Perancangan struktur, sintesis, uji antiplasmodia dan uji sitotoksisitas in vitro turunan andrografolida = Design, synthesis, in vitro antiplasmodial and cytotoxicity assays of andrographolide derivative.

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Abstrak

Senyawa andrografolida, metabolit sekunder pada tumbuhan Sambiloto (Andrographis paniculata), diketahui memiliki aktivitas antiplasmodia 50% in vitro (IC50) < 10 μM, sehingga layak dijadikan sebagai senyawa pemandu di dalam pencarian dan pengembangan obat antimalaria secara rasional. Enzim farnesil difosfat sintase P. falciparum (PfFPPS) merupakan target yang valid untuk obat antimalaria. Tujuan umum penelitian ini adalah membuktikan membuktikan hipotesis bahwa senyawa turunan andrografolida, yang rancangan strukturnya diperoleh melalui optimasi interaksi maya andrografolida dengan enzim PfFPPS berdasarkan pose penambatan maya substrat dan inhibitornya, memiliki aktivitas antiplasmodia in vitro yang lebih tinggi daripada aktivitas antiplasmodia in vitro andrografolida dan tidak toksik terhadap sel manusia. Melalui optimasi interaksi maya andrografolida dengan enzim PfFPPS berdasarkan pose penambatan maya substrat dan inhibitornya, telah diperoleh rancangan struktur turunan andrografolida yang baru yang berpotensi menghambat enzim PfFPPS. Melalui reaksi esterifikasi terhadap senyawa andrografolida, diperoleh senyawa 3,14-andrografolidabis(4'-kloro)benzoat (18). IC50 senyawa 18 terhadap P. falciparum galur 3D7 adalah: 131,60 μM. Persentase pertumbuhan sel DLD-1 di bawah pengaruh senyawa 18 hingga konsentrasi 63,74 μM adalah lebih dari 100%. Dengan demikian, senyawa turunan andrografolida tersebut memiliki aktivitas antiplasmodia in vitro yang lebih rendah daripada aktivitas antiplasmodia in vitro andrografolida, namun tidak toksik terhadap sel manusia.
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Andrographolide, a secondary metabolite of Sambiloto (Andrographis paniculata), has a 50% in vitro antiplasmodial activity (IC50) < 10 μM, that it is suitable as a lead compund in an antimalarial drug discovery and development. P. falciparum farnesyl diphosphate synthase (PfFPPS) is a valid target for antimalarial drug. The main objective of this research is to prove the hypothesis that andrographolide derivative, whose design was obtained throughout optimization of virtual interaction between andrographolide and PfFPPS based on the docking pose of its substrates and inhibitor, has a higher in vitro antiplasmodial activity than that of andrographolide and is not toxic towards human cells. Throughout optimization of virtual interaction between andrographolide and PfFPPS based on the docking pose of its substrates and inhibitor, design of novel andrographolide derivatives which are potential to inhibit PfFPPS was obtained. Throughout esterification on andrographolide, an andrographolide derivative was obtained: 3,14-andrographolidebis(4'-chloro)benzoate (18). IC50 of 18 against P. falciparum 3D7 was: 131.60 μM. Percentage of human DLD-1 cell growth under the influence of 18 up to 63.74 μM was more than 100%. Therefore, this andrographolide derivative has lower in vitro antiplasmodial activity than that of andrographolide, but is not toxic towards human cells.