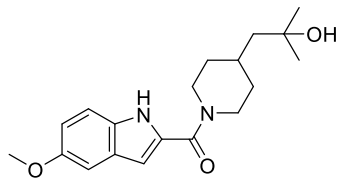
Product data sheet

MedKoo Cat#: 205818 Name: ASP9521 CAS#: 1126084-37-4 Chemical Formula: $C_{19}H_{26}N_2O_3$ Exact Mass: 330.19434 Molecular Weight: 330.42	
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:

ASP9521 is a novel, selective, orally bioavailable inhibitor of 17β-hydroxysteroid dehydrogenase type 5 (17βHSD5; AKR1C3). ASP9521 has demonstrated anti-tumour activity in in vitro and in vivo preclinical models. ASP9521 inhibited conversion of androstenedione (AD) into testosterone (T) by recombinant human or cynomolgus monkey AKR1C3 in a concentration-dependent manner (IC50,human: 11 nmol/L; IC50,monkey: 49 nmol/L). ASP9521 showed >100-fold selectivity for AKR1C3 over the isoform AKR1C2. In LNCaP-AKR1C3 cells, ASP9521 suppressed AD-dependent PSA production and cell proliferation. In patients with mCRPC, ASP9521 demonstrated dose-proportional increase in exposure over the doses evaluated, with an acceptable safety and tolerability profile. However, the novel androgen biosynthesis inhibitor showed no relevant evidence of clinical activity.

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	52.26	158.16
DMF	10.0	30.26
DMF:PBS (pH 7.2) (1:1)	0.5	1.51
Ethanol	36.35	110.01

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	3.03 mL	15.13 mL	30.26 mL
5 mM	0.61 mL	3.03 mL	6.05 mL
10 mM	0.30 mL	1.51 mL	3.03 mL
50 mM	0.06 mL	0.30 mL	0.61 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. Wangtrakuldee P, Adeniji AO, Zang T, Duan L, Khatri B, Twenter BM, Estrada MA, Higgins TF, Winkler JD, Penning TM. A 3-(4-nitronaphthen-1-yl) amino-benzoate analog as a bifunctional AKR1C3 inhibitor and AR antagonist: Head to head comparison with other advanced AKR1C3 targeted therapeutics. J Steroid Biochem Mol Biol. 2019 Sep;192:105283. doi: 10.1016/j.jsbmb.2019.01.001. Epub 2019 Jan 11. PMID: 30641225; PMCID: PMC6625945.

2. Kikuchi A, Furutani T, Azami H, Watanabe K, Niimi T, Kamiyama Y, Kuromitsu S, Baskin-Bey E, Heeringa M, Ouatas T, Enjo K. In vitro and in vivo characterisation of ASP9521: a novel, selective, orally bioavailable inhibitor of 17β-hydroxysteroid dehydrogenase type 5 (17βHSD5; AKR1C3). Invest New Drugs. 2014 Oct;32(5):860-70. doi: 10.1007/s10637-014-0130-5. Epub 2014 Jul 1. PMID: 24981575.

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In vivo study

1. Kikuchi A, Furutani T, Azami H, Watanabe K, Niimi T, Kamiyama Y, Kuromitsu S, Baskin-Bey E, Heeringa M, Ouatas T, Enjo K. In vitro and in vivo characterisation of ASP9521: a novel, selective, orally bioavailable inhibitor of 17β-hydroxysteroid dehydrogenase type 5 (17βHSD5; AKR1C3). Invest New Drugs. 2014 Oct;32(5):860-70. doi: 10.1007/s10637-014-0130-5. Epub 2014 Jul 1. PMID: 24981575.

7. Bioactivity

Biological target:

ASP-9521 is an AKR1C3 inhibitor with an IC50 of 11 nM for human AKR1C3.

In vitro activity

The AKR1C3 inhibition potency of the lead compounds were slightly less to those determined for two AKR1C3 inhibitors developed by industry GTx-560 and ASP9521, Table 2. Compound 1, GTx-560 and ASP9521 all inhibited the conversion of Δ4-AD to testosterone in LNCaP-AKR1C3 cells consistent with the competitive inhibition observed with these agents. However, there is a difference in potency of the compounds based on the in vitro enzyme assays and the assays performd in LNCaP-AKR1C3 cells, which may be related to cell permeability issues. All the inhibitors are carboxylic acids and would likely require transport by OATPs for cell entry.

Reference: J Steroid Biochem Mol Biol. 2019 Sep; 192: 105283. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6625945/

In vivo activity

To investigate ASP9521 accumulation, the concentration of ASP9521 in plasma and tumour tissue was measured over time in nude mice bearing HEK293 tumours with or without AKR1C3 expression. After single oral administration of ASP9521, plasma concentrations of ASP9521 reached maximum values within 0.25 h (mean: 767.3 ng/mL and 648.2 ng/mL for HEK293 and HEK293-AKR1C3 cells, respectively), but decreased rapidly thereafter (Fig. 10). Similarly, the intratumoural concentration of ASP9521 in HEK293 tumours lacking AKR1C3 expression rapidly decreased from 845.8 ng/g after 0.25 h to undetectable levels after 4 h. In contrast, in HEK293 tumours expressing AKR1C3, the maximum intratumoural ASP9521 concentration was considerably higher (mean: 1,905.0 ng/g after 0.25 h), and elevated ASP9521 levels were maintained for at least 4 h. These results suggest that accumulation of ASP9521 in tumour tissue may depend on AKR1C3 expression.

Reference: Invest New Drugs. 2014 Oct;32(5):860-70. https://pubmed.ncbi.nlm.nih.gov/24981575/