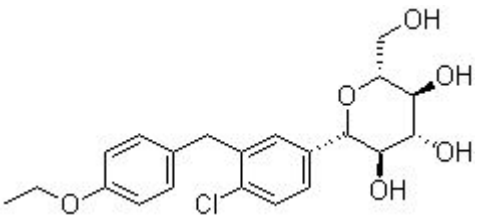
Product Introduction

Dapagliflozin

Dapagliflozin is a potent and selective **hSGLT2** inhibitor with **EC50** of 1.1 nM, exhibiting 1200-fold selectivity over hSGLT1. Phase 3.

Technical Data:

Molecular Weight (MW):	408.87	
Formula:	$C_{21}H_{25}ClO_6$	
Solubility (25°C) *** <1 mg/ml means slightly soluble or insoluble:**	DMSO 82 mg/mL	
	Water <1 mg/mL	
	Ethanol 17 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	461432-26-8	

Biological Activity

Dapagliflozin is not sensitive to hSGLT1 with a 1200-fold IC50. [1] Dapagliflozin is 32-fold more potent than phlorizin against hSGLT2 but 4-fold less than phlorizin against hSGLT1. Dapagliflozin is highly selective versus GLUT transporters and displays 8–9% inhibition in protein-free buffer at 20 μM and virtually no inhibition in the presence of 4% bovine serum albumin. [2] Dapagliflozin has good permeability across Caco-2 cell membranes and is a substrate for P-glycoprotein (P-gp) but not a significant P-gp inhibitor. Dapagliflozin is stable in rat, dog, monkey, and human serum at 10 μM. Dapagliflozin shows no inhibitory

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responses or induction to human P450 enzymes. The in vitro metabolic pathways Dapagliflozin are glucuronidation, hydroxylation, and O-deethylation. [3]

Dapagliflozin reduces blood glucose levels by 55% after 0.1 mg/kg oral dose in hyperglycemic streptozotocin (STZ) rats, which is in part to the metabolic stability conferred by the C-glucoside linkage. Dapagliflozin displays a favorable absorption, distribution, metabolism, and excretion (ADME) profile and is orally bioavailable. [1] Dapagliflozin (1 mg/kg) causes significant dose-dependent glucosuria and increase in urine volume in normal rats over 24 hours post-dose. Dapagliflozin induces increase in urine glucose and urine volume excretion at 6 hours post-dose in Zucker diabetic fatty (ZDF) rats. Dapagliflozin lowers fasting and fed glucose levels in ZDF rats even by 2 weeks of treatment, without any marker of renal or liver toxicity. [2] Dapagliflozin significantly reduces the development of hyperglycaemia, with lowered blood glucose. Dapagliflozin could improve the insulin sensitivity, reduce β-cell mass and the development of impaired pancreatic function. [4]

More potent stimulator of glucosuria than other SGLT2 inhibitors.

References

[1] Meng W, et al. J Med Chem, 2008, 51(5), 1145-1149.

[2] Han S, et al. Diabetes, 2008, 57(6), 1723-1729.

[3] Obermeier M, et al. Drug Metab Dispos, 2010, 38(3), 405-414.

[4] Macdonald FR, et al. Diabetes Obes Metab, 2010, 12(11), 1004-1012.

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