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Synthesis, antileishmanial and antimalarial activity evaluation of novel 2, 3-disubstituted-quinazoline-4(3h)-ones bearing biologically activequinoline and pyrazole moieties

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Due to fewer efficacies, costly and unsafe use of the currently available drugs, drug design and development for better drugs against leishmaniasis and malaria has become an active research area. Based on the progress reports on promising and diversified biological activities of 2,3-disubstituted-quinazoline-4(3H)-ones; this present investigation has attempted the synthesis of novel 2,3-disubstituted-quinazoline-4(3H)-ones bearing quinoline and pyrazole moieties and evaluate their antileishimanialand antimalarial activity. Upon condensation of the intermediates 3-aryl-2-methyl-quinazolin-4-(3H)-ones with various pyrazolyl aldehydes and 2-chloro-7-methyl-quinoline-4-carboxaldehyde, new 3-aryl-2-pyrazolyl-quinazoline-4(3H)-ones and 3-aryl-2-quinolinyl-quinazoline-4(3H)-ones respectively were successfully synthesized. Chemical structures of these compounds have been established on the basis of their elemental, analytical and spectral data. These compounds were evaluated for their in vitro antileishimanial and in vivo antimalarial activity against *Leishmania denovani* and *plasmodium berghei* respectively.All the compounds showed better antileishmanial activity compared to the standard drug miltefosine and moderate activity compared to amphotericin B phosphate. Compound 4a: (2-((E)-2-(1-(4-dimethylmethyleneaminosulfonylphenyl)-3-(4-chlorophenyl-1H-pyrazol-4-yl) vinyl)-3-p-tolylquinazolin-4(3H)-one) (IC50=0.0265 µg/ml) exhibited strongest antileishmanial activity; 120 folds more activity compared to miltefosine and 2 folds more active than amphotericin B phosphate. Among the compounds bearing quinoline moiety, compound 5c (2-((E)-2-(2-hydroxyquinoline-7-methyl-3-yl) vinyl)-3-o-tolylquinolin-4(3H)-one) (IC50=0.1862 µg/ml) showed good potency with 17 folds better activity than miltefosine. On the other hand, 3-aryl-2-quinolinyl-quinazoline-4(3H)-one derivatives had the highest antimalarial activity of all the compounds. From which, compound Va: (2-((E)-2-(2-hydroxyquinoline-7-methyl-3-yl) vinyl]-3-phenylquinazolin-4(3H)-one (percent suppression=85%) was the most active being chloroquine phosphate as standard drug. The acute toxicity test which was done for the most active compounds 4a and Va showed no sign of toxicity.

Biography

Roza G. Tesfahunegn has completed her M.Sc. at the age of 25 years in 2012 from Addis Ababa University, College of Health Sciences, School of Pharmacy. She is a lecturer of Medicinal Chemistry in Department of Pharmaceutical Chemistry and Pharmacognosy. She has taught and advised undergraduate and postgraduate courses for about 4 years. She has submitted two original articles and two reviews for publication to the peer reviewed journals.

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