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Research Article

Potential of Active Compounds in Water Hyacinth Leaves (*Eichhornia crassipes*) as Candidates for Leukemia Drugs: An In silico Approach

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Abstract:
Introduction — Leukemia is a major hematological malignancy with high mortality, particularly in pediatric populations. Conventional chemotherapy is often associated with severe side effects, creating an urgent need for safer and more selective therapeutic alternatives. Computational drug discovery offers an efficient strategy to identify potential bioactive compounds from natural resources. This study investigates active compounds derived from water hyacinth leaves (*Eichhornia crassipes*) as potential leukemia drug candidates using an *in silico* molecular docking approach.
Methods — A computational workflow was applied, including literature-based compound identification, molecular structure retrieval and preparation, target protein selection, and molecular docking analysis. Fms-related tyrosine kinase 3 (FLT3) was selected as the target protein for acute leukemia, while transforming growth factor beta receptor (TGF-βR) was used for chronic leukemia. Docking simulations were conducted to evaluate binding affinities and binding site similarities between test compounds and reference inhibitors.
Results — Ethyl 9,12,15-octadecatrienoate demonstrated a favorable interaction with FLT3, with a binding affinity of −7.2 kcal/mol and a binding site similarity of 88.89%. For TGF-βR, stigmasterol, dibutyl phthalate, and phytol showed notable interactions, with binding affinities of −9.4, −7.2, and −7.1 kcal/mol, respectively, and binding similarity values ranging from 62.5% to 75%.
Conclusion — Several active compounds from water hyacinth leaves exhibit promising interactions with leukemia-associated target proteins. These findings highlight the potential of natural bioactive compounds as alternative leukemia drug candidates and confirm the usefulness of *in silico* approaches for early-stage drug discovery, although further experimental validation is required.

Keywords: leukemia; molecular docking; bioinformatics; FLT3; TGF-β receptor

1. Introduction

Cancer is one of the non-communicable diseases that currently poses a major health problem worldwide, including in Indonesia [1]. Cancer is characterized by abnormal or continuous cell growth

that is uncontrolled, causing damage to surrounding tissues and potentially leading to metastasis [2]. Leukemia is the most common type of cancer, accounting for 28% of all cancer cases in children, with a mortality rate of 5.5% (14,862 people) in Indonesia in 2018 [3]. Clinical symptoms observed in children with leukemia include persistent flu-like symptoms, pallor, fatigue, fever, anorexia, weight loss, petechiae, unexplained bruising, bone and joint pain, abdominal pain, lymphadenopathy, and hepatosplenomegaly [4], [5].

The most effective treatment for leukemia is chemotherapy. Chemotherapy is a systemic treatment that can damage normal tissues in a chronic manner [6], [7]. On the other hand, chemotherapy has side effects such as nausea and vomiting [8]. Nausea and vomiting also occur due to the use of cytostatic drugs and are among the initial side effects that occur within 1 to 24 hours after administration of cytostatic drugs, sometimes even more than 24 hours [9]. Chemotherapy causes chronic side effects such as nausea, vomiting, alopecia, bone marrow suppression, and delayed side effects that vary and include pulmonary fibrosis and neuropathy. In addition to chemotherapy, drugs that act as anticancer agents are also used [8], [10], [11].

Protein identification studies can serve as one approach to identify drug target proteins that align with the intended therapeutic goals. In molecular research and drug development, the identification of target proteins and the study of their mechanisms of action can be highly significant. In chronic leukemia, abnormalities in the expression or function of the TGF-β receptor lead to the loss of control over cell growth, thereby promoting leukemic cell proliferation and disease progression [12]. Furthermore, Fms-related tyrosine kinase 3 is an important tyrosine kinase receptor for hematopoietic cell proliferation, contributing to aggressiveness and poor prognosis in acute myeloid leukemia [13].

Water hyacinth (*Eichhornia Crassipes)* is a floating aquatic plant belonging to the Pontederiaceae family. This plant can be found in tropical and subtropical environments and has a rapid growth rate, easily spreading to cover water surfaces. Therefore, it is generally considered an invasive plant (weed) due to its ability to quickly cover water surfaces [14], [15]. However, behind this, water hyacinth possesses several advantages that have been studied in various research. Its ability to absorb organic and inorganic pollutants, as well as heavy metals, has often been tested for its role as a phytoremediator [16], [17]. Additionally, water hyacinth can be beneficial, particularly in the field of pharmacology. Water hyacinth leaves contain secondary metabolites that have an anticancer role [18]. By isolating an active compound from water hyacinth leaves for use in cancer and inflammation treatment, water hyacinth leaves can enhance their potential as traditional medicine and pharmaceutical development [19]. The active compounds in water hyacinth leaves known to have anticancer potential include Propiolic acid, Phytol, 2-(octadecyloxy) Ethanol, 2-bromooctadecanal, Dibutyl phthalate, Ethyl 9,12,15-octadecatrienoate, 9,12,15 Octadecatrienoic acid, Stigmasterol, Oleic acid, eicosyl ester, and 17-Pentatriacontene [20].

