Potensi derivat andrografolid sebagai antiplasmodium kajian toksisitas dan target kerjanya pada status oksidatif P falciparum in vitro = Potency of andrografolid derivate as an antiplasmodium toxicity analysis and the target mechanism of P falciparum oxidative status in vitro / Ni Luh Putu Eka Kartika Sari

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Abstrak

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Latar belakang: Salah satu tantangan terbesar dalam upaya pengobatan malaria adalah terjadinya penurunan efikasi pada penggunaan obat antimalaria, seperti kasus resistensi. Kejadian resistensi terhadap beberapa jenis obat mendorong penemuan obat antimalaria baru terus dilakukan. Beberapa studi yang telah dilakukan menyebutkan bahwa andrografolid (ANDRO) memiliki efek sebagai antimalaria. Dehidroksiandrografolid (DeOH-AND) adalah senyawa yang memiliki kemiripan struktur dengan ANDRO. Penelitian ini bertujuan untuk mengetahui efek DeOH sebagai antiplasmodium dan mekanisme kerjanya.
Metode: Penelitian ini merupakan penelitian eksperimental dengan teknik in vitro. Pada penelitian ini digunakan galur parasit Plasmodium falciparum 3D7 (chloroquine sensitive). Percobaan dilakukan untuk menjawab tiga tujuan penelitian; pertama bertujuan untuk mengetahui potensi DeOH-AND sebagai antiplasmodium dengan melakukan uji IC50, uji hambatan bergantung stadium parasit dan melihat morfologi sel parasit menggunakan mikroskop cahaya dan TEM (Transmission Electron Microscope). Kedua bertujuan untuk mengetahui efek sitotoksik DeOH-AND terhadap sel mamalia yang diujikan pada sel hati galur sel HepG2 dan sel darah merah. Ketiga, bertujuan untuk mempelajari pengaruh DeOH-AND terhadap status oksidatif parasit dilihat dari kadar ROS intraseluler parasit, rasio GSH/GSSG dan aktivitas enzim SOD.
Hasil: DeOH-AND memiliki aktivitas antiplasmodium dengan nilai IC50 sebesar 4 μM sedangkan kontrol klorokuin yang digunakan memiliki nilai IC50 sebesar 0.06 μM (60x10-9 M). Kedua senyawa ini dapat menghambat pertumbuhan sel parasit pada stadium ring, tropozoit dan skizon. Hasil pengamatan menggunakan mikroskop cahaya dan TEM mempelihatkan kerusakan pada sel parasit bila dibandingkan dengan kontrol. Senyawa DeOH-AND tidak toksik terhadap sel hati (HepG2) dengan nilai CC50 yakni 394.67 μM serta tidak toksik pada sel darah merah. Hasil percobaan bagian ketiga menunjukkan bahwa DeOH-AND tidak mempengaruhi kadar ROS, rasio GSH/GSSG serta aktivitas enzim SOD.
Kesimpulan: Senyawa DeOH-AND memiliki potensi sebagai antiplasmodium dan tidak memiliki efek toksik terhadap sel mamalia baik hati (HepG2) dan sel darah merah. DeOH-AND tidak mempengaruhi status oksidatif parasit secara signifikan.
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ABSTRACT
Background: One of the biggest challenges in malaria treatment is the occurrence of decreasing efficacy on antimalarial drugs like resistancy cases. Insidence of some drug resistance encourages the new antimalarial drugs continue to discover. Severeal studies mentioned that andrographolide (ANDRO) has an antimalarial effect. Dehidroksiandrographolide (DeOH) is a compound which has structural similarities with ANDRO. This study aims to determine the effect of DeOH as antiplasmodium and its mechanism.
Methods: This is an experimental study using in vitro techniques. In this study were used Plasmodium falciparum 3D7 strains (chloroquine sensitive). The experiments has three aims; the first part was aimed to known about the potential of DeOH-AND as an antiplasmodium using IC50 assay technique, stage dependent antiplasmodium activity, and analyse the P. falciparum morphology using light microscope and TEM (Transmission Electron Miscroscope) technique. The second parts was aimed to investigate the cytotoxic effect of DeOH-AND on mamalian cell (hepar cell-HepG2 and red blood cell). And the third aims is to investigate the effect of DeOH-AND on parasite oxidative stress status with analyse the intracellular ROS (Reactive Oxygen Species) concentration, GSH/GSSG ratio and SOD (Superoxide Dismutase) enzyme activity.
Results: DeOH-AND has antiplasmodium activity with IC50 value of 4 μM whereas chloroquine has IC50 values of 0.06 μM (60x10-9M). These compounds was found to inhibit the ring, tropozoit and skizon stage of the parasite. Treated P. falciparum 3D7 parasites show the crisis of their morphology cell which compared with untreated parasites (control). DeOHAND is not toxic to liver cells (HepG2) with CC50 values 394.67 and also not toxic to red blood cells which were seen from the results of hemolysis potential test. DeOH antiplasmodium effect were seen on all stage of the parasite (either ring, trophozoit and schizont) and caused parasite cell damage effect activity at all stages of the parasite (either ring, trophozoit and schizonts) and shown to cause damage. The third experiment showed that DeOH-AND did not affect the intracellular ROS (Reactive Oxygen Species) concentration, GSH/GSSG ratio and also SOD enzyme activity.
Conclusions: DeOH compounds has antiplasmodium activity. These compound has no toxic effect on both of the liver cells (HepG2) and red blood cells. DeOH-AND did not affect parasit oxidative status with significantly, Background: One of the biggest challenges in malaria treatment is the occurrence of
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