Chempublish Journal
Journal Homepage: online-journal.unja.ac.id/chp
Department of Chemistry
Faculty of Science and Technology
Universitas Jambi
ISSN (Online): ISSN 2503-4588
No. 23/E/KPT/2019

Article

In silico and In vitro Study of The Anticancer Potential of Essential Oil from Sembung (*Blumea balsamifera*) Leaves against HeLa Cervical Cancer Cells

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Abstract

Blumea balsamifera (L.) DC. (sembung) is a medicinal plant widely recognized for its diverse pharmacological properties, including cytotoxic and anticancer activities. However, the anticancer potential of its leaf essential oil against cervical cancer remains poorly explored. This study aimed to evaluate the anticancer activity of *B. balsamifera* leaf essential oil against HeLa cervical cancer cells using integrated in silico and in vitro approaches. Molecular docking analysis against the anti-apoptotic Bcl-2 protein revealed favorable binding affinities for several major constituents, including camphor (-5.745 kcal/mol), caryophyllene (-7.077 kcal/mol), 7-epi-silphiperfol-5-ene (-7.311 kcal/mol), and γ-eudesmol (-7.083 kcal/mol), indicating potential interactions with apoptosis-related targets. Furthermore, cytotoxic activity assessed by the MTT assay demonstrated an IC_{50} value of 32.90 µg/mL against HeLa cells, indicating moderate cytotoxic potency. These findings suggest that *B. balsamifera* leaf essential oil possesses promising anti-cervical cancer activity and may serve as a potential natural source for the development of apoptosis-targeting anticancer agents.

Keywords: *Anticancer; Blumea balsamifera; molecular docking; MTT assay*

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DOI: https://doi.org/10.22437/chp.v10i1.49160
Received October 10th 2025; **Accepted** June 08th 2026; **Available online** June 30th 2026
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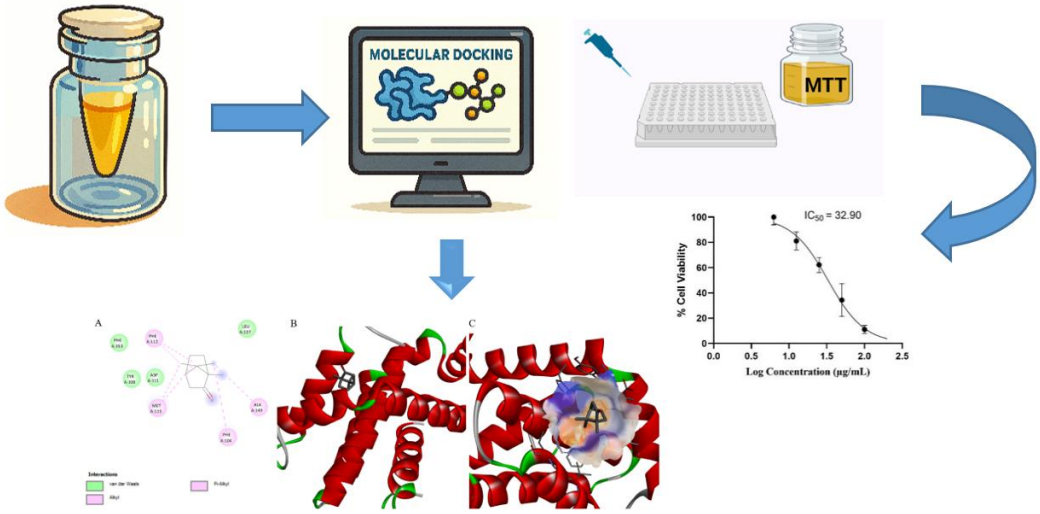
Graphical Abstract



Introduction

The medicinal plant *Blumea balsamifera* (L.) DC., commonly known as sembung, is a widely distributed shrub in Southeast Asia and has long been utilized in traditional medicine for the treatment of various ailments, including fever, wounds, hemorrhoids, diarrhea, diabetes, and cancer-related conditions [1]. Phytochemical investigations have revealed that *B. balsamifera* contains diverse bioactive constituents, such as flavonoids, terpenoids, phenolic compounds, and essential oils, which contribute to its broad pharmacological activities. Previous studies have demonstrated that extracts and fractions of sembung leaves possess significant biological properties, including antioxidant, anti-inflammatory, antimicrobial, and cytotoxic activities. Notably, several reports have shown cytotoxic and antiproliferative effects against different cancer cell lines, including A549 lung cancer cells, HL-60 leukemia cells, and HepG2 hepatocellular carcinoma cells [2][3][4]. These findings highlight the potential of *B. balsamifera* as a promising source of anticancer agents and warrant further investigation into its efficacy against other clinically relevant malignancies.

