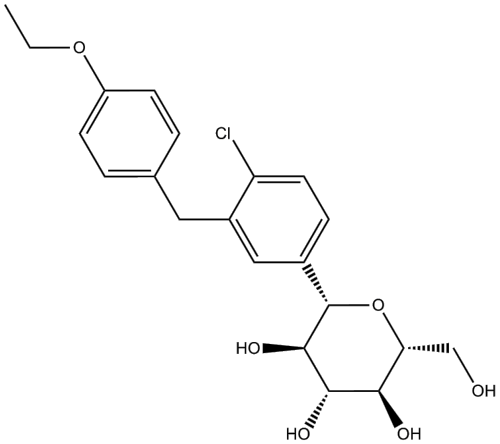
Product Data Sheet

Product Name: Dapagliflozin
Cat. No.: GC15530

Chemical Properties

Cas. No.	461432-26-8		
Chemical Name	(2S,3R,4R,5S,6R)-2-[4-chloro-3-[(4-ethoxyphenyl)methyl]phenyl]-6-(hydroxymethyl)oxane-3,4,5-triol		
SMILES	CCOC1=CC=C(C=C1)CC2=C(C=CC(=C2)C3C(C(C(C(O3)CO)O)O)O)Cl		
Formula	$C_{21}H_{25}ClO_6$	M.Wt	408.87
Solubility	≥ 15.1mg/mL in DMSO, ≥ 116.6 mg/mL in EtOH	Storage	Store at-20°C,sealed storage, away from moisture
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]:

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Cell lines	Human hepatocyte-derived liver cells (LO2) and human hepatocellular carcinoma cells (HepG2)
Preparation Method	Cells cultured in DMEM supplemented with 10% FBS at 37 ⊿in a humidified incubator containing 5% CO2, the cells were treated with 0.3 mM PA for 24 h to create the hepatocyte steatosis model in vitro. Then, hepatocytes were exposed to dapagliflozin at a concentration of 20 μM with or without chloroquine for 24 h.
Reaction Conditions	20 μM;24h
Applications	Exposure to 0.3 mM PA for 24 h dramatically increased the intracellular lipid accumulation in LO2 cells and HepG2 cells, whereas cotreatment with dapagliflozin could obviously attenuate the PA-induced lipid accumulation in both of hepatic cell lines.

Animal experiment [2]:

Animal models	Eight-week-old male BKS.Cg-Dock7m+/+Leprdb/Nju (db/db) mice
Preparation Method	Mice were group-housed conventionally and maintained on a 12-h light/dark cycle with free access to food and water. After a one-week adaptation, the diabetic condition was confirmed if the fasting blood glucose was 11.1 mmol/L. The diabetic mice were randomly assigned to two groups with 9 mice per group, and treated by daily intragastric administration of 1 mg/kg dapagliflozin or vehicle (water) for 6 weeks.
Dosage form	1 mg/kg;6 weeks;i.g.

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Applications	In db/db mice, treatment with dapagliflozin for 6 weeks had little effects on body weight. The fasting blood glucose level significantly declined after the 6-week treatment of dapagliflozin.

References:
[1]. Li L, Li Q, et,al.Dapagliflozin Alleviates Hepatic Steatosis by Restoring Autophagy via the AMPK-mTOR Pathway. Front Pharmacol. 2021 May 17;12:589273. doi: 10.3389/fphar.2021.589273. PMID: 34093169; PMCID: PMC8176308.
[2]. Wei R, Cui X, et,al. Dapagliflozin promotes beta cell regeneration by inducing pancreatic endocrine cell phenotype conversion in type 2 diabetic mice. Metabolism. 2020 Oct;111:154324. doi: 10.1016/j.metabol.2020.154324. Epub 2020 Jul 23. PMID: 32712220.

Background

Dapagliflozin, a sodium-glucose cotransporter 2 (SGLT2) inhibitor, is a novel antidiabetic agent that is approved for the treatment of T2DM by based on its ability to inhibit SGLT2-mediated renal glucose reabsorption. In addition to providing effective glycaemic control, dapagliflozin help decrease body weight, reduce rate of cardiovascular death, and possibly slow the progression of diabetic kidney diseases[1-3].

