

Publication

Antiprotozoal activity and DNA binding of N-substituted N-phenylbenzamide and 1,3-diphenylurea bisguanidines

JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)**ID** 2713846**Author(s)** Ríos Martínez, Carlos H.; Lagartera, Laura; Kaiser, Marcel; Dardonville, Christophe**Author(s) at UniBasel** [Kaiser, Marcel](#) ;**Year** 2014**Title** Antiprotozoal activity and DNA binding of N-substituted N-phenylbenzamide and 1,3-diphenylurea bisguanidines**Journal** European journal of medicinal chemistry**Volume** 81**Pages / Article-Number** 481-491**Keywords** Trypanosoma brucei, Plasmodium falciparum, Parasite chemotherapy, Guanidine, Minor groove binder, surface plasmon resonance (SPR) biosensor

Two series of N-alkyl, N-alkoxy, and N-hydroxy bisguanidines derived from the N-phenylbenzamide and 1,3-diphenylurea scaffolds were synthesised in three steps from the corresponding 4-amino-N-(4-aminophenyl)benzamide and 1,3-bis(4-aminophenyl)urea, respectively. All of the new compounds were evaluated *in vitro* against *T. b. rhodesiense* (STIB900) trypomastigotes and *Plasmodium falciparum* NF54 parasites (erythrocytic stage). N-alkoxy and N-hydroxy derivatives showed weak micromolar range IC₅₀ values against *T. b. rhodesiense* and *P. falciparum* whereas the N-alkyl analogues displayed sub-micromolar and low nanomolar IC₅₀ values against *P. falciparum* and *Trypanosoma brucei*, respectively. Two compounds, 4-(2-ethylguanidino)-N-(4-(2-ethylguanidino)phenyl)benzamide dihydrochloride (7b) and 4-(2-isopropylguanidino)-N-(4-(2-isopropylguanidino)phenyl)benzamide dihydrochloride (7c), which showed favourable drug-like properties and *in vivo* efficacy (100% cures) in the STIB900 mouse model of acute human African trypanosomiasis represent interesting leads for further *in vivo* studies. The binding of these compounds to AT-rich DNA was confirmed by surface plasmon resonance (SPR) biosensor experiments.

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