In silico testing is one of the studies that can predict the activity of a compound with potential as a drug and eliminate other compounds with low activity [21]. *In silico* testing has several advantages, including saving energy, time, and costs [22], [23]. Based on this, it is important to develop natural treatment innovations for leukemia patients through *in silico* testing by analyzing potential target proteins and plant compounds with anti-cancer potential. This study aims to describe the interaction between active compounds in water hyacinth leaves (*Eichhornia Crassipes*) and FLT3 and TGFβR proteins, which play a role in the mechanism of leukemia, through *in silico* analysis. It is hoped that this study can serve as a reference and recommendation for drug discovery efforts using natural active compounds from plants to address leukemia cases, potentially identifying candidate compounds for leukemia treatment.

2. Method

This study is a descriptive study using a computational approach (*in silico*). This descriptive method can be interpreted as a problem-solving procedure that is investigated through observation accompanied by recording what proteins are present and describing the state or behavior of the target object in the study based on apparent facts or what is actually observed. Data collection techniques used online web databases and literature studies of supporting data on the interaction between active compounds from water hyacinth leaves and target proteins from national and international journals. Data analysis techniques were performed using the PubChem web database (https://pubchem.ncbi.nlm.nih.gov/) [24], [25]. The first stage is to determine the content of active compounds in water hyacinth leaves (*Eichhornia Crassipes*) through literature studies based on Gas Chromatography-Mass Spectroscopy (GC-MS) test results [20]. A reference compound is also needed as a comparison for the binding formed by the active compounds in water hyacinth leaves. The reference compound used was pyrazole, which is known to play a role as an inhibitor in the anticancer mechanism [26].

The active compounds of water hyacinth leaves were minimized using the PyRx software [27]. The subsequent step involved analyzing and selecting receptors through the RCSB PDB website (https://www.rcsb.org/) [28]. The target proteins used were TGF-β receptor (PDB code: 3KCF) and Fms-related tyrosine kinase 3 (PDB code: 5X02). Both target proteins were then sterilized using AutoDock software. After the target receptor proteins were sterilized, the next step was molecular docking. Molecular docking is a computational procedure that can be used to predict chemical bonds between macromolecules (receptors) and small molecules (ligands) efficiently using their structures through molecular docking simulations [29]. The result of docking is the binding affinity value. The more negative the binding affinity value, the stronger the bond formed, and vice versa [30], [31]. After determining the binding affinity value, visualization was performed using PyMOL and Discovery Studio 2021 software to view the docking results in a representative manner [32], [33]. Based on the visualization results, the type of bond and the number of similarities in the attachment of amino acid residues formed between the active compounds of water hyacinth leaves and the reference compounds to the specific leukemia target protein were identified. This serves as a basis for understanding the relationship between the active compounds of water hyacinth leaves and a potential leukemia target protein, which is hoped to be used as a candidate drug for leukemia.

3. Results

The molecular docking process generates data on the binding affinity values and the location of the amino acid residue binding sites formed between the test compound and the target protein used. The results of the molecular docking data are presented in **Table 1**, while the visualization results of the molecular docking are shown in **Fig. 1** and **Fig. 2**.

Table 1. Results of molecular binding between *Eichhornia Crassipes* bioactive compounds and target proteins

Protein Name	PDB Code	Ligand	Binding Affinity (Kcal/mol)	Percentage of Similarity with Control (%)
FLT3	5X02	*Stigmasterol*	-10.2	66.67
		Pyrazole	-8.8	33.33
		Ethyl 9,12,15-	-7.2	88.89
		Octadecatrienoate		
		Phytol	-7.1	66.67
TGFβR1	3KCF	*Pyrazole*	-11.2	100
		Stigmasterol	-9.4	75

Protein Name	PDB Code	Ligand	Binding Affinity (Kcal/mol)	Percentage of Similarity with Control (%)
		Dibutyl phthalate	-7.2	62.5
		Phytol	-7.1	75