Dapagliflozin(20 μM;24h) promoted ACC1 phosphorylation and ACOX1 protein expression, promoted autophagy and alleviated lipid accumulation in PA-stimulated LO2 cells and HepG2 cells[4]. In diabetic proximal renal tubule cells, Dapaglide(20 μM;48h) net improved HG-induced autophagy flux reduction and inhibited mTOR by increasing AMPK activity, meanwhile dapagliflozin inhibited NF-κB pathway inflammatory changes[9].

In db/db mice, treatment with dapagliflozin(1 mg/kg;6 weeks;i.g.) for 6 weeks had little effects on body weight. The fasting blood glucose level significantly declined after the 6-week treatment of dapagliflozin[5]. Dapagliflozin(30mg/kg/day; p.o.) attenuated SGLT2 expression, which could prevent excessive glucose absorption and increase AMPK phosphorylation in HFD-induced obese mice or OA-stimulated HuS-E/2 cells[6]. Dapagliflozin (1mg/kg; i.v.) given pre-ischemia conferred the maximum level of cardioprotection quantified through the decrease in arrhythmia, attenuated infarct size, decreased cardiac apoptosis and improved cardiac mitochondrial function, biogenesis and

dynamics, leading to LV function improvement during cardiac I/R injury[7]. Dapagliflozin (1.5 mg/kg;23days; p.o.) provided glomerular protection in mice with protein-overload proteinuria induced by bovine serum albumin (BSA). Dapagliflozin limited proteinuria, glomerular lesions, and podocyte dysfunction and loss[8].

References:

[1]. Dhillon S. Dapagliflozin: A Review in Type 2 Diabetes. Drugs. 2019 Jul;79(10):1135-1146. doi: 10.1007/s40265-019-01148-3. Erratum in: Drugs. 2019 Dec;79(18):2013. PMID: 31236801; PMCID: PMC6879440.
[2]. Plosker GL. Dapagliflozin: a review of its use in type 2 diabetes mellitus. Drugs. 2012 Dec 3;72(17):2289-312. doi: 10.2165/11209910-000000000-00000. PMID: 23170914.
[3]. Plosker GL. Dapagliflozin: a review of its use in patients with type 2 diabetes. Drugs. 2014 Dec;74(18):2191-209. doi: 10.1007/s40265-014-0324-3. PMID: 25389049.
[4]. Li L, Li Q,et,al.Dapagliflozin Alleviates Hepatic Steatosis by Restoring Autophagy via the AMPK-mTOR Pathway. Front Pharmacol. 2021 May 17;12:589273. doi: 10.3389/fphar.2021.589273. PMID: 34093169; PMCID: PMC8176308.
[5]. Wei R, Cui X, et,al. Dapagliflozin promotes beta cell regeneration by inducing pancreatic endocrine cell phenotype conversion in type 2 diabetic mice. Metabolism. 2020 Oct;111:154324. doi: 10.1016/j.metabol.2020.154324. Epub 2020 Jul 23. PMID: 32712220.
[6]. Chiang H, Lee JC, et,al. Delayed intervention with a novel SGLT2 inhibitor NGI001 suppresses diet-induced metabolic dysfunction and non-alcoholic fatty liver disease in mice. Br J Pharmacol. 2020 Jan;177(2):239-253. doi: 10.1111/bph.14859. Epub 2019 Nov 12. PMID: 31497874; PMCID: PMC6989948.
[7]. Lahnwong S, Palee S, et,al. Acute dapagliflozin administration exerts cardioprotective effects in rats with cardiac ischemia/reperfusion injury. Cardiovasc Diabetol. 2020 Jun 15;19(1):91. doi: 10.1186/s12933-020-01066-9. PMID: 32539724; PMCID: PMC7296726.
[8]. Cassis P, Locatelli M, et,al. SGLT2 inhibitor dapagliflozin limits podocyte damage in proteinuric nondiabetic nephropathy. JCI Insight. 2018 Aug 9;3(15):e98720. doi: 10.1172/jci.insight.98720. PMID: 30089717; PMCID: PMC6129124.
[9]. Xu J, Kitada M, et,al. Dapagliflozin Restores Impaired Autophagy and Suppresses Inflammation in High Glucose-Treated HK-2 Cells. Cells. 2021 Jun 10;10(6):1457. doi: 10.3390/cells10061457. PMID: 34200774; PMCID: PMC8230404.