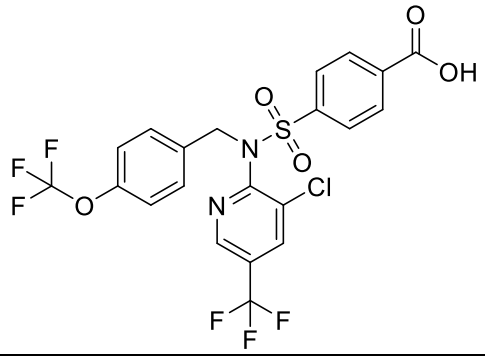
Product data sheet

MedKoo Cat#: 407141 Name: RQ-00203078 CAS#: 1254205-52-1 Chemical Formula: $C_{21}H_{13}ClF_6N_2O_5S$ Exact Mass: 554.01379 Molecular Weight: 554.84	
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:
RQ-00203078 is a potent, selective and orally active TRPM8 antagonist (IC50 values are 5.3 and 8.3 nM for rat and human channels respectively). RQ-00203078 blocks TRPM8 activity and reduces the invasion potential of oral squamous carcinoma cell lines. RQ-00203078 (RQ) profoundly reduced such agonist-induced cation currents. TRPM8 is reportedly an important player in carcinogenesis in human prostate cancer. 6).

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	40.0	72.09
Ethanol	40.0	72.09

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.80 mL	9.01 mL	18.02 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. Okamoto Y, Ohkubo T, Ikebe T, Yamazaki J. Blockade of TRPM8 activity reduces the invasion potential of oral squamous carcinoma cell lines. Int J Oncol. 2012 May;40(5):1431-40. doi: 10.3892/ijo.2012.1340. Epub 2012 Jan 20. PMID: 22267123.

In vivo study

1. Gong K, Jasmin L. Sustained Morphine Administration Induces TRPM8-Dependent Cold Hyperalgesia. J Pain. 2017 Feb;18(2):212-221. doi: 10.1016/j.jpain.2016.10.015. Epub 2016 Nov 12. PMID: 27845197; PMCID: PMC5291755.
2. Harrison E, Biswas L, Avusula R, Zhang M, Gong Y, Liu X. Effects of menthol and its interaction with nicotine-conditioned cue on nicotine-seeking behavior in rats. Psychopharmacology (Berl). 2017 Dec;234(23-24):3443-3453. doi: 10.1007/s00213-017-4736-0. Epub 2017 Sep 16. PMID: 28918457; PMCID: PMC5693741.

7. Bioactivity
Biological target:

RQ-00203078 is a highly selective TRPM8 antagonist with IC50s of 5.3 nM and 8.3 nM for rat and human TRPM8 channels, respectively as well as shows little inhibitory action against TRPV1, TRPA1, TRPV4, or TRPM2 channels.

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In vitro activity

To examine which types of TRP channels might be present in carcinoma cell lines derived from the human tongue, RT-PCR was performed using total RNA extracted from HSC3 and HSC4 cells by means of pairs of primers designed to recognize the mRNA of several TRP members (Table I). To try to determine whether TRPM8 is involved in the menthol-induced response, RQ (RQ-00203078) (10 μM) was used, a selective antagonist of TRPM8 (11). RQ completely inhibited thementhol-induced current (Fig. 2A). In HSC3 cells, RQ virtually abolished the response to menthol at all voltage steps within the range -100 to 100 mV. Both the menthol-induced effect and the WS-12-induced effect were significantly inhibited by RQ at either membrane potential in a concentration-dependent manner (1-10 μM). In addition to their sensitivity to menthol, HSC3 cells were sensitive to cooling (Fig. 2E). When the temperature of the external solution was decreased from 26˚C to 17˚C, the basal inward current recorded at -50 mV was progressively enhanced, and this effect was reversed in the presence of RQ. These results suggest that RQ is able to discriminate between the two classes of cold-sensing channels. Notably, the continued presence of RQ significantly attenuated both the menthol-induced [Ca2+]I elevation associated with intracellular Ca2+ release and the menthol-induced store-operated Ca2+ entry (open circles in Fig. 5A and B). These results suggest that intracellular TRPM8 channels function as Ca2+-release ER channels, and that these are sensitive to RQ. In the serum-free condition, menthol significantly increased migration in both cell types, while RQ significantly decreased the migration distance (both in the presence and absence of menthol) to a level below the migration distance measured in the control condition. These results suggest the involvement of both menthol-activated and basally activated TRPM8 in such RQ-blockable cell motility. RQ also suppressed the MMP-9 activity seen in the presence of menthol (Fig. 9A and B). The present study clearly demonstrates that RQ has a potent inhibitory effect on TRPM8-mediated responses associated with both the plasma membrane and ER channels.

Reference: Int J Oncol. 2012 May;40(5):1431-40. https://pubmed.ncbi.nlm.nih.gov/22267123/

In vivo activity

To verify that the TRPM8 channel mediated morphine induced cold hyperalgesia, RQ-00203078, a selective antagonist of TRPM8, was administed to both morphine treated and saline control rats. A dose of 3 mg/kg (i.p) RQ-00203078 blocked the cold plate induced paw lifts in both groups. In the morphine treated group, the antagonist reduced the number of paw lifts from 13.1 ± 2.5 to 2.2 ± 0.9 ($p < 0.01$, $n = 8$, Fig. 3). In the saline treated group, the number of paw lifts was reduced from 2.9 ± 1.1 to 0.6 ± 0.3 ($p < 0.01$, $n = 9$). Sustained morphine administration also induced mechanical hyperalgesia as determined by the response to von Frey hair stimulus ($p < 0.01$, $n = 7$, supplementary Fig. S2). Therefore the mechanical threshold was used to determine if RQ-00203078 blocked behaviors other than the cold behavior. In saline treated rats, administration of RQ-00203078 did not affect withdrawal from the mechanical stimulus, which was 25.4 ± 2.1 g (pre-administration) and 26.9 ± 2.2 g (post-administration) respectively ($p > 0.05$). Similarly, administration of RQ-00203078 did not have any significant effect on mechanosensitivity in morphine treated rats. The threshold was 16.9 ± 2.4 g before RQ-00203078 and 16.1 ± 2.5 g after RQ-00203078 (supplementary Fig. S2). Therefore, RQ-00203078 selectively blocked cold hyperalgesia without affecting mechanical hyperalgesia in morphine treated rats.

Reference: J Pain. 2017 Feb; 18(2): 212–221. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5291755/