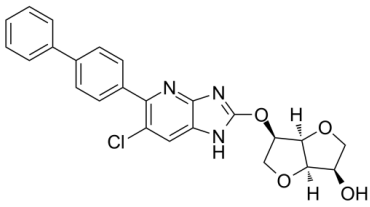
Data Sheet

Product Name:	MK8722
Cat. No.:	CS-0039843
CAS No.:	1394371-71-1
Molecular Formula:	C24H20ClN3O4
Molecular Weight:	449.89
Target:	AMPK
Pathway:	Epigenetics; PI3K/Akt/mTOR
Solubility:	DMSO : ≥ 62.5 mg/mL (138.92 mM)



BIOLOGICAL ACTIVITY:

MK8722 is a potent and systemic **pan-AMPK** activator. IC50 & Target: AMPK[1] **In Vitro:** MK8722 (MK-8722) is a potent, direct, allosteric activator of all 12 mammalian AMPK complexes. MK8722 activates pAMPK complexes with increased potency and magnitude versus AMP, with EC_{50} values of ~1 to 60 nM and increased activation by factors of ~4 to 24. Although MK8722 exhibits higher affinity for β1-containing (~1 to 6 nM) versus β2-containing (~15 to 63 nM) pAMPK complexes, it is the most potent activator of β2 complexes reported to date. pAMPK activation by maximal AMP plus MK8722 is synergistic, demonstrating that the agents act at distinct sites[1]. **In Vivo:** Chronic antihyperglycemic efficacy of MK8722 (MK-8722) is evaluated in db/db mice, a leptin receptor-deficient T2DM model. Once-daily administration of MK8722 results in dose-dependent lowering of ambient blood glucose. On treatment day 12, glucose reductions after MK8722 treatment (30 mpk/day) are comparable to those observed with the PPARγ agonist BRL49653 (3 mpk/day). Unlike BRL49653, the glucose-lowering action of MK8722 manifests without significant effects on body weight, which is a consistent finding. Dose-dependent increases in tissue pACC are maintained throughout the dosing period. Chronic efficacy, without tachyphylaxis, is also observed in additional dysmetabolic and diabetic rodent models. In all cases, efficacy is associated with trough MK8722 plasma levels comparable to the concentrations required to acutely stimulate skeletal muscle glucose uptake. Chronic MK8722 dosing in mice also increases muscle Glut4 protein levels, possibly contributing to efficacy[1].

PROTOCOL (Extracted from published papers and Only for reference)

Animal Administration: [1]Mice[1]

Housing Lean C57BL/6 mice at 10-12 weeks of age and **C57BL/6 eDIO mice** at 16 weeks of age are used. **db/db mice** at 7 weeks of age are used. Animals are maintained on a 12 hr/12 hr light-dark cycle with free access to food and water with the temperature maintained at 22°C. Four lean C57BL/6 mice are housed in a standard cage. eDIO mice are individually caged. Eight db/db mice are housed in a large rodent cage. C57BL/6 mice and db/db mice are maintained on regular rodent chow diet 7012 (5% dietary fat; 3.75 kcal/g) for 1-2 weeks before receiving compound treatments. eDIO mice are maintained on 60% kcal% fat diet. **Oral dosing of MK8722** in standard vehicle, or vehicle alone, is performed using **10 mL/kg** body weight. The effect of MK8722 on various metabolic parameters is established by comparison to vehicle treated animals[1].

References:

[1]. Myers RW, et al. Systemic pan-AMPK activator MK-8722 improves glucose homeostasis but induces cardiachypertrophy. Science. 2017 Aug 4;357(6350):507-511.

CAIndexNames:

D-Mannitol, 1,4:3,6-dianhydro-2-O-(5-[1,1'-biphenyl]-4-yl-6-chloro-3H-imidazo[4,5-b]pyridin-2-yl)-

SMILES:

O[C@H]1[C@@]([C@]2([H])OC1)([H])OC[C@H]2OC3=NC4=NC(C(C=C5)=CC=C5C6=CC=CC=C6)=C(Cl)C=C4N3

Caution: Product has not been fully validated for medical applications. For research use only.

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