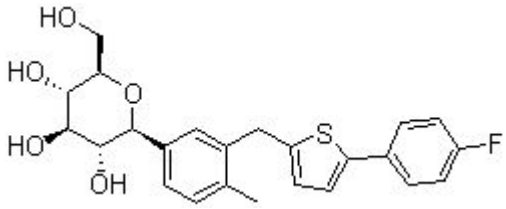
Product Introduction

Canagliflozin

Canagliflozin is a highly potent and selective SGLT2 inhibitor for **hSGLT2** with **IC50** of 2.2 nM, exhibits 413-fold selectivity over hSGLT1.

Technical Data:

Molecular Weight (MW):	444.52	
Formula:	$C_{24}H_{25}FO_5S$	
Solubility (25°C) * **<1 mg/ml means slightly soluble or insoluble:**	DMSO 89 mg/mL	
	Water <1 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	842133-18-0	

Biological Activity

Canagliflozin is a novel C-glucoside with thiophene ring. Canagliflozin inhibits Na^+-dependent ^{14}C-AMG uptake in a concentration-dependent fashion. Canagliflozin inhibits ^{14}C-AMG uptake in CHO-hSGLT1 and mSGLT1 cells with IC50 of 0.7 μM and >1 μM, respectively. Canagliflozin inhibits the facilitative (non-Na^+-linked) GLUT-mediated ^2H-2-DG uptake in L6 myoblasts by less than 50%. In sham-injected oocytes, Canagliflozin (10 μM) or phlorizin (3 mM) alone in the presence of 50 μM DNJ does not affect currents. In SGLT3-injected oocytes, DMSO and Canagliflozin 10 μM inhibits DNJ-induced currents by

15.6% and 23.4%, respectively.[1]

Canagliflozin shows pronounced anti-hyperglycemic effects in high-fat diet fed KK (HF-KK) mice. Oral administration at 30 mg/kg of Canagliflozin to male SD rats induces glucose excretion over 24 hours by 3,696 mg per 200 g body weight. Pharmacokinetic studies reveals a much higher exposure of Canagliflozin following oral administration. Following intravenous and oral doses of 3 and 10 mg/kg, respectively, to male SD rats, AUC_{0-inf}, po, $t_{1/2}$ and oral bioavailability are determined to be 35,980 ng·h/mL, 5.2 hours, and 85%, respectively. Thus, inhibition of SGLT2 in renal tubules after oral dosing of Canagliflozin is likely to continuously suppress reabsorption of glucose. The extensive UGE would reflect excellent pharmacokinetic properties of Canagliflozin in vivo as well as high potency of SGLT2 inhibition. Since most of the filtered glucose is reabsorbed by SGLT2 in the renal tubules, the novel compound would be useful for an anti-diabetic agent. Single oral administration of Canagliflozin at 3 mg/kg remarkably reduced blood glucose levels without influencing food intake in hyperglycemic high-fat diet fed KK (HF-KK) mice. There is a 48% reduction in blood glucose level versus vehicle at 6 hours. In contrast, Canagliflozin only slightly affects blood glucose levels in normoglycemic mice. Therefore, Canagliflozin would control hyperglycemia in the therapy of T2DM with low risk of hypoglycemia. [2]

References

[1] Liang Y, et al. PLoS One. 2012, 7(2), e30555.

[2] Nomura S, et al. J Med Chem. 2010, 53(17), 6355-6360.

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