Product Data Sheet

Product Name: CGS 21680
Cat. No.: GC10172

Chemical Properties

Cas. No.	120225-54-9		
Chemical Name	3-[4-[2-[[6-amino-9-[(2R,3R,4S,5S)-5-(ethylcarbamoyl)-3,4-dihydroxyoxolan-2-yl]purin-2-yl]amino]ethyl]phenyl]propanoic acid		
SMILES	CCNC(=O)C1C(C(C(O1)N2C=NC3=C2N=C(N=C3N)NCCC4=CC=C(C=C4)CCC(=O)O)O)O		
Formula	$C_{23}H_{29}N_7O_6$	M.Wt	499.52
Solubility	≥ 19.25mg/mL 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	CGS 21680		

Protocol

Cell experiment [1]:

Cell lines	UROtsa cells，human neutrophils
Preparation Method	Serum-free culture medium (without penicillin and streptomycin) containing 10^8 CFU/ml of UPEC strain IA2 was added to the bottom well of transwell inserts for 24h. Bacterial multiplication was limited by incubating the UROtsa cells with gentamicin (50μg/mL) 24h prior to infection. Human neutrophils were prepared as described above, and 3×10^6 neutrophils were added to the top well. Samples were taken from the bottom well after 0, 1, 2, and 3h. The number of neutrophils that had migrated was counted in a Bürker chamber. To examine the role of adenosine receptor activation in transuroepithelial neutrophil migration, adenosine (10μM) or the specific A_{2A} receptor agonist CGS 21680 (1μM) was added to the top well together with neutrophils after 24h of UPEC infection.

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Reaction Conditions	1μM; 3h
Applications	When cells were stimulated with the A_{2A} receptor agonist CGS 21680, UPEC-evoked migration was significantly decreased after 1h and 2h.

Animal experiment [2]:

Animal models	NSG mice
Preparation Method	Female NSG mice aged 6–8 weeks were injected i.p. daily (day 2 to day 11) with saline/0.2% DMSO (vehicle) or vehicle containing CGS 21680 (0.1mg/kg). hPBMCs, isolated by density centrifuga tion using Ficoll-Paque PLUS and resuspended in Dulbecco's phosphate-buffer saline , were injected i.p. (day 0) (10×10^6 hPBMCs/mouse). At 3 weeks post-hPBMC injection, mice were checked for en graftment by immunophenotyping of tail vein blood. Mice were monitored for signs of GVHD using a scoring system, giving a total clinical score out of 10. Mice were euthanized at 10weeks post-injection of hPBMCs, or earlier if exhibiting a clinical score of ≥8 or a weight loss of ≥10%, according to the approved animal ethics protocol.
Dosage form	0.1mg/kg; i.p.
Applications	CGS 21680 increased weight loss, and failed to reduce the clinical score or increase survival in this humanised mouse model of GVHD. CGS 21680 reduced T regulatory cells and increased serum human IL-6 concentrations. CGS 21680 reduced serum human tumor necrosis factor (TNF)-α concentrations and leukocyte infiltration into the liver.

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References:
[1]Säve S, Mohlin C, Vumma R, et al. Activation of adenosine A2A receptors inhibits neutrophil transuroepithelial migration[J]. Infection and immunity, 2011, 79(8): 3431-3437.
[2]Geraghty N J, Adhikary S R, Watson D, et al. The A2A receptor agonist CGS 21680 has beneficial and adverse effects on disease development in a humanised mouse model of graft-versus-host disease[J]. International Immunopharmacology, 2019, 72: 479-486.

Background

CGS 21680 is a selective adenosine A_{2A} receptor agonist with an IC_{50} value of 22nM[1]. This product is in free form, which is unstable, we recommend the stable salt form CGS 21680 Hydrochloride (GC11978) with the same biological activity. CGS 2168 enhances the release of excitatory transmitter amino acids in the ischemic rat cerebral cortex[2]. CGS 21680 accelerates the resequestration of cytoplasmic calcium and inhibits the proinflammatory activity of human neutrophils[3].

In vitro, CGS 21680 (1μM) treatment of human urothelial cell line (UROtsa cells) and human neutrophils for 3h significantly reduced cell migration induced by uropathogenic *Escherichia coli* (UPEC)[4].

In vivo, CGS 21680 (0.1mg/kg) treated humanized NSG mice by intraperitoneal injection had a

dual effect, increasing weight loss, reducing T cells, and increasing serum human IL-6 concentrations, but reducing hepatic leukocyte infiltration and serum human TNF-α concentrations[5]. CGS 21680 (0.1mg/kg) was intraperitoneally injected into mice with pleurisy, which significantly reduced the levels of inflammatory factors, neutrophil infiltration and the extent of lung injury[6]. CGS 21680 (0.1mg/kg) was intraperitoneally injected into mice with spinal cord injury, which reduced tissue damage, influx of myeloperoxidase-positive leukocytes, nuclear factor-κB activation and iNOS expression in spinal cord tissue, and reduced JNK MAPK activation in spinal cord oligodendrocytes[7].

References:

[1] Varani K, Gessi S, Merighi S, et al. Adenosine A2A receptors of human circulating blood elements[J]. Drug development research, 1998, 45(3-4): 253-260.
[2] O'regan M H, Simpson R E, Perkins L M, et al. The selective A2 adenosine receptor agonist CGS 21680 enhances excitatory transmitter amino acid release from the ischemic rat cerebral cortex[J]. Neuroscience letters, 1992, 138(1): 169-172.
[3] Anderson R, Visser S S, Ramafi G, et al. Accelerated resequestration of cytosolic calcium and suppression of the pro-inflammatory activities of human neutrophils by CGS 21680 in vitro[J]. British journal of pharmacology, 2000, 130(4): 717-724.
[4] Säve S, Mohlin C, Vumma R, et al. Activation of adenosine A2A receptors inhibits neutrophil transuroepithelial migration[J]. Infection and immunity, 2011, 79(8): 3431-3437.
[5] Geraghty N J, Adhikary S R, Watson D, et al. The A2A receptor agonist CGS 21680 has beneficial and adverse effects on disease development in a humanised mouse model of graft-versus-host disease[J]. International Immunopharmacology, 2019, 72: 479-486.
[6] Impellizzeri D, Di Paola R, Esposito E, et al. CGS 21680, an agonist of the adenosine (A2A) receptor, decreases acute lung inflammation[J]. European journal of pharmacology, 2011, 668(1-2): 305-316.
[7] Genovese T, Melani A, Esposito E, et al. The selective adenosine A2A receptor agonist CGS 21680 reduces JNK MAPK activation in oligodendrocytes in injured spinal cord[J]. Shock, 2009, 32(6): 578-585.