

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Applications	Guanfacine significantly reduced hyperactivity in Nf1+/- mice, decreasing total distance traveled in the OFT. Guanfacine improved behavioral inhibition in the CAR test by reducing entries into the edge zone and preventing falls. Guanfacine also attenuated impulsivity in the DDT, increasing the preference for larger delayed rewards over smaller immediate ones.

References:
[1] Wagener N, Lehmann W, Böker KO, et al. Chondral/Desmal Osteogenesis in 3D Spheroids Sensitized by Psychostimulants. J Clin Med. 2022 Oct 21;11(20):6218.
[2] Lukkes JL, Drozd HP, Fitz SD, et al. Guanfacine treatment improves ADHD phenotypes of impulsivity and hyperactivity in a neurofibromatosis type 1 mouse model. J Neurodev Disord. 2020 Jan 15;12(1):2.

Background

Guanfacine is a selective, orally active norepinephrine α2A receptor agonist with high specificity for the α2A receptor subtype[1-2]. By activating α2A-adrenergic receptors in the prefrontal cortex, Guanfacine inhibits excessive norepinephrine release, thereby enhancing prefrontal cortical function and improving cognitive abilities such as attention,

impulse control, and behavioral planning[3-4].

In vitro, incubation of P-glycoprotein-expressing LLC-PK1/MDR1 cells with Guanfacine (5μM and 50μM) for 60 minutes reduced P-glycoprotein levels[5]. Treatment of human mesenchymal stem cell (hMSC)-derived 3D spheroids with Guanfacine (17.7ng/mL) for 21 days (chondrogenic differentiation) or 28 days (osteogenic differentiation), Guanfacine significantly suppressed the proteoglycan synthesis, and reducing calcium nodule formation[6].

In vivo, a single intraperitoneal injection of Guanfacine (0.3–0.6mg/kg) in Wistar rats that had voluntarily consumed high amounts of alcohol (4.3 ± 0.2g/kg/24h; 5 months), Guanfacine significantly reduced 24-hour alcohol intake and attenuated alcohol deprivation effects as well as cue-induced alcohol-seeking behavior[7]. Daily intraperitoneal administration of Guanfacine (0.1–0.3mg/kg) for 6 consecutive days in 3–4 month old male Nf1+/- mice significantly improved impulsive choice behavior and behavioral inhibition deficits[8].

References:
[1] Arnsten AFT. Guanfacine's mechanism of action in treating prefrontal cortical disorders: Successful translation across species. Neurobiol Learn Mem. 2020 Dec;176:107327.
[2] Connor DF, Arnsten AF, Pearson GS, et al. Guanfacine extended release for the treatment of attention-deficit/hyperactivity disorder in children and adolescents. Expert Opin Pharmacother. 2014 Aug;15(11):1601-10..
[3] Rizzo R, Martino D. Guanfacine for the treatment of attention deficit hyperactivity disorder in children and adolescents. Expert Rev Neurother. 2015 Apr;15(4):347-54.
[4] Ota T, Yamamuro K, Okazaki K, et al. Evaluating Guanfacine Hydrochloride in the Treatment of Attention Deficit Hyperactivity Disorder (ADHD) in Adult Patients: Design, Development and Place in Therapy. Drug Des Devel Ther. 2021 May 11;15:1965-1969.
[5] Gillis NK, Zhu HJ, Markowitz JS. An in vitro evaluation of guanfacine as a substrate for P-glycoprotein. Neuropsychiatr Dis Treat. 2011;7:501-5.
[6] Wagener N, Lehmann W, Böker KO, et al. Chondral/Desmal Osteogenesis in 3D Spheroids Sensitized by Psychostimulants. J Clin Med. 2022 Oct 21;11(20):6218.
[7] Fredriksson I, Jayaram-Lindström N, Wirf M, et al. Evaluation of guanfacine as a potential medication for alcohol use disorder in long-term drinking rats: behavioral and

electrophysiological findings. Neuropsychopharmacology. 2015 Mar 13;40(5):1130-40.
[8] Lukkes JL, Drozd HP, Fitz SD, et al. Guanfacine treatment improves ADHD phenotypes of impulsivity and hyperactivity in a neurofibromatosis type 1 mouse model. J Neurodev Disord. 2020 Jan 15;12(1):2.

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