

Intisari

Micromelum minutum merupakan salah satu tanaman yang diketahui memiliki aktivitas sitotoksik terhadap beberapa sel kanker payudara dengan nilai $IC_{50} < 100 \mu\text{g/mL}$. Isolasi, identifikasi senyawa dan aktivitas farmakologi dari *M. minutum* yang tumbuh di beberapa negara telah dilakukan, dan diketahui adanya variasi struktur senyawa tergantung lokasi tumbuh dan varietasnya. Meskipun demikian, *M. minutum* yang tumbuh di Indonesia belum diteliti baik secara fitokimia maupun aktivitas farmakologinya. Penelitian ini bertujuan untuk mengetahui kandungan senyawa dalam ekstrak heksan *M. minutum* yang tumbuh di Taman Nasional Bantimurung, Bulusaraung, Sulawesi Selatan, serta aktivitas sitotoksik ekstrak heksan, fraksi dan isolatnya terhadap sel kanker payudara MCF-7 dan 4T1.

Serbuk simplisia daun *M. minutum* diekstraksi menggunakan heksan. Ekstrak heksan difraksinasi menggunakan teknik kromatografi. Ekstrak, fraksi dan isoalt diuji aktivitas sitotoksiknya terhadap sel kanker payudara MCF-7 dan 4T1. Konfirmasi stuktur senyawa menggunakan spektroskopi LC-MS, GC-MS, IR, H-NMR, C-NMR, DEPT, dan 2D-NMR (COSY, HSQC, dan HMBC).

Ekstrak heksan *M. minutum* memiliki rendamen sebesar 2.65% terhadap bobot simplisia. Ekstrak memiliki aktivitas sitotoksik terhadap sel kanker payudara MCF-7 dan 4T1 dengan IC_{50} berturut-turut sebesar 142 dan 77 $\mu\text{g/ml}$. Pemisahan ekstrak heksan dengan KCV menghasilkan sembilan fraksi (F1-F9). Fraksi 2, 3, dan 6 aktif terhadap sel MCF-7 dan 4T1 dengan IC_{50} fraksi berturut-turut sebesar 34, 84, dan 115 $\mu\text{g/mL}$ pada sel MCF-7, dan nilai IC_{50} fraksi berturut-turut sebesar 61, 111 dan 89 $\mu\text{g/mL}$ pada sel 4T1. Analisis F2 dan F3 dengan GC-MS menunjukkan bahwa kedua fraksi tersebut mengandung senyawa sesquiterpen beta elemen (35,36%), *longiphinolcarveol* (19,80%), dan *caryophyllene oxide* (14,43%). Pemisahan lebih lanjut F6 menghasilkan senyawa 5,7-dihidroksi-3,4',8-trimetoksiflavin ($C_{18}H_{16}O_7$) yang memiliki aktivitas sitotoksik sedang terhadap sel kanker payudara MCF-7 dan 4T1 dengan nilai IC_{50} berturut-turut sebesar 127 $\mu\text{g/mL}$ (369 μM) dan 78 $\mu\text{g/mL}$ (226 μM).

Berdasarkan hasil dapat disimpulkan ekstrak heksan *M. minutum* yang tumbuh di Taman Nasional Bantimurung, Bulusaraung, Sulawesi Selatan, mengandung senyawa terpenoid yaitu beta elemen, *longiphinolcarveol*, dan *caryophyllene oxide*, serta senyawa 5,7-dihidroksi-3,4',8-trimetoksiflavin. Ekstrak heksan *M. minutum*, fraksi, dan isolatnya memiliki aktivitas sitotoksik terhadap sel MCF-7 dan 4T1.

Kata Kunci : *Micromelum minutum*, beta elemen, *longiphinolcarveol*, *caryophyllene oxide*, 5,7-dihidroksi-3,4',8-trimetoksiflavin, aktivitas sitotoksik, MCF-7, dan 4T1.

Abstract

Micromelum minutum is an herb that known to have cytotoxic activity against some breast cancer cells with IC₅₀ values <100 µg/mL. Isolation, identification of compounds and pharmacological activity of *M. minutum* from several countries has been done, and it is known that there are structure variations of compound depended on location and its varieties. Nevertheless, *M. minutum* that grows in Indonesia has not been studied either phytochemically or pharmacologically. This study aimed to know the compounds in *M. minutum*'s leaves hexane extract which grow in Bantimurung National Park, Bulusaraung, South of Sulawesi, and evaluated cytotoxic activity of hexane extract, fraction and isolate against breast cancer cells MCF-7 and 4T1.

The powder of *M. minutum* leaves was macerated using hexane. Than, the hexane extract was fractionated using chromatographic techniques. Extract, fractions, and isolate were tested for cytotoxic activity against breast cancer MCF-7 and 4T1 cells. Structure Of compound was identified by using LC-MS spectroscopy, GC-MS, FT-IR, ¹H-NMR, ¹³C-NMR, DEPT 135°, and 2D-NMR (COSY, HSQC, and HMBC).

Micromelum minutum hexane extract had % yield about 2.65% of simplicia weight. The extract had cytotoxic activity against MCF-7 and 4T1 breast cancer cells with IC₅₀ 142 and 77 µg/mL, respectively. Fractionation of hexane extract with Vacuum Liquid Chromatography (VLC) resulted in nine fractions (F1-F9). Fraction 2, 3, and 6 were active as cytotoxic agent against MCF-7 and 4T1 cells with IC₅₀ 34, 84, and 115 µg /mL, respectively on MCF-7 cells, and IC₅₀ 61, 111 and 89 µg/mL, respectively in 4T1 cell. GC-MS analysis of F2 and F3 fractions showed that both fractions contain sesquiterpene β-elemene (35,36%), longiphinolcarveol (19,80%), and caryophyllene oxide (14,43%). Further separation of F6 resulted in a 5,7-dihydroxy-3,4,8-trimethoxyflavone (C₁₈H₁₆O₇) compound which had medium cytotoxic activity against MCF-7 and 4T1 breast cancer cells with IC₅₀ value about 127 µg/mL (369 µM) and 78 µg/mL (226 µM), respectively.

Based on the result, it could be concluded that hexane extract of *M. minutum* which grows in Bantimurung National Park, Bulusaraung, South Sulawesi contains terpenoid (beta element, longiphinolcarveol, and caryophyllene oxide), and 5,7-dihydroxy-3,4,8-trimethoxyflavone. The hexane extract of *M. minutum*, fractions, and its isolates have cytotoxic activity against MCF-7 and 4T1 breast cancer cell.

Keyword : *Micromelum minutum*, β-elemene, longiphinolcarveol, caryophyllene oxide, 5,7-dihydroxy-3,4,8-trimethoxyflavone, cytotoxic activity, MCF-7, and 4T1.