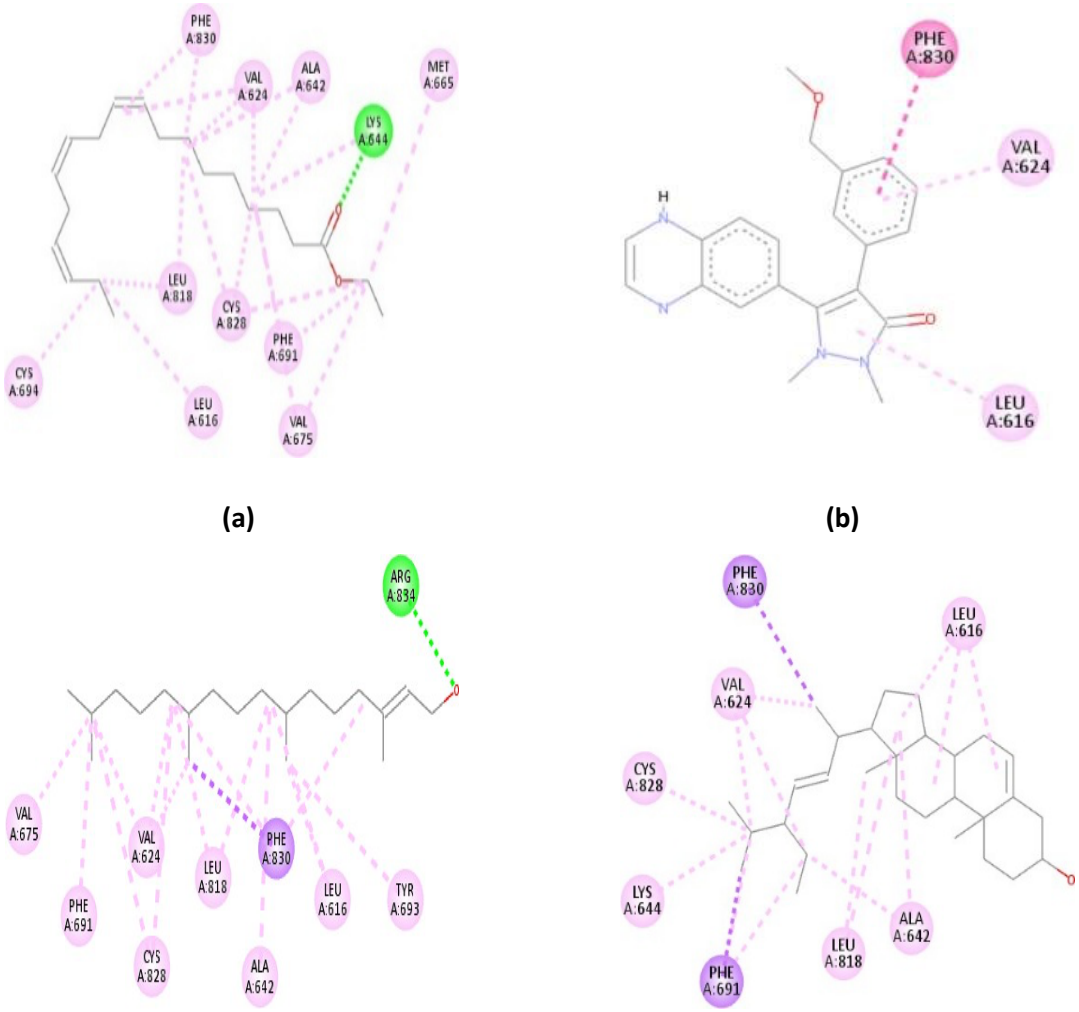


Figure 1. Visualization of the results of molecular binding between **(a)** Ethyl 9,12,15-octadecatrienoate, **(b)** Pyrazole, **(c)** Phytol, and **(d)** Stigmasterol with the target protein fms-related tyrosine kinase 3 (FLT3)

