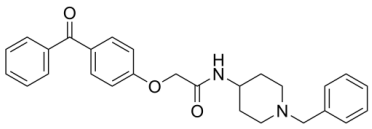
Data Sheet

Product Name:	AdipoRon
Cat. No.:	CS-2238
CAS No.:	924416-43-3
Molecular Formula:	$C_{27}H_{28}N_2O_3$
Molecular Weight:	428.52
Target:	Adiponectin Receptor
Pathway:	Metabolic Enzyme/Protease
Solubility:	DMSO : ≥ 44 mg/mL (102.68 mM); H2O : < 0.1 mg/mL (insoluble)



BIOLOGICAL ACTIVITY:

AdipoRon is an orally active and specific **AdipoR** agonist, binding to AdipoR1 and AdipoR2, with **K_d**s of 1.8 and 3.1 μM, respectively. IC50 & Target: Kd: 1.8 μM (AdipoR1), 3.1 μM (AdipoR2)[1] ***In Vitro:*** AdipoRon is an orally active and specific AdipoR agonist, binds to AdipoR1 and AdipoR2, with K_ds of 1.8 and 3.1 μM. AdipoRon (50 nM-50 μM) increases AMPK phosphorylation via AdipoR1[1]. AdipoRon (50 μM) dose-dependently attenuates the expression of TNF-α and TGF-β1 in the L02 cells. AdipoRon exhibits significant and dosage-dependent growth suppression on macrophages[2]. AdipoRon treatment significantly improves cardiac functional recovery after reperfusion, and inhibits post-MI apoptosis[3]. AdipoRon exerts vasodilation by mechanisms distinct to adiponectin and induces vasorelaxation without a marked decrease in VSMC $[Ca^{2+}]_i$[4]. ***In Vivo:*** AdipoRon (50 mg/kg, i.v.) cuases significant phosphorylation of AMPK in skeletal muscle and liver of wild-type mice but not Adipor1$^{-/-}$ Adipor2$^{-/-}$ double-knockout mice[1]. AdipoRon (0.02, 0.1, and 0.5 mg/kg, i.g.) alleviates D-GalN induced hepatotoxicity in mice, and prevents hepatic architecture distortion against D-GalN challenge. The hepatoprotective potential of AdipoRon is particularly evident in higher dosages (0.1 and 0.5 mg/kg)[2]. Enhanced cardiomyocyte apoptosis in APN-deficient mice is rescued by AdipoRon (50 mg/kg, p.o.) administration. Antiapoptotic effect of AdipoRon is attenuated but not lost in AMPK-DN mice[3].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: [2]The effects of **AdipoRon** on the proliferation of parenchymal and non-parenchymal hepatocytes are evaluated in vitro via **L02 and RAW264.7**, by MTT assay as described with slight modification: 100 μL cells suspension (**6×10^4/mL**) are seeded in a 96-well plate and incubated for 18 h. Fresh media with **AdipoRon** are added at **specified concentrations**, and the incubations continue for a further 24 h. Then cells are incubated for 4 h with 0.5 mg/mL of MTT, and analyzed in a microplate reader at 490 nm. Each group is performed in six replications. The mean absorbance values corrected for a blank (medium only) are calculated as percentages of survival[2].

Animal Administration: AdipoRon is dissolved in DMSO and diluted by saline containing 0.5% sodium carboxymethyl cellulose (CMC-Na) [final vehicle: 5% DMSO (v/v) saline solution].[2]Mice[2]

After 3 days of acclimation, mice are randomLy divided into six groups (9 mice in each): control, model, bicyclol (20 mg/kg), **AdipoRon (0.02 mg/kg, 0.1 mg/kg, 0.5 mg/kg)**. The synthetic AdipoRon and bicyclol are dissolved in **DMSO** and diluted by **saline containing 0.5% sodium carboxymethyl cellulose (CMC-Na) [final vehicle: 5% DMSO (v/v) saline solution]**. All test groups are administered with vehicle (control and model groups) or therapeutic agents (bicyclol or AdipoRon groups) at a dosing volume of **10 mL/kg**, by **intragastric (i.g.) gavage** twice per day for three consecutive days prior to D-GalN administration. 2 h after last treatment, mice are challenged with a single intraperitoneal (i.p.) administration of D-GalN saline solution at a dose of 600 mg/kg to induce acute liver injury, while the control group mice receive saline instead. Then mice are fasted for 20 h before orbital blood collection. Finally,

all animals are sacrificed by cervical dislocation, and livers are harvested for biochemical or histopathology analysis[2].

References:

[1]. Okada-Iwabu M, et al. A small-molecule AdipoR agonist for type 2 diabetes and short life in obesity. Nature. 2013 Nov 28;503(7477):493-9.

[2]. Wang Y, et al. Hepatoprotective effects of AdipoRon against d-galactosamine-induced liver injury in mice. Eur J Pharm Sci. 2016 Aug 9;93:123-131.

[3]. Zhang Y, et al. AdipoRon, the first orally active adiponectin receptor activator, attenuates postischemic myocardial apoptosis through both AMPK-mediated and AMPK-independent signalings. Am J Physiol Endocrinol Metab. 2015 Aug 1;309(3):E275-82.

[4]. Hong K, et al. Adiponectin Receptor Agonist, AdipoRon, Causes Vasorelaxation Predominantly Via a Direct Smooth Muscle Action. Microcirculation. 2016 Apr;23(3):207-20.

CAIndexNames:

Acetamide, 2-(4-benzoylphenoxy)-N-[1-(phenylmethyl)-4-piperidinyl]-

SMILES:

O=C(NC1CCN(CC2=CC=CC=C2)CC1)COC3=CC=C(C(C4=CC=CC=C4)=O)C=C3

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