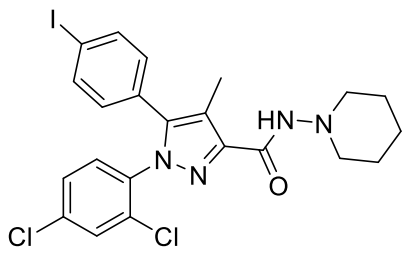
Product data sheet

MedKoo Cat#: 510338 Name: AM251 CAS#: 183232-66-8 Chemical Formula: $C_{22}H_{21}Cl_2IN_4O$ Exact Mass: 554.01371 Molecular Weight: 555.24	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
AM251 is a cannabinoid receptor antagonist. AM251 improves recognition memory in rats and produces nocifensive behavior via activation of ERK signaling pathway. Moreover, AM251 alters mitochondrial physiology via proteolytic degradation of ERRα and attenuates mechanical allodynia and thermal hyperalgesia after burn injury.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	36.38	65.52
DMF	10.0	18.01
Ethanol	14.0	25.21

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.80 mL	9.01 mL	18.01 mL
5 mM	0.36 mL	1.80 mL	3.60 mL
10 mM	0.18 mL	0.90 mL	1.80 mL
50 mM	0.04 mL	0.18 mL	0.36 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Correia-Sá IB, Carvalho CM, Serrão PV, Machado VA, Carvalho SO, Marques M, Vieira-Coelho MA. AM251, a cannabinoid receptor 1 antagonist, prevents human fibroblasts differentiation and collagen deposition induced by TGF-β - An in vitro study. Eur J Pharmacol. 2021 Feb 5;892:173738. doi: 10.1016/j.ejphar.2020.173738. Epub 2020 Nov 19. PMID: 33220269.
2. Yoshinaga T, Uwabe K, Naito S, Higashino K, Nakano T, Numata Y, Kihara A. AM251 Suppresses Epithelial-Mesenchymal Transition of Renal Tubular Epithelial Cells. PLoS One. 2016 Dec 9;11(12):e0167848. doi: 10.1371/journal.pone.0167848. PMID: 27936102; PMCID: PMC5148003.

In vivo study

1. Parihar VK, Syage A, Flores L, Lilagan A, Allen BD, Angulo MC, Song J, Smith SM, Arechavala RJ, Giedzinski E, Limoli CL. The Cannabinoid Receptor 1 Reverse Agonist AM251 Ameliorates Radiation-Induced Cognitive Decrements. Front Cell Neurosci. 2021 Jun 28;15:668286. doi: 10.3389/fncel.2021.668286. PMID: 34262437; PMCID: PMC8273551.
2. Pryce G, Baker D. Antidote to cannabinoid intoxication: the CB1 receptor inverse agonist, AM251, reverses hypothermic effects of the CB1 receptor agonist, CB-13, in mice. Br J Pharmacol. 2017 Nov;174(21):3790-3794. doi: 10.1111/bph.13973. Epub 2017 Sep 20. PMID: 28800377; PMCID: PMC5647190.

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7. Bioactivity

Biological target:

AM251 is a selective cannabinoid 1 (CB1) receptor antagonist with an IC50 of 8 nM, also acts as a potent GPR55 agonist with an EC50 of 39 nM.

In vitro activity

However, TGF-β effect was inhibited in the presence of CB_1 agonist ACEA 1 μM in association with CB_1 selective antagonist AM251 10 μM (24.76 ± 6.43 *vs* 2.03 ± 0.87, P = 0.0451, statistically significant). Moreover, CB_1 antagonist alone also prevented TGF-β effect on α-SMA expressions (24.76 ± 6.43 *vs* 1.74 ± 1.15, P = 0.0451, statistically significant). In this context, this study evaluated the effect of this drug at concentrations of 1 μM, 5 μM and 10 μM in the fibroblast primary culture activated with TGF-β. AM251 inhibited the TGF-β effect on α-SMA expression in a concentration-dependent manner (Fig. 4). This effect was significant at concentrations ≥1 μM (all P < 0.05*vs*TGF-β), reaching a maximum at the concentration of 5 μM.

Reference: Eur J Pharmacol. 2021 Feb 5;892:173738. https://pubmed.ncbi.nlm.nih.gov/33220269/

In vivo activity

As anticipated, a 5 $mg \cdot kg^{-1}$, i.p. dose of CB-13 induced hypothermia in ABH mice (Figure 1), which has been shown previously to be CB_1 receptor-mediated and completely absent in CB_1 receptor-deficient mice. This induced significant visible sedation and also induced hypothermia, which was measured to provide a quantitative readout. The hypothermic effect was rapidly antagonized with AM251 (5 $mg \cdot kg^{-1}$, i.v.; Figure 1), and the significant marked sedation, associated with the relative lack of motility, was lost within 20 min. The hypothermia was lost by 40 min after treatment with AM251 (Figure 1). Therefore, a CB_1 receptor inverse agonist can reverse CB_1 receptor-mediated cannabimimetic effects.

Reference: Br J Pharmacol. 2017 Nov; 174(21): 3790–3794. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5647190/