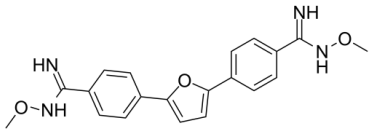
Data Sheet

Product Name:	Pafuramidine
Cat. No.:	CS-1470
CAS No.:	186953-56-0
Molecular Formula:	C20H20N4O3
Molecular Weight:	364.40
Target:	Parasite
Pathway:	Anti-infection
Solubility:	H2O : < 0.1 mg/mL (insoluble); DMSO : 33.33 mg/mL (91.47 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

Pafuramidine (DB289) is an orally bioavailable prodrug of furamidine, which has clinical activity against Pneumocystis pneumonia. IC50 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:

[1]. Lanteri CA, Trumpower BL, Tidwell RR, DB75, a novel trypanocidal agent, disrupts mitochondrial function in Saccharomyces cerevisiae. Antimicrob Agents Chemother. 2004 Oct;48(10):3968-74.

[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 dihydrochloride). Drug Metab Dispos. 2007 Jun;35(6):955-67.

[3]. Sturk LM, Brock JL, Bagnell CR, Distribution and quantitation of the anti-trypanosomal diamidine 2,5-bis(4-amidinophenyl)furan (DB75) and its N-methoxy prodrug DB289 in murine brain tissue. Acta Trop. 2004 Jul;91(2):131-43.

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

CAIndexNames:

Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-methoxy-

SMILES:

N=C(C1=CC=C(C2=CC=C(C3=CC=C(C(NOC)=N)C=C3)O2)C=C1)NOC

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

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