Cervical cancer remains a major global health burden and is one of the leading causes of cancer-related mortality among women, particularly in low- and middle-income countries. According to the Global Cancer Observatory (GLOBOCAN) 2022, cervical cancer accounted for 662,301 new cases and 348,874 deaths worldwide, ranking among the most prevalent cancers affecting women. In Indonesia, cervical cancer is the third most frequently diagnosed cancer, with 36,633 new cases reported in 2022 [5]. Despite advances in surgery, radiotherapy, chemotherapy, and targeted therapies, treatment outcomes remain limited by adverse side effects, drug resistance, tumor recurrence, and high treatment costs. Consequently, the identification of novel, effective, and safer anticancer compounds from natural resources has become an important area of research in cancer drug discovery.

Among the various bioactive fractions of *B. balsamifera*, essential oil represents a particularly attractive source of pharmacologically active compounds due to

its richness in volatile terpenoids and oxygenated derivatives, many of which have demonstrated anticancer properties. However, current knowledge regarding the anticancer potential of *B. balsamifera* essential oil remains limited. Most previous studies have focused on crude extracts or solvent fractions and have primarily evaluated their activity against non-cervical cancer models. To the best of our knowledge, comprehensive investigations combining molecular docking and experimental cytotoxicity assessments of sembung leaf essential oil against cervical cancer cells are still scarce. This knowledge gap limits our understanding of the molecular mechanisms underlying its potential anticancer effects.

The B-cell lymphoma-2 (Bcl-2) protein was selected as the molecular target in this study because it plays a critical role in regulating apoptosis and is frequently overexpressed in cervical cancer cells, including HeLa cells [6][7]. Overexpression of Bcl-2 contributes to cancer cell survival by suppressing programmed cell death, thereby promoting tumor progression and resistance to anticancer therapy. Inhibition of Bcl-2 has therefore emerged as an attractive therapeutic strategy for inducing apoptosis in cervical cancer cells. Accordingly, evaluating the interaction of essential oil constituents with Bcl-2 may provide valuable insights into their potential mechanism of action as anticancer agents.

Therefore, this study aimed to investigate the anticancer potential of *B. balsamifera* leaf essential oil against cervical cancer through an integrated in silico and in vitro approach. Molecular docking was employed to predict the binding affinity and interaction patterns of major essential oil constituents toward the Bcl-2 protein, while cytotoxic activity was evaluated using the MTT assay on HeLa cervical cancer cells. The findings of this study are expected to provide scientific evidence supporting the development of *B. balsamifera* essential oil as a potential natural source of anti-cervical cancer agents and contribute to the discovery of novel apoptosis-targeting therapeutics.

Materials and Methods

Materials, Apparatus, and Software

The materials used in this study included: essential oil from sembung leaves (*Blumea balsamifera*), cervical cancer cells (HeLa), DMEM (Gibco, 2323000), fetal bovine serum/FBS (Gibco, 2445956RP), antibiotic and antimycotic/ABAM (Gibco, 2321098), phosphate buffer saline (PBS), and trypsin (Gibco, 2391466). The equipment used included: Biosafety Cabinet (Thermo Scientific 1300 Series A2 Class II), CO2 Incubator (ARA P170), 96 well plate (TPP, 92696), Centrifuge Tube (SPL, 61015), Haemocytometer, Inverted Microscope (EVOS, AMEX1000), Plate reader (iMax Biorad). The software used included: GraphPad Prism 10, AutoDock Vina Tools-1.5.7, PyMOL 3.1.6.1, and BOVIA Discovery Studio 2022.

Molecular docking of major compounds against Bcl-2

In molecular docking analysis, the major compounds Camphor, Caryophyllene, 7-epi-Silphiperfol-5-ene, and Gamma-Eudesmol (obtained from GC-MS analysis of sembung leaf essential oil in the author's preliminary study) were used as ligands. Venetoclax (ABT-199), a clinically approved Bcl-2 inhibitor, was used as the positive control ligand. The Bcl-2 protein with PDB codes 6QGK was used as the receptor. The docking process was performed using AutoDock Vina Tools, PyMOL, and BIOVIA Discovery Studio software. The three-

dimensional structure of the protein was obtained from the Research Collaboratory for Structural Bioinformatics (RCSB) Protein Data Bank (https://www.rcsb.org/), while the ligand structure was downloaded from PubChem(https://pubchem.ncbi.nlm.nih.gov/). Receptor preparation was performed with PyMOL by removing water molecules and non-essential residues and separating the native ligand from the receptor. Next, polar hydrogen atoms were added, and the docking process was performed in AutoDock Vina Tools. The interaction results were visualised in two and three dimensions using BIOVIA Discovery Studio. The docking protocol was validated by redocking the native ligand, and the Root Mean Square Deviation (RMSD) was calculated.

