INTISARI

Prevalensi penyakit yang melibatkan proses inflamasi di Indonesia cukup tinggi, sehingga diperlukan pencarian dan pengembangan senyawa penuntun baru yang berpotensi sebagai agen antiinflamasi. Salah satu tanaman yang berpotensi sebagai antiinflamasi adalah *Murraya koenigii*. Penelitian ini bertujuan mengidentifikasi senyawa aktif *M. koenigii* yang berpotensi sebagai agen antiinflamasi dan analgesik, serta mengkaji mekanisme kerjanya melalui penghambatan enzim siklooksigenase.

Ekstraksi dilakukan menggunakan etanol 90% dengan metode remaserasi. Aktivitas antiinflamasi ekstrak diuji secara *in vivo* melalui model *paw oedema* tikus terinduksi karagenan, sedangkan kadar sitokin proinflamasi (TNF-α, IL-1β, IL-6) dianalisis menggunakan metode ELISA. Uji analgesik ekstrak dilakukan dengan metode *tail-flick* pada tikus. Fraksinasi menghasilkan fraksi larut dan tidak larut etil asetat, yang kemudian diuji kandungan total fenolik, flavonoid, serta aktivitas antioksidan menggunakan metode DPPH, FRAP, dan ABTS. Fraksi aktif dimurnikan dengan *flash column chromatography* dan KLT preparatif. Aktivitas penghambatan COX-1 dan COX-2 diuji secara *in vitro* menggunakan *COX Inhibitor Screening Assay Kit* untuk menentukan nilai IC_{50}. Uji statistik menggunakan uji normalitas data yaitu uji Kolmogorov-Smirnov, uji homogenitas menggunakan Levene's Test, yang dilanjutkan dengan uji one way Anova. Identifikasi struktur dilakukan melalui spektroskopi UV-Vis, FTIR, MS, dan NMR.

Ekstrak etanol daun *M. koenigii* dosis 100, 200, dan 400 mg/kg BB menunjukkan aktivitas antiinflamasi dan menurunkan kadar sitokin proinflamasi (TNF-α, IL-6, dan IL-1β) pada tikus terinduksi karagenan, serta memiliki aktivitas analgesik pada uji *tail-flick* secara *in vivo*. Secara *in vitro*, ekstrak etanol daun *M. koenigii*, fraksi larut etil asetat, dan fraksi tak larut etil asetat menghambat enzim COX-1 dengan nilai IC_{50} berturut-turut 74,91 µg/mL, 83,92 µg/mL, dan 66,16 µg/mL, serta menghambat enzim COX-2 dengan nilai IC_{50} berturut-turut 33,84 µg/mL, 42,41 µg/mL, dan 70,49 µg/mL. Isolat FLEA-1 menunjukkan aktivitas paling kuat dengan nilai IC_{50} 23,07 µg/mL terhadap COX-1 dan 13,22 µg/mL terhadap COX-2, yang teridentifikasi sebagai mahanimbine ($C_{23}H_{25}NO$). Mahanimbine sebagai komponen aktif daun *M. koenigii* terbukti memiliki aktivitas antiinflamasi melalui penghambatan enzim COX. Berdasarkan temuan ini, senyawa mahanimbine direkomendasikan sebagai senyawa penanda (marker) dan berpotensi untuk dikembangkan sebagai kandidat herbal antiinflamasi yang efektif.

Kata Kunci: antiinflamasi, mahanimbine, *Murraya koenigii*, siklooksigenase, dan sitokin proinflamasi.

ABSTRACT

The prevalence of diseases involving inflammatory processes in Indonesia remains high, highlighting the need for the discovery and development of new lead compounds with potential anti-inflammatory activity. *Murraya koenigii* is one of the medicinal plants with promising anti-inflammatory properties. This study aimed to identify active compounds from *M. koenigii* with potential anti-inflammatory and analgesic activities and to elucidate their mechanisms of action through cyclooxygenase (COX) enzyme inhibition.

Extraction was performed using 90% ethanol by the remaceration method. The anti-inflammatory activity of the extract was evaluated in vivo using a carrageenan-induced paw edema model in rats, while pro-inflammatory cytokine levels (TNF-α, IL-1β, and IL-6) were quantified using enzyme-linked immunosorbent assay (ELISA). Analgesic activity was assessed using the tail-flick test in rats. Fractionation yielded ethyl acetate–soluble and ethyl acetate–insoluble fractions, which were subsequently evaluated for total phenolic and flavonoid contents as well as antioxidant activity using DPPH, FRAP, and ABTS assays. The active fraction was further purified by flash column chromatography and preparative thin-layer chromatography. In vitro COX-1 and COX-2 inhibitory activities were determined using a COX Inhibitor Screening Assay Kit to calculate IC_{50} values. Statistical analysis was performed using the Kolmogorov–Smirnov test for data normality and Levene's test for homogeneity of variance, followed by one-way ANOVA. Structural elucidation was conducted using UV–Vis, FTIR, MS, and NMR spectroscopy.

The ethanolic leaf extract of *M. koenigii* at doses of 100, 200, and 400 mg/kg body weight exhibited significant anti-inflammatory activity and reduced pro-inflammatory cytokine levels (TNF-α, IL-6, and IL-1β) in carrageenan-induced rats, along with notable analgesic effects in the tail-flick test in vivo**.** In vitro, the ethanolic extract, ethyl acetate–soluble fraction, and ethyl acetate–insoluble fraction inhibited COX-1 with IC_{50} values of 74.91, 83.92, and 66.16 µg/mL, respectively, and inhibited COX-2 with IC_{50} values of 33.84, 42.41, and 70.49 µg/mL, respectively. The isolate FLEA-1 demonstrated the strongest inhibitory activity, with IC_{50} values of 23.07 µg/mL against COX-1 and 13.22 µg/mL against COX-2, and was identified as mahanimbine ($C_{23}H_{25}NO$). These findings confirm that mahanimbine is an active constituent of *M. koenigii* leaves that exerts anti-inflammatory effects through COX enzyme inhibition. Therefore, mahanimbine is recommended as a chemical marker and holds strong potential for development as an effective herbal anti-inflammatory candidate.

Keywords: anti-inflammatory, cyclooxygenase, mahanimbine, *Murraya koenigii*, dan pro-inflammatory cytokines.