# Fosfluconazole

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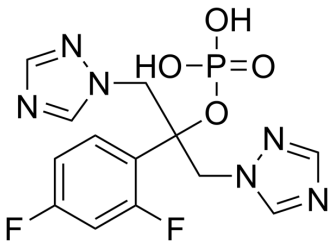
|---|---|
| **Cat. No.:** | HY-100666 |
| **CAS No.:** | 194798-83-9 |
| **Molecular Formula:** | $C_{13}H_{13}F_2N_6O_4P$ |
| **Molecular Weight:** | 386.25 |
| **Target:** | Fungal |
| **Pathway:** | Anti-infection |
| **Storage:** | Powder -20°C 3 years<br>4°C 2 years<br>In solvent -80°C 2 years<br>-20°C 1 year |



## 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 |

Please refer to the solubility information to select the appropriate solvent.

**In Vivo**

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 6.25 mg/mL (16.18 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 6.25 mg/mL (16.18 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 6.25 mg/mL (16.18 mM); Clear solution

## BIOLOGICAL ACTIVITY

**Description**

Fosfluconazole is a proagent 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].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

**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].

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## PROTOCOL

**Kinase Assay** [2]

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].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## 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.





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