The anticancer potential of essential oil from sembung leaves against cervical cancer cells

Essential oil samples were dissolved in DMSO to obtain a stock solution of 1000 µg/mL, then diluted with DMEM medium to obtain test concentrations of 200, 100, 50, 25, 12.5 and 6.25 µg/mL, with the final DMSO concentration kept below 1% (v/v) to avoid cytotoxic effects. HeLa cancer cells were grown in complete medium (DMEM + 10% FBS + 1% antibiotic-antimycotic) and incubated at 37 °C, 95% humidity, and 5% CO_2 until they reached a confluence of ≥ 80%. Confluent cells were harvested, suspended, and seeded in a 96-well plate for 24 hours. After adding 20 µL of the test solution, the culture was incubated for an additional 48 hours. The medium was then discarded, and the cells were washed with 100 µL of PBS. This was followed by the addition of MTT reagent (0.5 mg/mL) and incubation for 4 hours. The formazan crystals formed were dissolved with 100 µL of DMSO, then the absorbance was measured at 570 nm using a microplate reader. The percentage of cell viability was calculated based on the absorbance value, and the IC_{50} value was determined using GraphPad Prism. All experiments were performed in quadruplicate, and the results are presented as mean ± standard deviation (SD). Untreated cells were used as the growth control, while wells without cells were used as the negative control (blank). No standard anticancer drug was included as a positive control in this study.

Results and Discussions

Molecular Docking Analysis against BCL-2 Protein

Molecular docking testing is an in silico method used to predict the cytotoxic activity potential of the major compound (Table 1) in sembung leaves essential oil against cervical cancer cells. The receptor selected was the Bcl-2 protein, because this protein plays an essential role in inhibiting programmed cell death (apoptosis). Overexpression of the Bcl-2 protein results in a decrease in the ability of cells to undergo apoptosis, allowing abnormal cells to survive and potentially accelerating the progression of precancerous lesions to invasive cervical cancer. In addition, Bcl-2 overexpression has been reported in cervical cancer cells, including HeLa cells, where it contributes to apoptosis resistance, making it a relevant molecular target for anticancer studies [8][9][10].

Table 1. Major constituents of *Blumea balsamifera* leaf essential oil identified by GC–MS.

No	Retention Time	Compound	Area (%)
1	14.766	Camphor	32.56
2	22.829	Caryophyllen	17.04
3	20.674	7-epi-Silphiperfol-5-ene	5.33
4	28.246	Gamma-Eudesmol	5.01

The Bcl-2 protein structures used in this study was obtained from the Protein Data Bank (PDB ID: 6QGK). This structure was selected due to its X-ray diffraction resolution of ≤2.5 Å, which indicates a high level of accuracy in the atomic position and active site conformation of the protein. This value has a direct impact on the accuracy of ligand-receptor interaction predictions, so that the docking results obtained can be considered reliable for in silico analysis [11]. The docking protocol was validated by redocking the native ligand (J1Q) into the Bcl-2 receptor (PDB ID: 6QGK), resulting in an RMSD value of 0.611 Å, indicating acceptable docking accuracy because the RMSD value was below 2.0 Å. The grid box parameters for the Bcl-2 receptor (PDB ID: 6QGK) were defined with center coordinates of x = 1.861, y = 0.439, and z = 19.153, and a grid size of 16 × 16 × 16 Å.

Table 2 presents the molecular docking results of the major compounds in essential oils. The binding affinity values indicate the strength of interaction between ligands and target proteins, where more negative values correspond to more stable ligand–protein complexes [12]. In general, binding affinity values around −5 kcal/mol are often considered to indicate relatively weak interactions, whereas values lower than −7 kcal/mol may suggest stronger interactions. These classifications are based on previously reported literature and should be interpreted cautiously, as binding affinity alone does not fully represent biological activity [13,14].

Table 2 Molecular docking results of the major compound in essential oils

Ligands	PDB ID	Binding Affinity (kcal/mol)
Camphor	6QGK	-5.745
Caryophyllene	6QGK	-7.077
7-epi-Silphiperfol-5-ene	6QGK	-7.311
Gamma-Eudesmol	6QGK	-7.083
Venetoclax	6QGK	-10.76

As a comparison, Venetoclax, a clinically approved Bcl-2 inhibitor used as a positive control ligand, showed a binding affinity value of −10.76 kcal/mol, indicating a very strong interaction with the Bcl-2 protein. Although the binding affinity values of the major compounds from sembung leaf essential oil were lower than that of Venetoclax, but caryophyllene, 7-epi-silphiperfol-5-ene, and γ-eudesmol still showed relatively strong interactions, with binding affinity values of −7.077, −7.311, and −7.083 kcal/mol, respectively. Meanwhile, camphor exhibited a binding affinity value of -5.745 kcal/mol, which may be classified as a moderate interaction.

