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产品名称：2-(2,4-二氟苯基)-1,3-二(1H-1,2,4-三氮唑-1-基)丙基二氢磷酸酯
产品别名：Fosfluconazole ；福司氟康唑

生物活性：

Description	Fosfluconazole is a prodrug of Fluconazole that is widely used as an antifungal agent.
IC_{50} & Target	Antifungal[1]
In Vitro	To investigate the polarized bioconversion and the Transwell transport of phosphate prodrugs in Caco-2 monolayer, 10 μM Fosfluconazole or Fosphenytoin is dosed either in the apical or basal compartment in Transwell plates. Both prodrugs are efficiently cleaved in the apical compartment after a 2 h incubation. To further investigate the kinetics of ALP-mediated bioconversion, the concentration-dependent ALP-mediated bioconversions are conducted to determine the Michaelis-Menten constant (K_m) of prodrug bioconversion in Caco-2 monolayers. The saturation curves of Fosphenytoin and Fosfluconazole with the concentration increase are found. The estimated K_m values of Fosphenytoin and Fosfluconazole are 1160 and 357 μM, respectively[2].
In Vivo	The apparent half-life for Fosfluconazole bioconversion in intestinal mucosa scraps is 10 min[2]. Fluconazole (FLCZ) is an antifungal agent that is efficacious in the treatment of fungal peritonitis. Fosfluconazole (F-FLCZ) is the phosphate prodrug of FLCZ, which is highly soluble compared with FLCZ. F-FLCZ is useful against fungal peritonitis in continuous ambulatory peritoneal dialysis (CAPD) patients because it has a high water solubility. The aims of the present study are to characterize the peritoneal permeability of FLCZ and the pharmacokinetics of FLCZ and F-FLCZ after intraperitoneal (i.p.) administration to peritoneal dialysis rats. FLCZ or F-FLCZ is administered intravenously and intraperitoneally. After the i.p. administration of F-FLCZ, FLCZ is detected in circulating blood and the dialyzing fluid in peritoneal dialysis rats. The concentration of plasma FLCZ after the i.p. F-FLCZ administration is lower than that after the intravenous (i.v.) F-FLCZ administration. It is considered that the dose should be increased appropriately when F-FLCZ is administered intraperitoneally. The profiles of plasma FLCZ after i.v. and i.p. administrations are analyzed using a two-compartment model in which the distribution volume of the peripheral compartment is fixed at a volume of the dialyzing fluid (peritoneal dialysis PK model). The peritoneal dialysis PK model could describe the profiles of plasma and dialyzing fluid FLCZ. These results suggest that FLCZ and F-FLCZ could be administered intraperitoneally for the treatment of fungal peritonitis in CAPD patients[3].
Solvent&Solubility	***In Vitro:*** **DMSO : 6.2 mg/mL (16.05 mM;** Need ultrasonic and warming)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.5890 mL	12.9450 mL	25.8900 mL
5 mM	0.5178 mL	2.5890 mL	5.1780 mL
10 mM	0.2589 mL	1.2945 mL	2.5890 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]. Hagiya H, et al. Successful treatment of recurrent candidemia due to candidal thrombophlebitis associated with a central venous catheter using a combination of Fosfluconazole and micafungin. Intern Med. 2013;52(18):2139-43. [2]. Yuan H, et al. Evaluation of in vitro models for screening alkaline phosphatase-mediated bioconversion of phosphate ester prodrugs. Drug Metab Dispos. 2009 Jul;37(7):1443-7. [3]. Aoyama T, et al. Pharmacokinetics of fluconazole and Fosfluconazole after intraperitoneal administration to peritoneal dialysis rats. Drug Metab Pharmacokinet. 2005 Dec;20(6):485-90.
实验参考：	
Kinase Assay	An aliquot of 200 μL of mucosa scrap lysate solution is mixed with 100 mM phosphate buffer, pH 7.4, to a final volume at 1 ml. The concentration of the test compounds (Fosphenytoin and Fosfluconazole) is 10 μM. The incubation medium is prewarmed at 37°C before the reaction is initiated by addition of the tested compounds. An aliquot of 100 μL is collected from the incubation vial at the time points 0, 5, 10, 20, 30, 45, and 60 min and transferred to a 96-well plate, in which 100 μL of Acetonitrile is prefilled to terminate the reaction. The samples are diluted 5-fold with acetonitrile containing 1 μM Tolbutamide as an analytical internal standard. The samples are centrifuged at 4000 rpm for 5 min to precipitate protein. The supernatant is transferred to a new 96-well plate for concentration analysis by liquid chromatography/tandem mass spectrometry (LC/MS/MS)[2].
References	[1]. Hagiya H, et al. Successful treatment of recurrent candidemia due to candidal thrombophlebitis associated with a central venous catheter using a combination of Fosfluconazole and micafungin. Intern Med. 2013;52(18):2139-43. [2]. Yuan H, et al. Evaluation of in vitro models for screening alkaline phosphatase-mediated bioconversion of phosphate ester prodrugs. Drug Metab Dispos. 2009 Jul;37(7):1443-7. [3]. Aoyama T, et al. Pharmacokinetics of fluconazole and Fosfluconazole after intraperitoneal administration to peritoneal dialysis rats. Drug Metab Pharmacokinet. 2005 Dec;20(6):485-90.