# Uji efektivitas nanoemulgel kombinasi ekstrak ageratum conyzoides (l.) L dan oldenlandia corymbosa l. serta senyawa aktifnya pada tikus model osteoartritis yang diinduksi monoiodoasetat = The effectiveness study of nanoemulgel combination of ageratum conyzoides (l.) l. extract and oldenlandia corymbosa l. extract and its active compound on monoiodoacetic induced osteoarthritis rat model

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Abstrak

Di Indonesia, daun Babandotan (Ageratum conyzoides (L.) L.) (EAC) dan herba Rumput Mutiara (Oldenlandia corymbosa L.) (EOC) telah digunakan secara empiris turun-temurun untuk mengobati penyakit sendin dengan cara ditumbuk kemudian dioleskan. Kuersetin (KU) dan asam ursolat (AU) yang merupakan zat aktif di dalam ekstrak tersebut memiliki aktivitas antiinflamasi pada hewan model yang diinduksi osteoartritis. Di dalam penelitian ini, kombinasi ekstrak babandotan dan rumput mutiara serta kombinasi kuersetin dan asam ursolat diformulasikan dalam sistem pembawa nanoemulsi sehingga memiliki karakteristik fisik yang baik serta dapat menghambat proses inflamasi dan dapat digunakan sebagai obat osteoartritis. Sebanyak 50 (lima puluh) ekor tikus dibagi dalam 10 kelompok (n=5) yaitu: (1) kelompok kontrol normal (normal) (2) kelompok kontrol negatif (negatif) (3) kelompok kombinasi EAC-EOC (EAC-EOC) (4) kelompok EAC tunggal (EAC) (5) kelompok EOC tunggal (EOC) (6) kelompok kombinasi KU-AU (KU-AU) (7) kelompok KU tunggal (KU) (8) kelompok AU tunggal (9) kelompok kombinasi KU-AU non-nano (Emulgel KU-AU) (10) kelompok kontrol positif (positif). Pada hari ke-0, tikus diinduksi monoiodoasetat secara intraartikular 3,0mg/0.05 mL kecuali kelompok normal. Pemberian sediaan topikal sesuai dengan kelompok dosis dilakukan mulai hari ke-29. Dilakukan evaluasi terhadap volume udem (setiap 7 hari), analisis kadar sitokin serum dengan enzyme-linked immunoabsorbent assay (ELISA) dan histopatologi serta imunohistokimia pada hari ke-57. Volume udem lutut tikus tidak berbeda bermakna dengan kelompok normal sejak hari ke-42. Penurunan kadar sitokin serum terjadi pada biomarker Protein S100A8, Interleukin-1β, inducible nitric oxide synthase (iNOS), matrix metalloproteinase-13 (MMP-13), a disintegrin and metalloproteinase thrombospondin-like motifs-5 (ADAMTS-5), Kolagen Tipe 2 dan Aggrecan Core Protein. Perbedaan bermakna semua kelompok perlakuan dengan kelompok negatif terjadi pada biomarker penanda proses inflamasi yaitu Protein S100A8, Interleukin-1ß dan iNOS (#P<0,05). Hasil evaluasi histopatologi dan imunohistokimia menunjukkan bahwa terjadi penghambatan degradasi proteoglikan. Sediaan nanoemulgel yang dikembangkan baik komposisi tunggal maupun kombinasi dapat memperbaiki kerusakan kartilago yang bermanfaat sebagai obat osteoartritis.
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In Indonesia, babandotan leaves (ageratum conyzoides (L.) L.) (ACE) and pearl grass herbs (Oldenlandia corymbosa L.) (OCE) have been used empirically as topical preparation for traditional medicine in the treatment of joint disease. Their active compound namely quercetin (QU) and ursolic (UA) acid has appearance anti-inflammatory activity in osteoarthritis (OA) animal model. We investigated nanoemulgel of combination QU and UA as well as the combination ACE and OCE from nanoemulsion carrier systems as the new drug focused on plant-based natural products with a good physical characteristic

that inhibit inflammatory process and applied in managing osteoarthritis (OA). Fifty animals were randomly designated to the 10 groups (n=5) as follows: (1) normal control group (Normal), (2) negative control groups (negative), (3) combination ACE-OCE, (4) single ACE, (5) single OCE, (6) combination QU-UA, (7) single QU, (8) single UA, (9) combination QU-UA non-nano formula (emulgel QU-UA), (10) positive control group (positive). Rats were receiving intraartikular monoiodoacetate injection 3.0mg/0.05 mL on day 0 exluding for normal control group. All groups were administered topical preparations allow to each dose group on day 29. We evaluated knee edema profile (every 7 days), serum cytokine level (on day 57) with enzyme-linked
immunoabsorbent assay (ELISA) and histopatological and immunhostochemistry evaluation. Since day 42, knee edema profile of all group treatment has been similar with normal control group ($p>0.05$). Serum cytokines level for some biomarkers, such as S100A8 Protein, Interleukin-1β, inducible nitric oxide synthase (iNOS), matrix metalloproteinase-13 (MMP-13), a disintegrin and metalloproteinase thrombospondin-like motifs-5 (ADAMTS-5), Collagen Type II and Aggrecan Core Protein were decrease. A significant difference compared with negative group showed for all groups treatment on measurement of inflammation process biomarker of S100A8 Protein, IL-1β, and iNOS (#$P<0.05$). Based on histological and immunohistochemistry evaluation showed that there was inhibition of proteoglycan degradation. The developed nanoemulgel ACE-OCE and QU-UA either combination or not has good physical characteristic and promising effect to enhance MIA induced cartilage damage as potential therapeutic agent for OA and encouraging to conduct further study as clinical trials.