ISOLASI SENYAWA AKTIF DARI DAUN BANGUN-BANGUN (*Coleus amboinicus,* L.) DAN UJI POTENSINYA SEBAGAI ANTIKANKER SECARA *IN VITRO* DAN *IN SILICO*

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INTISARI

Penyakit kanker terus mengalami peningkatan jumlah kasus dan menjadi masalah bagi kesehatan sebagai penyumbang kematian tertinggi kedua di dunia. Kondisi ini menjadi semakin serius mengingat penggunaan obat kanker saat ini masih belum efektif dan memiliki bioavailabilitas yang buruk. Penelitian ini bertujuan untuk mengisolasi senyawa aktif, menguji potensi aktivitas dan selektivitas antikanker secara *in vitro* dari daun bangun-bangun (*Coleus amboinicus*, Lour), serta melakukan kajian penambatan molekul secara *in silico* isolat aktif dengan protein hasil kajian bioinformatika melalui pendekatan farmakologi jaringan pada jalur kanker. Skrining fitokimia menunjukkan ekstrak etanol daun *Coleus amboinicus* memiliki kandungan golongan senyawa metabolit sekunder seperti fenolik dan polifenolat, flavonoid, alkaloid, triterpenoid/steroid, dan saponin. Skrining awal aktivitas antikanker dilakukan secara *in vitro* dengan metode MTT terhadap sel kanker payudara (MCF-7), kanker serviks (HeLa), dan kanker paru (A549) dari masing-masing ekstrak meliputi ekstrak etanol awal dan ekstrak hasil partisi (*n*-heksana, kloroform, etil asetat, dan etanol-air/residu) menunjukkan aktivitas kategori sedang-lemah (IC_{50} = 84,24–251,20 ppm). Ekstrak dengan aktivitas antikanker yang paling potensial yaitu ekstrak *n*-heksana dan etil asetat sehingga dilanjutkan ke tahap pemurnian. Isolat aktif dikarakterisasi, ditentukan titik leleh, dan dielusidasi struktur menggunakan spektrometer UV-Vis, FT-IR, GC-MS, ^{1}H- dan ^{13}C-NMR. Isolat aktif diuji potensi aktivitas antikanker terhadap sel kanker MCF-7, HeLa, dan A549 dan dibandingkan dengan sel normal (CV-1). Isolat aktif (kode **2**) dengan senyawa 7α-etoksi-16-hidroksiroileanon hasil pemurnian ekstrak *n*-heksana menunjukkan aktivitas paling baik terhadap sel A549 dengan IC_{50} 31,74 ppm dan selektivitas 10,53; serta terhadap sel HeLa dengan IC_{50} 37,43 ppm dan selektivitas 9,71. Isolat aktif (kode **1**) dari ekstrak etil asetat menunjukkan aktivitas paling baik terhadap sel MCF-7 (IC_{50} 80,05 ppm dan selektivitas 6,96) dengan lima senyawa dengan kadar tertinggi yaitu (1) etil heksadekanoat (19,74%); (2) bis(2-etilheksil)-1,4-benzenakarboksilat (14,63%); (3) etil-9*Z*,12*Z*,15*Z*-okatdekatrienoat (12,31%); (4) 2,4-di-tersier-butilfenol (9,67%), dan (5) 3,7,11,15-tetrametilheksadek-2-en-1-il asetat (9,46%). Senyawa 7α-etoksi-16-hidroksiroileanon hasil kajian bioinformatika pendekatan farmakologi jaringan pada jalur kanker menargetkan tiga protein utama yaitu PPARG, BCl2, dan ITGB1 dari protein kanker paru dan kanker serviks, sedangkan isolat (**1**) dari ekstrak etil asetat menargetkan protein MMP2, MDM2, dan STAT3 dari kanker payudara. Prediksi profil *absorption, distribution, metabolism, excretion, and toxicity* (ADMET) memberikan sifat farmakokinetika yang baik dan efek toksisitas yang relatif rendah serta memenuhi aturan Lipinski sebagai dasar pengembangan obat oral yang baik. Hasil penelitian ini memberikan harapan yang menjanjikan di masa depan untuk dapat dikembangkan lebih lanjut sebagai alternatif obat kanker berbasis bahan alam mulai dari penggunaan sebagai obat tradisional dan fitofarmaka hingga obat modern.