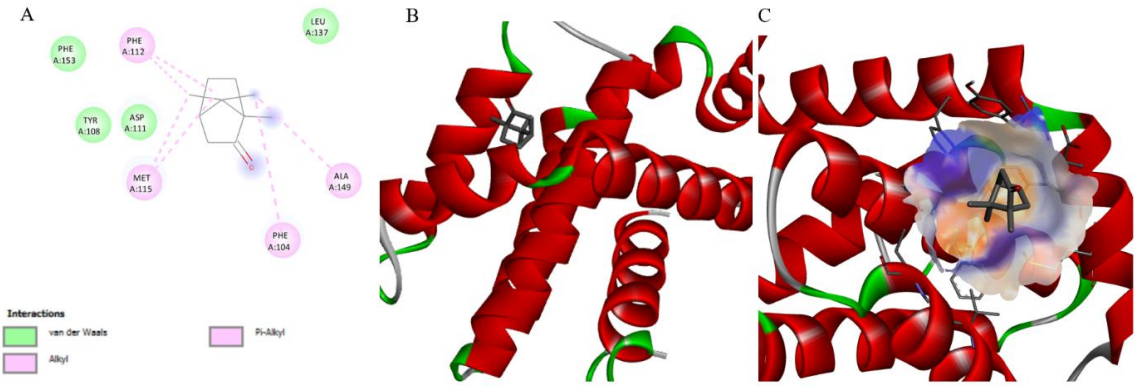


Figure 1. Interaction of camphor ligand with 6QGK receptor (A) 2D Interaction Diagram (B) 3D ligand-receptor complex (C) View of binding pocket surface

Figure 1 shows the results of the interaction between the caryophyllene ligand and the Bcl-2 receptor (PDB ID: 6QGK). The 2D interaction diagram shows alkyl and π–alkyl interactions (light purple) with residues Met115, Ala149, Phe104, and Phe112. In addition, van der Waals interactions (green) were observed with residues Asp111, Tyr108, Phe153, and Leu137. The 3D ligand–receptor complex shows that the ligand is positioned within the binding pocket surrounded by α-helical structures (red) and loop regions (green and gray). The surface view indicates that the ligand occupies a hydrophobic binding pocket, which may contribute to the stability of the caryophyllene–6QGK complex and support the binding affinity obtained from the docking results.

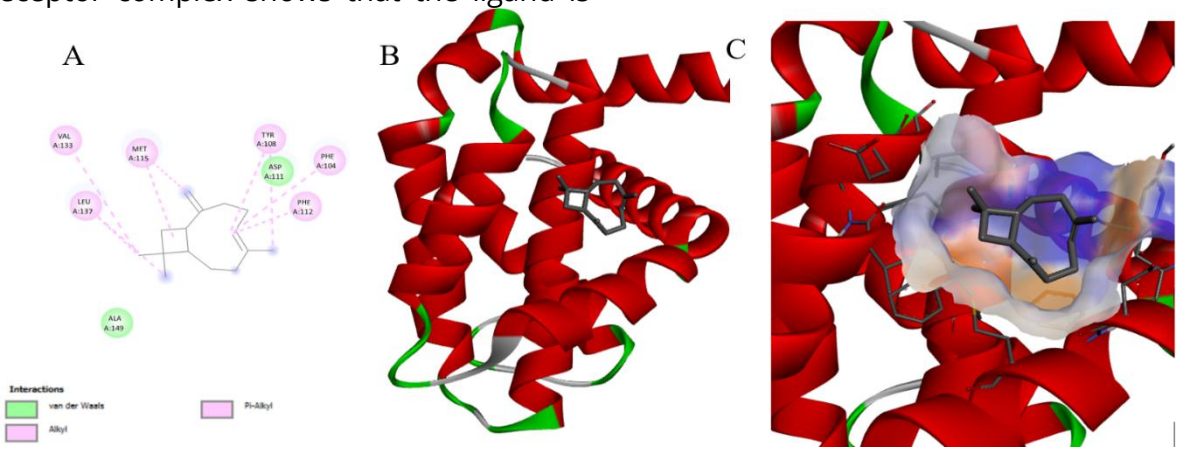


Figure 2. Interaction of the caryophyllene ligand with the 6QGK receptor (A) 2D interaction diagram (B) 3D ligand-receptor complex (C) View of the binding pocket surface

Figure 2 shows the interaction of the caryophyllene compound with the Bcl-2 receptor (PDB ID: 6QGK). The ligand interacts via π–alkyl forces (light purple) with residues Phe104, Tyr108, Phe112, Met115, Val133, and Leu137, as well as van der Waals forces (green) with residues Asp111 and Ala149. The ligand appears to be stably oriented within the hydrophobic pocket, which plays a crucial role in maintaining the caryophyllene-6QGK complex and enhancing the binding affinity, as indicated by the docking results.

