Fosfomycin

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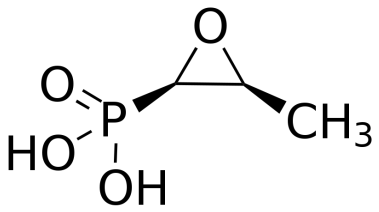

Systematic (IUPAC) name	
[(2*R*,3*S*)-3-methyloxiran-2-yl]phosphonic acid	
Identifiers	
CAS number	23155-02-4 [1] 78964-85-9 [2] (tromethamine)
ATC code	J01 XX01 [3]
PubChem	CID 446987 [4]
DrugBank	APRD00987 [5]
Chemical data	
Formula	$C_3H_7O_4P$
Mol. mass	138.059 g/mol
Pharmacokinetic data	
Bioavailability	30–37% (oral, fosfomycin tromethamine); varies with food intake
Protein binding	Nil
Metabolism	Nil
Half-life	5.7 hours (mean)
Excretion	Renal and fecal, unchanged
Therapeutic considerations	
Pregnancy cat.	B(US)
Legal status	-only (US)
Routes	Oral
✓ **(what is this?) (verify)** [6]	

Fosfomycin (also known as phosphomycin and phosphonomycin) is a broad-spectrum antibiotic[7] produced by certain *Streptomyces* species.

Uses

Fosfomycin is indicated in the treatment of urinary tract infections, where it is usually administered as a single oral megadose.[8]

The drug is well tolerated and has a low incidence of harmful side-effects.[8] However, development of bacterial resistance under therapy is a frequent occurrence and makes fosfomycin unsuitable for sustained therapy of severe infections.

Additional uses have been proposed.[9] The global problem of advancing antimicrobial resistance has led to a renewed interest in its use more recently.[10]

Mechanism of action

Fosfomycin inhibits bacterial cell wall biogenesis by inactivating the enzyme UDP-*N*-actetylglucosamine-3-enolpyruvyltransferase, also known as MurA.[11] This enzyme catalyzes the committed step in peptidoglycan biosynthesis, namely the ligation of phosphoenolpyruvate (PEP) to the 3'-hydroxyl group of UDP-*N*-acetylglucosamine. This pyruvate moiety provides the linker that bridges the glycan and peptide portion of peptidoglycan. Fosfomycin is a PEP analog that inhibits MurA by alkylating an active site cysteine residue (Cys 115 in the *Escherichia coli* enzyme).[12]

Fosfomycin enters the bacterial cell through the glycerophosphate transporter.

Biosynthetic gene cluster

The complete fosfomycin biosynthetic gene cluster from *Streptomyces fradiae* has been cloned and sequenced and the heterologous production of fosfomycin in *Streptomyces lividans* has been achieved by Ryan Woodyer of the Huimin Zhao and Wilfred van der Donk research groups.[13]

Resistance

Mutations that inactivate the non-essential glycerophosphate transporter render bacteria resistant to fosfomycin.[14] [15]

Fosfomycin resistance enzymes

Enzymes conferring resistance to fosfomycin have also been identified and are encoded both chromosomally and on plasmids.[16]

Glyoxalase superfamily enzymes

Three related but mechanistically distinct fosfomycin resistance enzymes (named, FosA, FosB and FosX) function by nucleophilic attack on carbon 1 of fosfomycin. This opens the epoxide ring and renders the drug ineffective. The enzymes differ by the identity of the nucleophile utilized in the reaction; glutathione for FosA, cysteine for FosB, and water for FosX.[16]

FosC

FosC utilizes ATP and adds a phosphate group to fosfomycin, thus altering its properties and making the drug ineffective.[17]

See also

- Fosmidomycin

External links

- Fosfomycin information at RxList [18]

References

[1] http://www.nlm.nih.gov/cgi/mesh/2009/MB_cgi?term=23155-02-4&rn=1

[2] http://toolserver.org/~magnus/cas.php?language=en&cas=78964-85-9&title=

[3] http://www.whocc.no/atc_ddd_index/?code=J01XX01

[4] http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=446987

[5] http://www.drugbank.ca/cgi-bin/show_drug.cgi?CARD=APRD00987

[6] http://en.wikipedia.org/w/index.php?&diff=cur&oldid=307781151

[7] Grif K, Dierich MP, Pfaller K, Miglioli PA, Allerberger F (August 2001). "In vitro activity of fosfomycin in combination with various antistaphylococcal substances" (http://jac.oxfordjournals.org/cgi/pmidlookup?view=long&pmid=11481290). *The Journal of antimicrobial chemotherapy* **48** (2): 209–17. doi:10.1093/jac/48.2.209. PMID 11481290. .

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[18] http://www.rxlist.com/cgi/generic/fosfomycin.htm

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