Kata kunci: *Coleus amboinicus,* antikanker, bioinformatika, *in vitro*, *in silico*, farmakologi jaringan.

ISOLATION OF ACTIVE COMPOUNDS FROM BANGUN-BANGUN (*Coleus amboinicus*, L.) LEAVES AND ITS POTENTIAL AS ANTICANCER THROUGH *IN VITRO* AND *IN SILICO*

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ABSTRACT

Cancer cases continue to increase and have become a health problem as the second highest cause of death worldwide. This condition becomes a serious concern considering that the use of current cancer drugs remain ineffective and have poor bioavailability. This research aims to isolate active compounds, test their potential anticancer activity and selectivity *in vitro* from bangun-bangun (*Coleus amboinicus*, Lour) leaves, and conduct an *in silico* molecular docking study of active isolates with proteins from bioinformatics studies through a network pharmacology approach from pathways in cancer. Phytochemical screening showed that the ethanolic extract of *Coleus amboinicus* leaves contains secondary metabolite compounds, including phenolics and polyphenolics, flavonoids, alkaloids, triterpenoids/steroids, and saponins. Initial screening of anticancer activity was performed in vitro using the MTT method against breast cancer cells (MCF-7), cervical cancer (HeLa), and lung cancer (A549) from each extract, including the initial ethanolic extract and the partition extracts (*n*-hexane, chloroform, ethyl acetate, and ethanol-water/residue), and showed moderate-weak activity (IC_{50} = 84.24–251.20 ppm). The most potent extracts were *n*-hexane and ethyl acetate extracts, thus, they were further studied to purification method. Active isolates were characterized, subjected for melting points determination, and their structures elucidated using UV-Vis, FT-IR, GC-MS, ^{1}H- and ^{13}C-NMR spectrometry. These active isolates were tested for potential anticancer activity against MCF-7, HeLa, and A549 cancer cells and compared with normal cells (CV-1). The active isolate (code **2**), with the compound 7α-ethoxy-16-hydroxyroyleanone resulting from the purification of *n*-hexane extract, showed the best activity against A549 cells with an IC_{50} of 31.74 ppm and a selectivity of 10.53; and against HeLa cells with an IC_{50} of 37.43 ppm and a selectivity of 9.71. The active isolate (code **1**) from the ethyl acetate extract showed the best activity against MCF-7 cells (IC_{50} of 80.05 ppm and a selectivity of 6.96) with the five main compounds, namely (1) ethyl hexadecanoate (19.74%); (2) bis(2-ethylhexyl)-1,4-benzenecarboxylate (14.63%); (3) ethyl-9*Z*,12*Z*,15*Z*-ocatedecarenoate (12.31%); (4) 2,4-di-tertiary-butylphenol (9.67%); and (5) 3,7,11,15-tetramethylhexadec-2-en-1-yl acetate (9.46%). The compound 7α-ethoxy-16-hydroxyroyleanone, according to a bioinformatic study using a network pharmacology approach on cancer pathways, targets three main proteins, namely PPARG, BCl2, and ITGB1, from lung cancer and cervical cancer proteins, while isolate (**1**) from ethyl acetate extract targets MMP2, MDM2, and STAT3 proteins from breast cancer. Predictions of absorption, distribution, metabolism, excretion, and toxicity (ADMET) profiles provide good pharmacokinetic properties and relatively low toxicity effects, as well as fulfill Lipinski's rules as a basis for developing good oral drugs. The results of this study offer promising hope in the future for further development of alternative natural-based cancer drugs, ranging from its application as traditional medicine and phytopharmaceuticals to modern medicines.

Keywords: *Coleus amboinicus,* anticancer, bioinformatic, *in vitro*, *in silico,* network pharmacology.