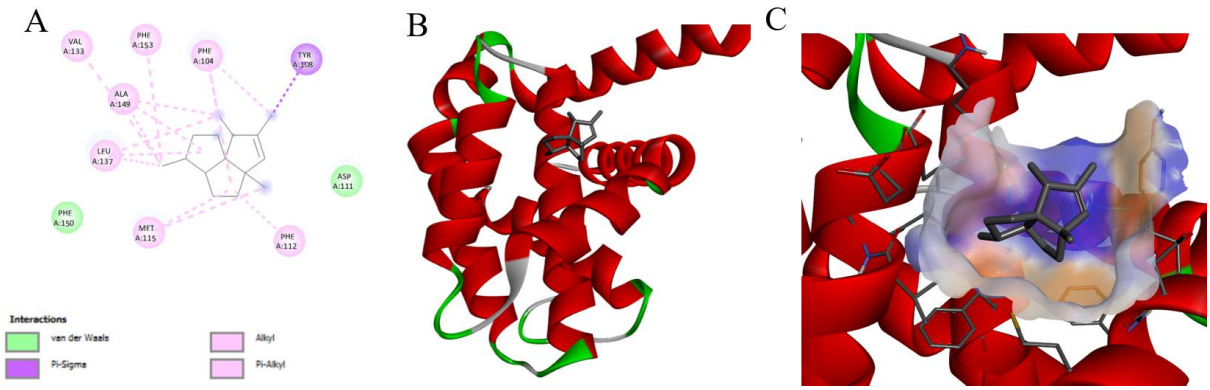


Figure 3. Interaction of the 7-epi-Silphiperfol-5-ene ligand with the 6QGK receptor (A) 2D Interaction Diagram (B) 3D ligand-receptor complex (C) View of the binding pocket surface

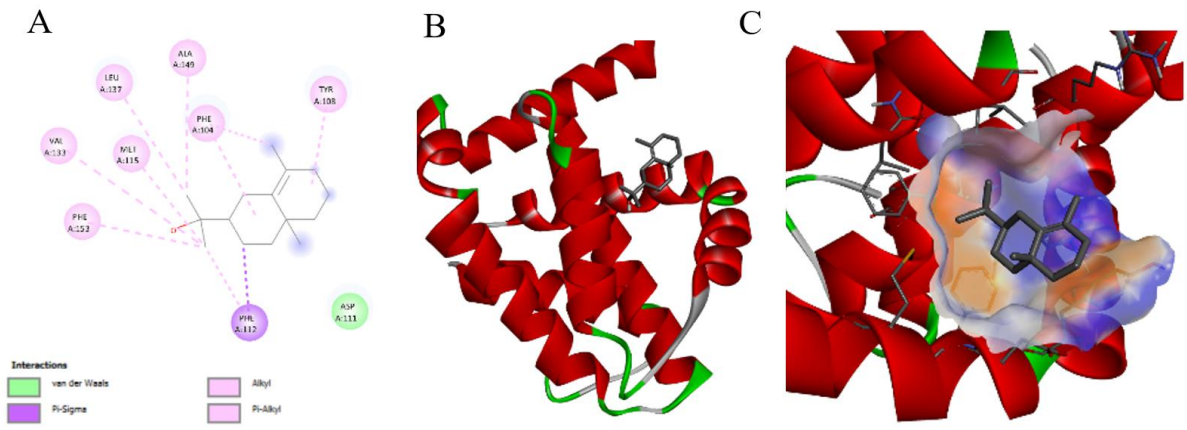


Figure 4. Interaction of the Gamma-Eudesmol ligand with the 6QGK receptor (A) 2D Interaction Diagram (B) 3D Ligand-Receptor Complex (C) View of the binding pocket surface

Figure 3 shows the interaction of the 7-epi-Silphiperfol-5-ene ligand compound with the Bcl-2 receptor (PDB ID: 6QGK) through van der Waals bonds (green) with residues Asp111 and Phe150, as well as π–sigma interactions (dark purple), alkyl, and π–alkyl (light purple) interactions with residues Met115, Leu137, Ala149, Val133, Phe112, Phe104, Phe153, and Tyr108. These interactions suggest that the stability of the 7-epi-Silphiperfol-5-ene–hydrophobic interactions primarily support the 6QGK complex, while the other residues contribute through weak nonpolar interactions.

Figure 4 shows the interaction of the γ-eudesmol compound with the Bcl-2 receptor (PDB ID: 6QGK). The ligand interacts via π–sigma forces (dark purple) with residue Phe112, as well as π–alkyl forces (light purple) with Phe104, Tyr108, Met115, Val133, Leu137, Ala149, and Phe153. In addition, there is a van der Waals interaction (green) with Asp111. This combination of hydrophobic interactions plays an important role in maintaining the stability and binding affinity of the complex.

Based on the results of molecular docking tests on the major compound of sembung leaves, which were reviewed in terms of RMSD values, binding affinity energy, and the types of interactions formed between ligands and amino acid residues such as π–sigma, π–alkyl, and van der Waals, it was found that sembung plants may have potential as anticancer agents, particularly for cervical cancer. Therefore, further in vitro research using the MTT assay method is required to validate these findings.

The anticancer potential of essential oil from Sembung Leaves against Cervical Cancer Cells

Anticancer testing was conducted using the MTT (Microculture Tetrazolium Test) method, which aims to determine the ability of essential oils to inhibit cell growth. This test is based on cell viability percentage and the determination of the IC_{50} value. The cell viability percentage at a given sample absorbance value determines the IC_{50} value. The sample absorbance values from various concentrations can be used to calculate the cell viability percentage, which represents the number of cells that survive after exposure to a test sample. The test results are shown in Figure 5.

Figure 5a shows that the absorbance value decreases with increasing concentration. This indicates that higher concentrations

contain greater amounts of active compounds in the sample, which may inhibit cell growth. A similar trend is observed in Figure 5b, where cell viability decreases as the concentration increases. The decrease in absorbance and cell viability is associated with reduced activity of succinate dehydrogenase, which catalyses the reduction of tetrazolium salt to formazan crystals, as cell viability decreases at higher concentrations.

