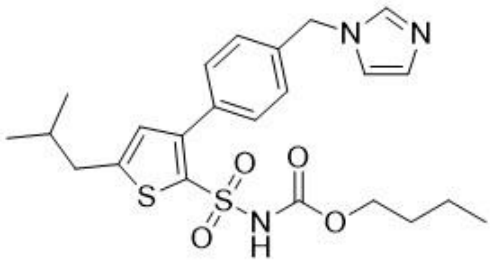
Product data sheet

MedKoo Cat#: 527400 Name: AT2 Agonist C21 CAS#: 477775-14-7 Chemical Formula: $C_{23}H_{29}N_3O_4S_2$ Exact Mass: 475.1599 Molecular Weight: 475.622	
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:

AT2 Agonist C21 is the first potent and selective agonist of angiotensin AT2 receptors, preventing endothelial inflammation and leukocyte adhesion in vitro and in vivo. AT2 Agonist C21 prevents cognitive decline after permanent stroke in aged animals-A randomized double- blind pre-clinical study. AT2 Agonist C21 attenuates pulmonary inflammation in a model of acute lung injury. AT2 Agonist C21 attenuates the Progression of Lung Fibrosis and Pulmonary Hypertension in an Experimental Model of Bleomycin-Induced Lung 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	100	210.25

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.10	10.51	21.03
5 mM	0.42	2.10	4.21
10 mM	0.21	1.05	2.10
50 mM	0.04	0.21	0.42

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. Sampson AK, Irvine JC, Shihata WA, Dragoljevic D, Lumsden N, Huet O, Barnes T, Unger T, Steckelings UM, Jennings GL, Widdop RE, Chin-Dusting JP. Compound 21, a selective agonist of angiotensin AT2 receptors, prevents endothelial inflammation and leukocyte adhesion in vitro and in vivo. Br J Pharmacol. 2016 Feb;173(4):729-40. doi: 10.1111/bph.13063. Epub 2015 Jun 29. PMID: 25560767; PMCID: PMC4742292.
2. Fouda AY, Pillai B, Dhandapani KM, Ergul A, Fagan SC. Role of interleukin-10 in the neuroprotective effect of the Angiotensin Type 2 Receptor agonist, compound 21, after ischemia/reperfusion injury. Eur J Pharmacol. 2017 Mar 15;799:128-134. doi: 10.1016/j.ejphar.2017.02.016. Epub 2017 Feb 10. PMID: 28192099; PMCID: PMC5411859.

In vivo study

1. Ali Q, Hussain T. AT2 receptor non-peptide agonist C21 promotes natriuresis in obese Zucker rats. Hypertens Res. 2012 Jun;35(6):654-60. doi: 10.1038/hr.2012.13. Epub 2012 Feb 2. PMID: 22297475; PMCID: PMC3912844.
2. Ali Q, Patel S, Hussain T. Angiotensin AT2 receptor agonist prevents salt-sensitive hypertension in obese Zucker rats. Am J Physiol Renal Physiol. 2015 Jun 15;308(12):F1379-85. doi: 10.1152/ajprenal.00002.2015. Epub 2015 Apr 8. PMID: 25855512; PMCID: PMC4469886.

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7. Bioactivity

Biological target:

AT2 receptor agonist C21 is a druglike selective angiotensin II AT2 receptor agonist with Ki values of 0.4 nM and >10 μM for the AT2 receptor and AT1 receptor, respectively.

In vitro activity

The effect of direct AT2 receptor stimulation with Compound 21 (C21) on the leukocyte adhesion cascade in vitro was examined. Effects of C21 on TNFα-induced inflammation were assessed in human umbilical vein endothelial cells (HUVECs), activation of monocytes, and polarisation of monocyte-derived macrophages. C21 attenuated TNFα-induced: monocyte adhesion to cultured HUVECs, adhesion molecule expression and abolished TNFα-induced ROS production. TNFα-induced NFκB translocation from the cytoplasm to the nucleus, essential for cytokine production, was prevented by C21. C21 did not influence monocyte activation or macrophage polarisation but did reduce TNFα and IL-6 mRNA expression in M1 macrophages. The anti-inflammatory effects of C21 were abolished by an AT2 receptor antagonist confirming that the effects of C21 were AT2 receptor-mediated. C21 prevented TNFα-induced and HFD-induced vascular inflammation in vitro. The data provides strong evidence that the anti-atherosclerotic actions of C21 were due to vascular anti-inflammatory effects, mediated by AT2 receptors.

Br J Pharmacol. 2016 Feb;173(4):729-40. https://pubmed.ncbi.nlm.nih.gov/25560767/

In vivo activity

In the present study, the role of a novel, non-peptide agonist, C21, in natriuresis via AT2 receptor activation in OZR was investigated. Infusion of C21 caused dose-dependent increases in UF (urine flow) and UNaV (urinary Na volume) relative to basal rates, and these increases were highly significant with the 5 μg kg−1 min−1 dose (Figure 2), which was used in subsequent sets of the experiment. To demonstrate that C21-induced Na excretion is mediated via the AT2 receptor, the AT2 receptor antagonist, PD123319 (50 μg kg−1 min−1 i.v.), was infused before the infusion of C21. Although PD123319 alone did not affect UF or UNaV, when compared with basal rates, it completely abolished increases in UF and UNaV in response to C21 (Figure 3), suggesting the involvement of the AT2 receptor. Infusion of C21 (5 μg kg−1 min−1) caused a significant increase in FENa (Basal: 3.033±0.9%, C21: 14.63±2.3%, $P<0.05$), suggesting a tubular effect of the drug (Figure 4a). Similarly, C21 infusion (5 μg kg−1 min−1) caused a significant increase in FELi (Basal: 24.6±2.9, C21: 56.8±5.5 %, $P<0.05$) (Figure 4b). The C21 infusion in AM + BFTZ-infused rats caused a further increase in both the UF and the UNaV. These findings suggest that the majority of C21-induced natriuresis originates from the proximal nephron segments; however, the findings do not rule out the possibility of involvement at the loop of Henle.

Hypertens Res. 2012 Jun; 35(6): 654–660. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3912844/