
Product Data Sheet

Product Name: GR 46611

Cat. No.: GC14373

Chemical Properties

Cas. No. 185259-85-2

Chemical Name (Z)-3-(3-(2-(dimethylamino)ethyl)-1H-indol-5-yl)-N-(4-methoxybenzyl)acrylamide

SMILES O=C(/C=C\C1=CC=C2NC=C(C2=C1)CCN(C)C)NCC(C=C3)=CC=C3OCFormula $C_{23}H_{27}N_3O_2$ M.Wt 377.49

Solubility Soluble to 50 mM in DMSO and to 10 mM in ethanol Storage Store at RT

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 CCRF CEM cells

Preparation Method CCRF CEM cells were cultured in RPMI-1640 medium supplemented with 10% heat-inactivated fetal bovine serum, 100U/ml penicillin, 100µg/ml streptomycin in a humidified incubator at 37°C and 5% CO₂. CCRF CEM cells were plated at a density of 2×10^5 cells/well in a 6-well plate with growth medium for 24h, and then were incubated with 1µM GR 46611 for 48h, the cell proliferation was analyzed.**Caution: Product has not been fully validated for medical applications. For research use only.**

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Reaction Conditions 1 μ M; 48h

Applications GR 46611 treatment significantly enhanced cell proliferation of CCRF CEM cells.

Animal experiment [2]:

Animal models Dravet syndrome (DS) mice

Preparation Method DS mice were primed with a hyperthermia-induced seizure on postnatal day of age (P) 18 \pm 1 day. After a 5-min acclimation to a RET-3 rectal temperature probe, body temperature was raised at a rate of 0.25 $^{\circ}$ C per minute using a heat lamp until the first generalized seizure resulting in a loss of posture. Subsequently, the same mice were tested for seizure threshold at P21 after receiving drug pretreatment (GR 46611 was dissolved in 5% DMSO, 30% propylene glycol in saline and administered intraperitoneally at 1mg/kg) 20min before repeating the hyperthermia protocol.

Dosage form 1mg/kg for once; i.p.

Applications GR 46611 treatment increased the threshold of hyperthermia-induced seizure and lowered seizure severity in DS mice.

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References:

[1] Sibella-Argüelles C.

The proliferation of human T lymphoblastic cells induced by 5-HT1B receptors activation is regulated by 5-HT-moduline[J]. Comptes Rendus de l'Académie des Sciences-Series III-Sciences de la Vie, 2001, 324(4): 365-372.

[2] Hatini P G, Commons

K G. A 5-HT1D-receptor agonist protects Dravet syndrome mice from seizure and early death[J]. European Journal of Neuroscience, 2020, 52(10): 4370-4374.

Background

GR 46611 is a 5-HT1B and 5-HT1D receptor agonist, which can regulate the feeding behavior of animals^[1]. GR 46611 enhances transporter ZnT8-dependent zinc import into insulin granules through stimulation of V-ATPase-driven acidification in β -cells and increases β -cell zinc content and augments β -cell-targeted drug delivery^[2]. GR 46611 has been widely used in rat formalin tests to alleviate inflammatory pain^[3].

In vitro, GR 46611 treatment (1 μ M) for 48 hours significantly promoted the proliferation of CCRF-CEM cells^[4].

In vivo, GR 46611 treatment via daily intraperitoneal injection at a dose of 1mg/kg for 14 days significantly increased the seizure threshold of Dravet syndrome (DS) mice induced

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by hyperthermia, and reduced the severity of seizures and increased the survival rate of the mice^[5]. A single injection of GR 46611 (30mg/kg) was administered, lasting for 3 hours, which significantly caused a decrease in rectal temperature in adult guinea pigs^[6]. A single injection of GR 46611 (0.6nM; 1 μ l) via anterior portion of paraventricular thalamic nucleus reduced the pain threshold of mice within 24 hours and prolonged the immobility time in the forced swimming test (FST) and tail suspension test (TST)^[7].

References:

- [1] Da Silva R A, de Oliveira S T, Hackl L P N, et al. Ingestive behaviors and metabolic fuels after central injections of 5-HT1A and 5-HT1D/1B receptors agonists in the pigeon[J]. Brain research, 2004, 1026(2): 275-283.
- [2] Lee S, Fraser H P, Schugar R C, et al. Pharmacologic stimulation of insulin granule acidification increases β -cell zinc content and augments β -cell-targeted drug delivery[J]. Journal of Biological Chemistry, 2025, 301(10).
- [3] Granados-Soto V, Argüelles C F, Rocha-González H I, et al. The role of peripheral 5-HT1A, 5-HT1B, 5-HT1D, 5-HT1E and 5-HT1F serotonergic receptors in the reduction of nociception in rats[J]. Neuroscience, 2010, 165(2): 561-568.
- [4] Sibella-Argüelles C. The proliferation of human T lymphoblastic cells induced by 5-HT1B receptors activation is regulated by 5-HT-moduline[J]. Comptes Rendus de l'Académie des Sciences-Series III-Sciences de la Vie, 2001, 324(4): 365-372.
- [5] Hatini P G, Commons K G. A 5-HT1D-receptor agonist protects Dravet syndrome mice from seizure and early death[J]. European Journal of Neuroscience, 2020, 52(10): 4370-4374.
- [6] Skingle M, Higgins G A, Feniuk W. Stimulation of central 5-HT1D receptors causes hypothermia in the guinea-pig[J]. Journal of Psychopharmacology, 1994, 8(1): 14-21.
- [7] Cui M, Ji R, Song L, et al. Neuronal and molecular mechanisms underlying chronic pain and depression comorbidity in the paraventricular thalamus[J]. Journal of Neuroscience, 2024, 44(13).

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