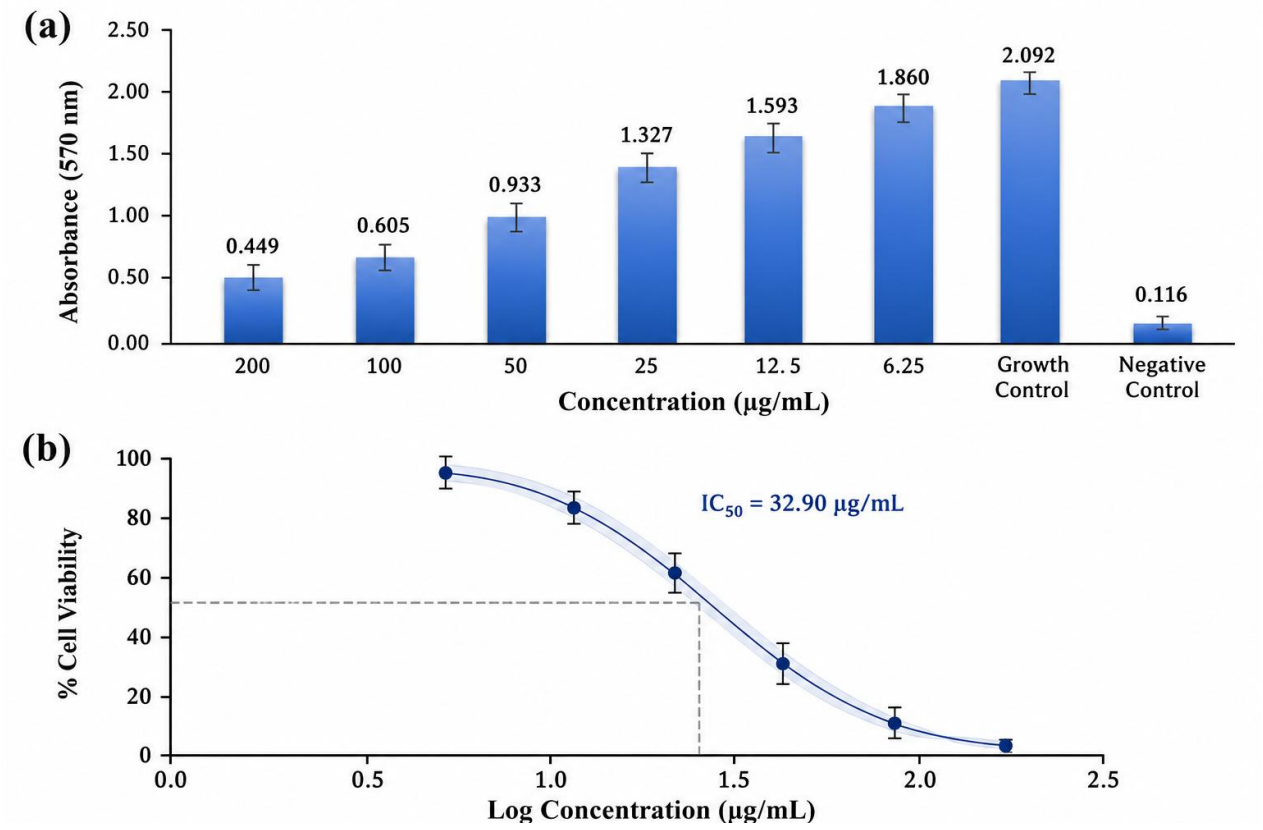


Figure 5. MTT assay results of *Blumea balsamifera* leaf essential oil on HeLa cervical cancer cells. (a) Absorbance at 570 nm after treatment with different concentrations. (b) Dose–response curve showing cell viability (%) versus log concentration, yielding an IC_{50} value of 32.90 µg/mL.

Figure 5b shows that at the highest concentration (200 µg/mL), cell viability was 16.86%, indicating that cell growth was not completely inhibited at this concentration. Meanwhile, at the lowest concentration (6.25 µg/mL), the cell viability percentage was 88.25%, indicating that cell growth was inhibited by approximately 12% at this concentration. The test results showed that the essential oil exhibited cytotoxic activity, with an IC_{50} value of 32.90 µg/mL, which may be classified as moderate cytotoxic activity based on the National Cancer Institute (NCI) criteria, where IC_{50} values between 20–100 µg/mL are considered moderate [15][16]. This IC_{50} value indicates that the essential oil has potential cytotoxic activity against HeLa cervical cancer cells.

However, the absence of a standard anticancer drug (e.g., doxorubicin) as a positive control represents a limitation of this study and should be considered in interpreting the cytotoxicity results. The molecular docking results suggest that the major compounds of sembung leaf

essential oil may interact with the Bcl-2 protein. However, the relationship between Bcl-2 binding affinity and the observed cytotoxic activity in the MTT assay has not been experimentally confirmed in this study and requires further investigation. Nevertheless, the observed cytotoxic activity, together with the molecular docking results, suggests that the essential oil has potential biological activity against the Bcl-2 target. Further studies using standard anticancer agents and mechanistic analysis are recommended to strengthen these findings.

