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产品名称：ASP-9521
产品别名：ASP-9521

生物活性：

Description	ASP-9521 is a potent, selective and orally available AKR1C3 inhibitor with an IC50 of 11 nM for human AKR1C3.
IC_{50} & Target	IC50:11 nM (human AKR1C3), 49 nM (monkey AKR1C3)[1]
In Vitro	AKR1C3 is a promising therapeutic target in castrationresistant prostate cancer, as combination of an AKR1C3 inhibitor and a gonadotropin-releasing hormone analogue may lead to complete androgen blockade.ASP-9521 inhibits conversion of androstenedione (AD) into androstenediol and testosterone (T) by recombinant human or cynomolgus monkey AKR1C3 in a concentrationdependent manner (IC50, human: 11 nM; IC50,monkey: 49 nM). ASP-9521 shows more than 100-fold selectivity for AKR1C3 over the isoform AKR1C2. In LNCaP-AKR1C3 cells, ASP-9521 suppresses AD-dependent PSA production and cell proliferation[1].
In Vivo	In CWR22R xenografts, single oral administration of ASP-9521 (3 mg/kg) inhibits AD-induced intratumoural T production and this inhibitory effect is maintained for 24 h. After oral administration, ASP-9521is rapidly eliminated from plasma, while its intratumoural concentration remained high. The bioavailability of ASP-9521 after oral administration (1 mg/kg) is 35 %, 78 % and 58 % in rats, dogs and monkeys, respectively[1].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 300 mg/mL (907.94 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.0265 mL	15.1323 mL	30.2645 mL
5 mM	0.6053 mL	3.0265 mL	6.0529 mL
10 mM	0.3026 mL	1.5132 mL	3.0265 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

References	[1]. Kikuchi A, et al. 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.

实验参考：

Cell Assay	LNCaP-AKR1C3 cells stably expressing human AKR1C3 are seeded in 96-well plates at 10000 cells/100 μL/well in RPMI-1640 medium supplemented with heat-inactivated charcoal-dextran-stripped FBS (1 % for the PSA expression assay and T measurement and 5 % for the cell proliferation assay). After 24 h incubation, AD is added to each well with or without ASP-9521 (0.3-100 nM). The cell culture media are collected 24 h after administration of AD to

	measure T concentration and 6 days after administration of AD to measure cell proliferation using Cell-Titer Glo assay[1].
Animal Administration	Mice carrying HEK293 or HEK293-AKR1C3 tumours with similar sizes are selected and randomly divided into 5 groups (N=3 for each group). All groups are treated with ASP-9521 (single oral administration; 3 mg/kg). Plasma (from the central vein) and tumour tissues are collected at 0.25, 0.5, 1, 2 and 4 h after administration of ASP-9521, and ASP-9521 concentrations are determined using the HPLCMS/MS method[1].
References	[1]. Kikuchi A, et al. 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.