OMICS Group Conferences
Accelerating Scientific Discovery

International Congress on
Bacteriology & Infectious Diseases
November 20-22, 2013 DoubleTree by Hilton Baltimore-BWI Airport, MD, USA

Synthesis of some novel 2-pyrazolyl-4(3H)-quinazolinone derivatives of potential antimalarial and anti-leishmanial activities

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In this work, some novel 2-pyrazolyl-4(3H)-quinazolinone derivatives have been synthesized by cyclization and condensation reactions. The synthesized compounds were obtained in a good yield (55.9-94%). The chemical structures of the final compounds were also verified by spectroscopic tools (IR, 1H NMR and elemental microanalyses). The *in vivo* anti-malarial activity of these compounds against *P.berghei* infected mice was found to be moderate at oral dose of 48.46 μmol/kg/day. This dose is equivalent to 25 mg/kg of chloroquine phosphate which causes 100% inhibition of the parasite. Among the synthesized compounds, 2-(3-(thiophen-2-yl)-4,5-dihydro-1H-pyrazol-5-yl)-3-phenylquinazolin-4(3H)-one, Xa, showed better activity with percent suppression of 65.89. The synthesized compounds were also evaluated for their *in vitro* anti-leishmanial activity against *L. donovani.* Among the synthesized compounds, compound IXe (IC50=0.0121 μg/ml) was found to be four times more potent than amphotericine B (IC50=0.0460 μg/ml) while it was two hundred sixty four (264X) times more potent than miltefosine (IC50=3.1911 μg/ml). Compound Xa (IC50=0.0211 μg/ml) was twice more potent than amphotericine B and this is the second most active compound as anti-leishmanial agent among the synthesized compounds. The synthesized compounds exhibited better inhibitory activity as indicated by their lower IC50 than miltefosine, except for compound XI. Compound XI showed the least activity which might be due to the presence of a phenyl group on the pyrazole N1. Furthermore, in the thiophen series cyclization of α,β-unsaturated compounds to the corresponding pyrazoline analogs led to improvement in activity while the phenyl series showed conflicting results. Results of acute toxicity test of the most active compounds (IXe and Xa) showed that the median lethal dose (LD50) is much greater than 300 mg/kg.

Biography

Addisu Asfaw Azene has completed his B.Pharm at the age of 23 years from University of Gondar, School of Pharmacy and M.Sc. in Medicinal Chemistry from Addis Ababa University, School of Pharmacy. He is lecturer and researcher at Mekelle University, Ethiopia. He has conducted different researches awaiting publication on reputed journals.

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