This cytotoxic ability is attributed to the active compounds in sembung leaves essential oil, which are primarily terpenoid compounds. Terpenoid compounds have been widely reported to exhibit cytotoxic and pharmacological bioactivity, such as anticancer [17][18]. Additionally, compounds in essential oils have been reported to inhibit cancer cell growth by inducing apoptosis and increasing oxidative stress, as reported in previous studies. This mechanism is suggested to contribute to cancer cell damage [19][20][21]. However, these proposed mechanisms have not been experimentally confirmed in this study and are presented based on previously reported findings, while further studies are needed to validate these mechanisms.

Conclusions

The results of this study suggest that sembung leaf essential oil has potential anticancer activity against HeLa cervical cancer cells based on molecular docking and MTT assay results. Caryophyllene, 7-epi-silphiperfol-5-ene, and γ-eudesmol showed relatively strong interactions with the Bcl-2 protein, while the essential oil exhibited moderate cytotoxic activity with an IC_{50} value of 32.90 µg/mL. However, further studies are needed to confirm the proposed anticancer mechanism.

Acknowledgement

This study was conducted as a part of the research activities supported by the Directorate of Research, Technology, and Community Service (DRTPM), Ministry of Education, Culture, Research, and Technology of the Republic of Indonesia, under the Penelitian Dosen Pemula (2025) scheme. The authors also acknowledge the support and facilitation provided by the Institute for Research and Community Service (LPPM), Universitas Teknologi Nusantara.

Author Contributions

Conceptualization, Rahmi Vika Ulia and Toto Raharto; Methodology, Rahmi Vika Ulia; Software, Toto Raharto and Yoan De Nanda Herru; Validation, Rahmi Vika Ulia, Suryati, and Adlis Santoni; Formal Analysis, Toto Raharto; Investigation, Rahmi Vika Ulia, Toto Raharto, Suryati, Adlis Santoni, and Yoan De Nanda Herru; Resources, Rahmi Vika Ulia and Toto Raharto; Data Curation, Yoan De Nanda Herru; Writing – Original Draft Preparation, Rahmi Vika Ulia; Writing – Review & Editing, Suryati; Visualization, Adlis Santoni; Supervision, Rahmi Vika Ulia; Project Administration, Toto Raharto; Funding Acquisition, Rahmi Vika Ulia.

Conflict of Interest

The authors declare no conflict of interest.

References

[1]. Widhiantara, G., and Jawi, I.M. Phytochemical composition and health properties of Sembung plant (*Blumea balsamifera*): A review. *Veterinary World.* 2021, 14(5), 1185–1196. DOI: 10.14202/vetworld.2021.1185-1196.

[2]. Norikura, T., Kojima-Yuasa, A., Shimizu, M., Huang, X., Xu, S., Kametani, S., Rho, S.-N.,

Kennedy, D. O., and Matsui-Yuasa, I. Anticancer activities and mechanisms of *Blumea balsamifera* extract in hepatocellular carcinoma cells. *The American Journal of Chinese Medicine.* 2008, 36(2), 411-424). DOI: 10.1142/S0192415X08005862.

[3]. Ismail, N. A., Matawali, A., Lee, P.-C., How, S.-E., Lee, B. H., Goh, L. P. W., and Gansau, J. A. *Blumea balsamifera* (L.) DC. Elicit Anti-Kinase, Anti-Phosphatase and Cytotoxic Activities against Acute Promyelocytic Leukemia Cells (HL-60). *Tropical Journal of Natural Product Research*. 2023, 5(4), 656-660. DOI: 10.26538/tjnpr/v5i5.8.

[4]. Nurlailiyah, F. A., Dwijayanti, D. R., Hermanto, F. E., Masruri, M., and Widodo, N. Cytotoxicity of *Blumea balsamifera* on A549 Lung Cancer Cells : Integrating in Vitro Analysis with Computational Study of AKT-1 Inhibition. *Tropical Journal of Natural Product Research*. 2025, 9(2), 495–503. DOI: 10.26538/tjnpr/v9i2.12.

[5]. World Health Organization. Global Cancer Observatory. 2022.

[6]. Permatasari, H. K., Wewengkang, D. S., Tertiana, N. I., Muslim, F. Z., Yusuf, M., Baliulina, S. O., Daud, V. P. A., Setiawan, A. A., and Nurkolis, F. Anti-cancer properties of Caulerpa racemosa by altering expression of Bcl-2, BAX, cleaved caspase 3 and apoptosis in HeLa cancer cell culture. *Frontiers in Oncology*. 2022, 12, 964816. DOI: 10.3389/fonc.2022.964816.

