

Publication

Antiprotozoal activity of dicationic 3,5-diphenylisoxazoles, their prodrugs and aza-analogues

JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)**ID** 2383699**Author(s)** Patrick, Donald A.; Bakunov, Stanislav A.; Bakunova, Svetlana M.; Wenzler, Tanja; Brun, Reto; Tidwell, Richard R.**Author(s) at UniBasel** [Wenzler, Tanja](#) ; [Brun, Reto](#) ;**Year** 2014**Title** Antiprotozoal activity of dicationic 3,5-diphenylisoxazoles, their prodrugs and aza-analogues**Journal** Bioorganic & medicinal chemistry**Volume** 22**Number** 1**Pages / Article-Number** 559-576**Keywords** Diarylisoxazole, Diamidine, Prodrug, Antiprotozoal, Antitrypanosomal

Fifty novel prodrugs and aza-analogues of 3,5-bis(4-amidinophenyl)isoxazole and its derivatives were prepared. Eighteen of the 24 aza-analogues exhibited IC₅₀ values below 25 nM against Trypanosoma brucei rhodesiense or Plasmodium falciparum. Six compounds had antitrypanosomal IC₅₀ values below 10 nM. Twelve analogues showed similar antiplasmodial activities, including three with sub-nanomolar potencies. Forty-four diamidines (including 16 aza-analogues) and the 26 prodrugs were evaluated for efficacy in mice infected with T. b. rhodesiense STIB900. Six diamidines cured 4/4 mice at daily 5 mg/kg intraperitoneal doses for 4 days, giving results far superior to pentamidine and furamidine. One prodrug attained 3/4 cures at daily 25 mg/kg oral doses for 4 days.

Publisher Elsevier**ISSN/ISBN** 0968-0896**edoc-URL** <http://edoc.unibas.ch/dok/A6233654>**Full Text on edoc** No;**Digital Object Identifier DOI** 10.1016/j.bmc.2013.10.050**PubMed ID** <http://www.ncbi.nlm.nih.gov/pubmed/24268543>**Document type (ISI)** Article