Antiprotozoal activities of tetrazole-quinolines with aminopiperidine linker

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Human African Trypanosomiasis (HAT, sleeping sickness) and Malaria both are insect vectored tropical diseases. Only a couple of drugs is able to cure HAT, but all of them are toxic, prone to resistance and require parenteral administration. Malaria is responsible for high morbidity and mortality in humans. It is one of the global killers of children. Wide-spread drug resistance against traditional therapeutics which were once highly effective makes them almost useless. Therefore new drugs against both diseases are urgently needed.; Recently, we reported the synthesis and antiprotozoal activities of a number of new 2- substituted 4-carbamoyl- and 4-aminoquinolines. This study focussed on the synthesis of novel tetrazole derivatives which are linked to the quinoline core via a piperidine ring.; Novel compounds exhibiting a 7-chloroquinoline and a tetrazole ring were prepared via Ugi-azide reaction. Modifications were restricted to the orientation and the substitution of the linker. Compounds were tested for their activities against Trypanosoma brucei rhodesiense (STIB 900). Their antiplasmodial activities were determined against a sensitive (NF54) and a multiresistant strain (K1) of Plasmodium falciparum.; Eighteen tetrazole derivatives were prepared. The results of the biological tests were compared with the activities of drugs in use and structure-activity relationships were discussed. Their antitrypanosomal activities were only moderate. In contrast some of the compounds showed promising activity against both strains of Plasmodium falciparum and good to excellent resistance indices.; The antiplasmodial activities depended on the orientation of the 4-aminopiperidine linker. Compounds with a tertiary amino group in position 4 of the quinoline ring exhibited equal activity against both strains, whereas those with a secondary amino group were mainly active against the sensitive strain.
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