[7]. Leisching, G., Loos, B., Botha, M., and Engelbrecht, A.-M. Bcl-2 confers survival in cisplatin treated cervical cancer cells: Circumventing cisplatin dose-dependent toxicity and resistance. *Journal of Translational Medicine*. 2015, 13(1), 328. DOI: 10.1186/s12967-015-0689-4

[8]. Yumol, J., Gabrielli, B., Tayyar, Y., McMillan, N. A., and Idris, A. Smart drug combinations for cervical cancer: Dual targeting of Bcl-2 family of proteins and aurora kinases. *American Journal of Cancer Research*. 2020, 10(10), 3406–3414. PMID: 33163279

[9]. Abdul Rahman, S. F., Muniandy, K., Soo, Y. K., Hamdan, M. A., Shunmugam, L., and Idris, A. Co-inhibition of BCL-XL and MCL-1 with selective BCL-2 family inhibitors enhances cytotoxicity of cervical cancer cell lines. *Biochemistry and Biophysics Reports*. 2020, 22, 100756. DOI: 10.1016/j.bbrep.2020.100756.

[10]. Tuohetimulati, G., Zhu, M., Chen, J., and Niyazi, M. Expressions and clinical significance of Bcl-2, Bcl-xL and c-IAP1 protein in cervical cancer. *International Journal of Clinical and Experimental Medicine*. 2018, 11(11), 12361–12367.

[11]. Ferreira de Freitas, R., and Schapira, M. A systematic analysis of atomic protein–ligand interactions in the PDB. *Medicinal Chemistry Communications*. 2017, 8(10), 1970–1981. DOI: 10.1039/C7MD00381A.

[12]. Ramírez, D., and Caballero, J. Is It Reliable to Take the Molecular Docking Top Scoring Position as the Best Solution without Considering Available Structural Data?. *Molecules.* 2018, 23(5), 1038. DOI: 10.3390/molecules23051038.

[13]. Sharma, A., Vora, J., Patel, D., Sinha, S., Jha, P. C., and Shrivastava, N. Identification of natural inhibitors against prime targets of SARS-CoV-2 using molecular docking, molecular dynamics simulation and MM-PBSA approaches. *Journal of Biomolecular Structure and Dynamics*. 2022, 40(7), 3296–3311. DOI: 10.1080/07391102.2020.1846624.

[14]. Ivanova, L., and Karelson, M. The Impact of Software Used and the Type of Target Protein on Molecular Docking Accuracy. *Molecules*. 2022, 27(24), 9041. DOI: 10.3390/molecules27249041.

[15]. Niksic, H., Becic, F., Koric, E., Gusic, I., Omeragic, E., Muratovic, S., Miladinovic, B., and Duric, K. Cytotoxicity screening of *Thymus vulgaris* L. essential oil in brine shrimp nauplii and cancer cell lines. *Scientific Reports*. 2021, 11(1), 13178. DOI: 10.1038/s41598-021-92679-x.

[16]. Zulkipli, N. N., Rahman, S. A., Taib, W. R. W., Razali, R. M., Ismail, I., Ahmad, W. A. N. W., and Daud, C. K. D. C. The cytotoxicity effect and identification of bioactive compounds of *Prismatomeris glabra* crude leaf extracts against breast cancer cells. *Beni-Suef University Journal of Basic and Applied Sciences*. 2024, 13(1), 33. DOI:

10.1186/s43088-024-00490-0.

[17]. Kamran, S., Sinniah, A., Abdulghani, M. A. M., and Alshawsh, M. A. Therapeutic Potential of Certain Terpenoids as Anticancer Agents: A Scoping Review. *Cancers*. 2022, 14(5), 1100. DOI: 10.3390/cancers14051100.

[18]. Wu, Z. L., Li, N., Huang, J. L., Sang, H. Y., and Chen, X. Essential oil and its major compounds from oil camphor inhibit human lung and breast cancer cell growth by cell-cycle arresting. *International Journal of Clinical and Experimental Medicine*. 2016, 9(7), 12852–12861.

[19]. Madrid, A., Silva, V., Russo, A., Moller, A. C., Sánchez, E., Villena, J., Jara-Gutiérrez, C., and Montenegro, I. Selective cytotoxicity of Gomortega keule essential oil through a ROS-mediated pro-apoptotic mechanism. *Frontiers in Pharmacology*. 2025, 16, 1722619. DOI: 10.3389/fphar.2025.1722619.

[20]. Abdoul-Latif, F. M., Ainane, A., Aboubaker, I. H., Mohamed, J., and Ainane, T. Exploring the Potent Anticancer Activity of Essential Oils and Their Bioactive Compounds: Mechanisms and Prospects for Future Cancer Therapy. *Pharmaceuticals*. 2023, 16(8), 1086. DOI: 10.3390/ph16081086.

[21]. Bayala, B., Bassole, I. H. N., Scifo, R., Gnoula, C., Morel, L., Lobaccaro, J. M. A., Simpore, J., and Fancellu, A. Anticancer activity of essential oils and their chemical components – a review. *American Journal of Cancer Research*. 2014, 4(6), 591–607. PMID: 25520854.