Anti-trypanosomal activity of Fexinidazole: a new oral nitroimidazole drug candidate for the treatment of sleeping sickness

JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

ID 1022831
Author(s) Kaiser, Marcel; Bray, Michael A.; Cal, Monica; Trunz, Bernadette Bourdin; Torreele, Els; Brun, Reto
Author(s) at UniBasel Kaiser, Marcel ; Brun, Reto ;
Year 2011
Title Anti-trypanosomal activity of Fexinidazole: a new oral nitroimidazole drug candidate for the treatment of sleeping sickness
Journal Antimicrobial agents and chemotherapy : AAC
Volume 55
Number 12
Pages / **Article-Number** 5602-5608
Fexinidazole is a 5-nitroimidazole drug currently in clinical development for the treatment of human sleeping sickness (human African trypanosomiasis (HAT)) caused by infection with species of the protozoan parasite Trypanosoma brucei. The compound and its two principal metabolites the sulfoxide and sulfone have been assessed for their ability to kill a range of T. brucei parasite strains in vitro and to cure both acute and chronic HAT disease models in the mouse. The parent molecule and both metabolites have shown trypanocidal activity in vitro in the 0.7 - 3.3 muM (0.2 to 0.9 mug/ml) range against all parasite strains tested. In vivo fexinidazole is orally effective in curing both acute and chronic disease in the mouse at doses of 100 mg/kg/day for 4 days and 200 mg/kg/day for five days respectively. Pharmacokinetic data indicate that it is likely that the sulfoxide and sulfone metabolites provide most if not all of the in vivo killing activity (33). Fexinidazole and its metabolites require up to 48 hours exposure in order to induce maximal trypanocidal efficacy in vitro. The parent drug and its metabolites show no in vitro cross reactivity in terms of trypanocidal activity with either themselves or other known trypanocidal drugs in use in man. The in vitro and in vivo anti-trypanosomal activity of fexinidazole and its two principal metabolites provides evidence that the compound has the potential to be an effective oral treatment for both the T. b. gambiense and T. b. rhodesiense forms of human sleeping sickness and both stages of the disease
Publisher American Society for Microbiology
ISSN/ISBN 0066-4804
edoc-URL http://edoc.unibas.ch/dok/A6002117
Full Text on edoc No;
Digital Object Identifier DOI 10.1128/AAC.00246-11
PubMed ID http://www.ncbi.nlm.nih.gov/pubmed/21911566
ISI-Number WOS:000296920600025
Document type (ISI) Article