Pafuramidine

Cat. No.: HY-14932
CAS No.: 186953-56-0
Molecular Formula: C₂₀H₂₀N₄O₃
Molecular Weight: 364.4
Target: Parasite
Pathway: Anti-infection
Storage:
- Powder: -20°C, 3 years; 4°C, 2 years; In solvent: -80°C, 6 months; -20°C, 1 month

SOLVENT & SOLUBILITY

In Vitro
- DMSO: 33.33 mg/mL (91.47 mM; Need ultrasonic)
- H₂O: < 0.1 mg/mL (insoluble)

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent</th>
<th>Mass Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
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<tr>
<td></td>
<td></td>
<td>1 mM</td>
<td>2.7442 mL</td>
<td>13.7212 mL</td>
<td>27.4424 mL</td>
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<tr>
<td></td>
<td></td>
<td>5 mM</td>
<td>0.5488 mL</td>
<td>2.7442 mL</td>
<td>5.4885 mL</td>
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<tr>
<td></td>
<td></td>
<td>10 mM</td>
<td>0.2744 mL</td>
<td>1.3721 mL</td>
<td>2.7442 mL</td>
</tr>
</tbody>
</table>

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: ≥ 2.5 mg/mL (6.86 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.86 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
Pafuramidine (DB289) is an orally bioavailable prodrug of furamidine, which has clinical activity against Pneumocystis pneumonia. ICS0 Value: 4.5 nM (In vitro inhibitory activity against Trypanosoma brucei rhodesiense) [4]

Target:
Antiparasitic DB289 (pafuramidine maleate; 2,5-bis[4-(N-methoxyamidino)phenyl]furan monomaleate) is a prodrug of DB75 (furamidine dihydrochloride; 2,5-bis(4-guanylphenyl)furan dihydrochloride), an aromatic dication related to pentamidine that has demonstrated good efficacy against African trypanosomiasis, Pneumocystis carinii pneumonia, and malaria, but lacks adequate oral availability. In vitro: The results of this investigation suggest that DB75 inhibits mitochondrial function. Yeast cells relying upon mitochondrial metabolism for energy production are especially sensitive to DB75 [1]. In vivo: Clearance of DB289 approximated the liver plasma flow and its large volume of...
distribution was consistent with extensive tissue binding. Plasma protein binding of DB289 was 97 to 99% in four animal species and humans, but that of DB75 was noticeably less and more species- and concentration-dependent [2]. Despite excellent oral activity against early-stage sleeping sickness, oral administration of DB289 exhibited limited efficacy in mouse models of late-stage disease [3]. Clinical trial: DB289, a novel orally active prodrug of DB75, is undergoing phase IIb clinical trials for early-stage human African trypanosomiasis, Pneumocystis jiroveci carinii pneumonia, and malaria [1].

REFERENCES


[2]. Midgley I, Fitzpatrick K, Taylor LM, Pharmacokinetics and metabolism of the prodrug DB289 (2,5-bis[4-(N-methoxyamidino)phenyl]furan monomaleate) in rat and monkey and its conversion to the antiprotozoal/antifungal drug DB75 (2,5-bis(4-guanylphenyl)furan d


[4]. In vitro inhibitory activity against Trypanosoma brucei rhodesiense - BioAssay Summary.