

Product Data Sheet

Product Name: Fosmidomycin (sodium salt)

Cat. No.: GC12939

Chemical Properties

Cas. No. 66508-37-0

Chemical Name P-[3-(formylhydroxyamino)propyl]-phosphonic acid, monosodium salt

SMILES ON(C([H])=O)CCCP([O-])(O)=O.[Na+]

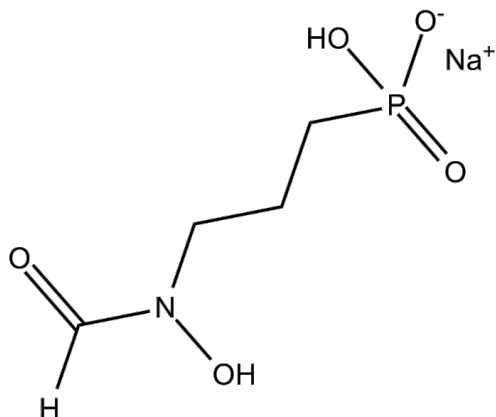
Formula $C_4H_9NO_5P \cdot Na$ M.Wt 205.1

Solubility $\leq 5\text{mg/ml}$ in PBS, pH 7.2 Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines *E. coli* cells

Caution: Product has not been fully validated for medical applications. For research use only.

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Preparation Method A 3h-old wild-type *E. coli* strain suspension was spread out on LB-agar plates containing Fosmidomycin (from 0 to 100µM). After 24h, 48h and 72h, the number of colonies was counted. Exceeding the value of 200 colonies indicates the formation of a lawn of bacteria.

Reaction Conditions 0-100µM; 24h, 48h and 72h

Applications *E. coli* developed resistance to Fosmidomycin within 24h, with resistance developing more rapidly at lower concentrations.

Animal experiment [2]:

Animal models *Plasmodium vinckei* mouse model

Preparation Method Mice were inoculated by intraperitoneal injection with approximately 5×10^7 infected erythrocytes from a donor mouse. Fosmidomycin was dissolved in phosphate-buffered saline and administered orally (75mg/kg of body weight). Clindamycin hydrochloride was dissolved in distilled water and administered by intraperitoneal injection (5mg/kg). Four mice were used for each treatment group, and three mice were used for the control group. Drugs were given on days 1 and 2 postinfection, and parasitemia was monitored on days 3 to 5. Parasitemia was monitored by Giemsa staining of blood smears. Mice were sacrificed when parasitemia exceeded 40%.

Dosage form 75mg/kg, on days 1 and 2; p.o.

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Applications

On day 3, the parasitemia of mice treated with 75mg/kg of Fosmidomycin or 5mg/kg of clindamycin was 7.8 or 20%, respectively, in comparison to 42% in untreated control mice. When the mice were treated with a combination of 75 mg/kg of Fosmidomycin and 5.0mg/kg of clindamycin, the parasitemia was approximately 0.1% on day 3, increasing to 0.2% on day 5.

References:

[1] Hemmerlin A, Tritsch D, Hammann P, et al. Profiling of defense responses in *Escherichia coli* treated with fosmidomycin[J]. *Biochimie*, 2014, 99: 54-62.

[2] Wiesner J, Henschker D, Hutchinson D B, et al. In vitro and in vivo synergy of fosmidomycin, a novel antimalarial drug, with clindamycin[J]. *Antimicrobial Agents and Chemotherapy*, 2002, 46(9): 2889-2894.

Background

Fosmidomycin (sodium salt) is a specific inhibitor of 1-deoxy-d-xylulose 5-phosphate reductoisomerase (DXP)^[1]. Fosmidomycin is a phosphate antibiotic isolated from *Streptomyces* that is active against both Gram-negative and Gram-positive bacteria^[2]. Fosmidomycin is an effective and safe antimalarial drug^[3]. Fosmidomycin inhibits the second reaction in the non-mevalonate pathway of isoprene biosynthesis, which is an important pathway for many obligate intracellular pathogens, including *mycobacteria* and *apicomplexan parasites*^[4].

In vitro, *Escherichia coli* cells treated with Fosmidomycin (0-100µM) for 24-72h developed resistance to Fosmidomycin within 24h, and resistance developed more rapidly at lower concentrations^[5]. Fosmidomycin (0.25-2mM) treatment of HeLa cells infected with *Chlamydia* does not inhibit the ability of *Chlamydia* to infect HeLa cells, but it does prevent the development and production of inclusion bodies in infectious offspring^[6].

In vivo, Fosmidomycin (75mg/kg) was administered orally to treat mice infected with *Plasmodium vinckei* for 2 days and effectively treated the parasitemia of mice. The effect was better when

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combined with clindamycin^[7].

References:

- [1] Kuzuyama T, Shimizu T, Takahashi S, et al. Fosmidomycin, a specific inhibitor of 1-deoxy-D-xylulose 5-phosphate reductoisomerase in the nonmevalonate pathway for terpenoid biosynthesis[J]. Tetrahedron letters, 1998, 39(43): 7913-7916.
- [2] Parkinson E I, Erb A, Eliot A C, et al. Fosmidomycin biosynthesis diverges from related phosphonate natural products[J]. Nature chemical biology, 2019, 15(11): 1049-1056.
- [3] Missinou M A, Borrmann S, Schindler A, et al. Fosmidomycin for malaria[J]. The Lancet, 2002, 360(9349): 1941-1942.
- [4] Sparr C, Purkayastha N, Kolesinska B, et al. Improved efficacy of fosmidomycin against Plasmodium and Mycobacterium species by combination with the cell-penetrating peptide octaarginine[J]. Antimicrobial agents and chemotherapy, 2013, 57(10): 4689-4698.
- [5] Hemmerlin A, Tritsch D, Hammann P, et al. Profiling of defense responses in Escherichia coli treated with fosmidomycin[J]. Biochimie, 2014, 99: 54-62.
- [6] Slade J A, Brockett M, Singh R, et al. Fosmidomycin, an inhibitor of isoprenoid synthesis, induces persistence in Chlamydia by inhibiting peptidoglycan assembly[J]. PLoS pathogens, 2019, 15(10): e1008078.
- [7] Wiesner J, Henschker D, Hutchinson D B, et al. In vitro and in vivo synergy of fosmidomycin, a novel antimalarial drug, with clindamycin[J]. Antimicrobial Agents and Chemotherapy, 2002, 46(9): 2889-2894.

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