

2nd International Conference and Exhibition on Pharmacognosy, Phytochemistry & Natural Products

August 25-27, 2014 DoubleTree by Hilton Beijing, China

Synthesis and anti-malarial screening, of (*N*¹, *N*¹,-diethyl-*N*⁴,-dihydroartemisinin-10-yl) pentane-1, 4-diamine (PdP)

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Antimalarials are chemotherapeutic agents used for the prevention and treatment of malaria. Artemisinin and its derivatives has been discovered to be the anti-malarial drug of first choice because it is highly curative, effective on most stages of plasmodium life cycle, safe during the first, second and third trimesters, and safe for all ages. WHO, nevertheless, has recommended artemisinin based combination therapy (ACT) to guard against possible development of resistance like observed with chloroquine. In view of this fact we proposed coupling dihydroartemisinin, a derivative of artemisinin and 2-amino, 5-diethyl amino pentane, the chloroquine handle by using an SN2 reaction mechanism. The Mitsunobu (1967) coupling method, involving diisopropyl azodicarboxylate (DIAD), triphenyl phosphine (Ph3P), 2-amino, 5-diethyl amino pentane and dihydroartemisinin (DHA) at room temperature was adopted to synthesis our target compound, (*N*¹, *N*¹,-diethyl-*N*⁴,-dihydroartemisinin-10-yl)pentane-1,4-diamine (PdP) (IUPAC Name: *N*¹,*N*¹-diethyl-*N*⁴-(3,6,9-trimethyldecahydro-3,12-epoxy[1,2]dioxepino[4,3-*i*] isochromen -10-yl) pentane-1,4-diamine). The structure of "PdP" was confirmed by its mass spectra fragmentation patterns. The compound was screened at three dose levels of 3 mg/Kg, 10 mg/Kg and 30 mg/Kg, for *in-vivo* curative anti-malaria activity against infected mice with *Plasmodium berghei* with an LD₅₀ of 330 mg/Kg in mouse by oral route.

Biography

Ezekiel O Afolabi is a Senior Lecturer in the Department of Pharmaceutical Chemistry, University of Jos, Jos, Nigeria. His first degree was in Chemistry, (BSc (Hons.) Chemistry, Ibadan, 1976). After teaching for a while at secondary school level, he was appointed a Graduate Assistant at Ahmadu Bello University, Zaria, in September 1979, where he obtained MSc in Pharmaceutical Chemistry in August 1982. In 1983 and 1993 respectively, he was a visiting research student for nine months to Professor Keith Bowden, University of Essex, Colchester, and Professor Stephen Matlin, University of Warwick, Coventry, both in England (U.K.). In September 2011, he defended his PhD Thesis and has supervised more than 60 undergraduate student projects and has twelve Journal Papers.

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