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Efek andrografolida dan ekstrak sambiloto andrographis paniculata ness. terhadap viabilitas, siklus sel, serta faktor transkripsi diferensiasi bone marrow mesenchymal stem cells bmmsc menjadi osteoblas = The effects of andrographolide and the extract of andrographis paniculata ness. on viability, cell cycle, and transcription factors of osteoblast differentiation on human bone marrow mesenchymal stem cells bmmsc

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Abstrak

ABSTRAK
belakang: Sambiloto Andrographis paniculata Ness. telah digunakan secara luas sebagai obat tradisional. Tanaman ini mempunyai potensi sebagai antikanker. Andrografolida sebagai senyawa aktif utama sambiloto telah terbukti bersifat sitotoksik terhadap berbagai jenis sel kanker. Evaluasi toksisitas penting dilakukan untuk memastikan keamanan andrografolida dan tanaman sambiloto. Penelitian ini bertujuan menganalisis efek andrografolida dan ekstrak/fraksi sambiloto terhadap viabilitas, siklus, serta faktor transkripsi diferensiasi sel punca mesenkimal asal sumsum tulang manusia bone marrow mesenchymal stem cells/BMMSC menjadi osteoblas. Metode: Penilaian efek andrografolida dan fraksi etil asetat sambiloto FEAS terhadap viabilitas, siklus sel serta tingkat ekspresi mRNA CDK4 dan p21 dilakukan dengan memaparkan andrografolida konsentrasi 5, 10 dan 15 g/mL dan FEAS konsentrasi 20, 40 dan 60 g/mL selama 12, 24 dan 36 jam. Viabilitas sel diperiksa berdasarkan prinsip reduksi garam formazan WST-8, analisa siklus sel menggunakan flow cytometer dan tingkat ekspresi mRNA dengan quantitative RT-PCR. Penilaian terhadap diferensiasi osteoblas dilakukan dengan menginduksi BMMSC dengan medium osteogenik disertai pemberian andrografolida konsentrasi 5 dan 10 g/mL serta FEAS konsentrasi 20 dan 40 g/mL selama 7, 14 dan 21 hari, kemudian dinilai intensitas pewarnaan alizarin red AR , kadar deposit kalsium ekstraseluler serta tingkat ekspresi runx2 dan osterik. Hasil: Andrografolida dan FEAS menurunkan viabilitas BMMSC sesuai tingkatan konsentrasi dan waktu paparan. Kedua bahan uji tersebut menghambat proliferasi BMMSC dengan meningkatkan secara bermakna persentase populasi sel pada fase G1 dan menurunkan populasi sel yang memasuki fase S dan G2 siklus sel pada paparan 24 jam. Tidak terdapat efek terhadap tingkat ekspresi mRNA CDK4 namun ekspresi mRNA p21 meningkat bermakna. Andrografolida dan FEAS menurunkan intensitas warna merah AR, kadar matriks kalsium ekstraseluler dan ekspresi mRNA runx2 secara bermakna, namun meningkatkan ekspresi mRNA osterik pada proses diferensiasi BMMSC menjadi osteoblas Kesimpulan: Andrografolida konsentrasi 5, 10 dan 15 g/mL maupun fraksi etil asetat sambiloto konsentrasi 20, 40 da 60 g/mL mempunyai efek toksik terhadap viabilitas, proliferasi dan diferensiasi osteoblas pada BMMSC secara in vitro. Kata kunci : Andrografolida, Andrographis paniculata, BMMSC, siklus sel, osteoblas.<hr />Background: Sambiloto Andrographis paniculata Ness./AP , has been used extensively as a traditional medicine. Andrographolide as the main active component of this plant showed cytotoxic activity in vitro on various type of cancer cells line. Toxicity evaluation is important to ensure the safety of andrographolide and this bitter plant. The objective of this study was to investigate the effects of andrographolide and the extract of AP on viability, cell cycle, and transcription factors of osteoblast differentiation on human bone marrow mesenchymal stem cells BMMSC Methods: BMMSC

were treated with andrographolide at 5, 10 and 15 ?g/mL and ethyl acetate fraction of AP EAFA at 20, 40 and 60 ?g/mL for 12, 24 and 36 hours. The cells viability was assessed using tetrazolium salt WST-8 assay, the cell cycle was evaluated using flow cytometer with propidium iodide DNA?binding fluorescent dyes and the expression of CDK4 mRNA and p21 was analyzed by RT-PCR. Further examination was investigated the effects of the compounds on the osteogenic differentiation of BMMSC. The cells were cultured on osteogenic medium and treated with andrographolide at 5 and 10 ?g/mL and EAFA at 20 and 40 ?g/mL for 7, 14 and 21 days. The matrix mineralization was assessed by alizarin red-s staining AR , the semi-quantification of calcium was determined by acetic acid extraction of calcium binding AR and the expression of runx2 and osterix were analysed by RT-PCR Results: This research was revealed that andrographolide and EAFA decreased the cell viability, arrested the cell cycle at G1 phase, and up regulated the expression of mRNA p21. Moreover andrographolide and EAFA supplementation decreased the intensity of AR and calcium deposition on cell culture. The expression of transcriptor factors runx2 was down regulated while osterix was up regulated. Conclusion: Andrographolide at 20, 40 and 60 ?g/mL and EAFA at 20, 40 and 60 ?g/mL showed potentially toxic on cell viability, arrested cell cycle and impaired osteoblast differentiation of BMMSC in vitro.