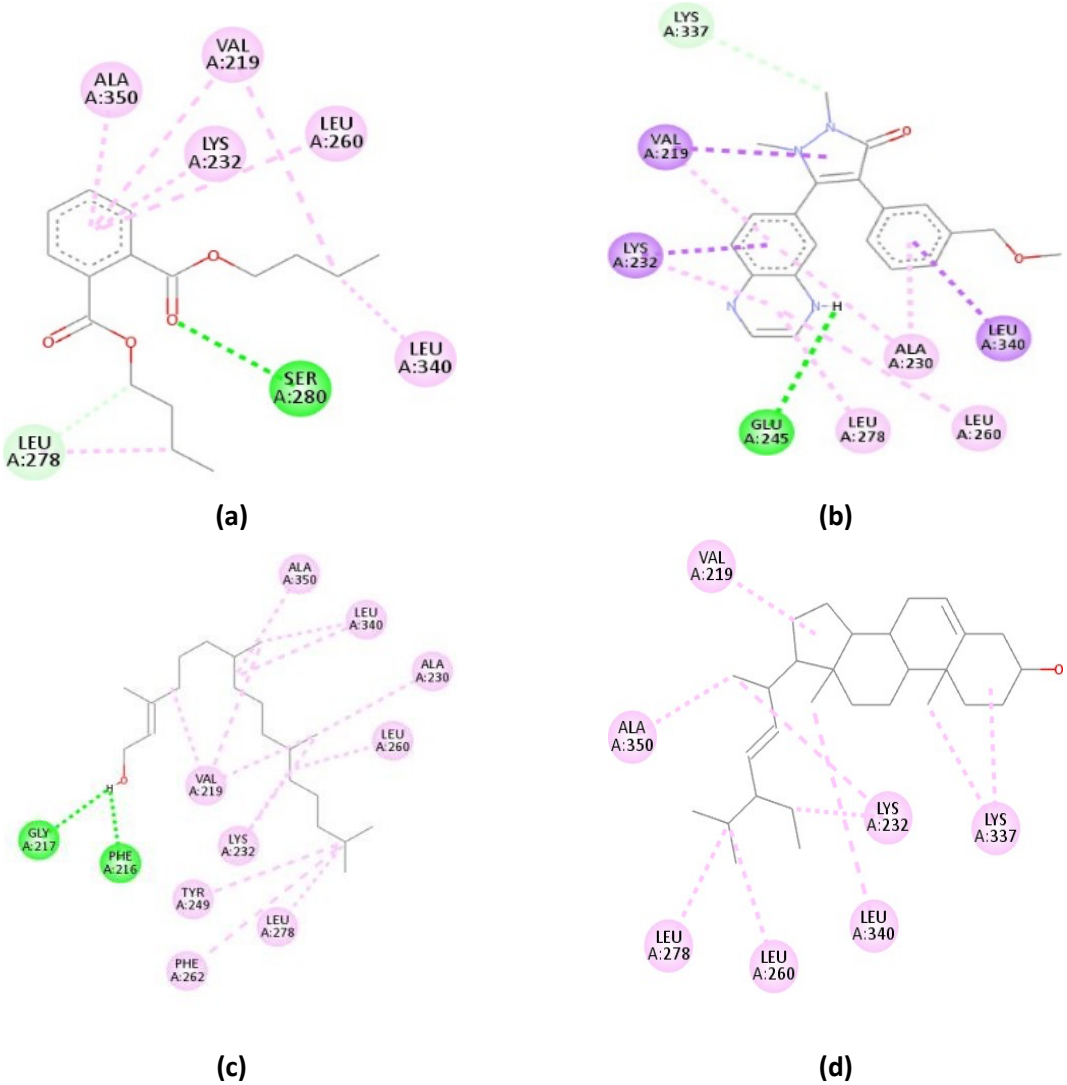
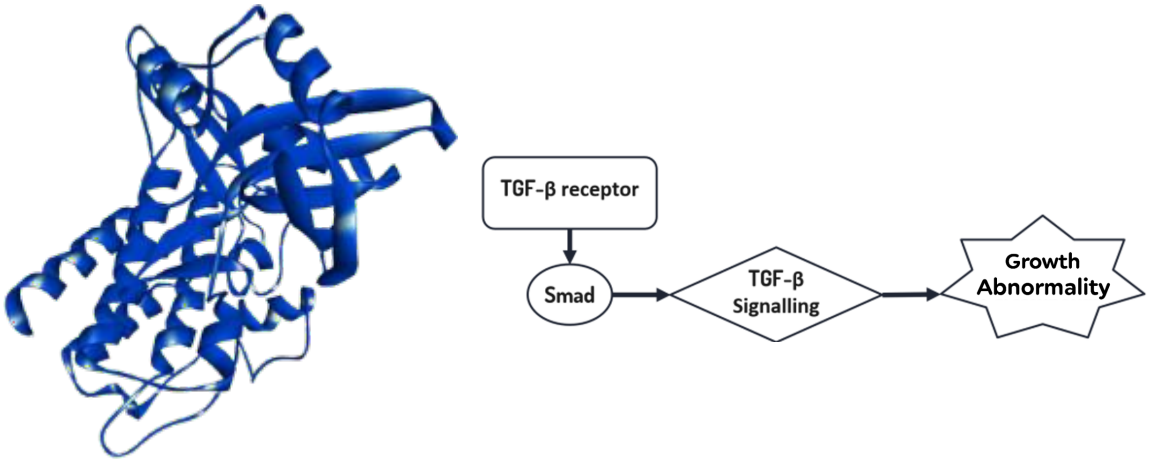


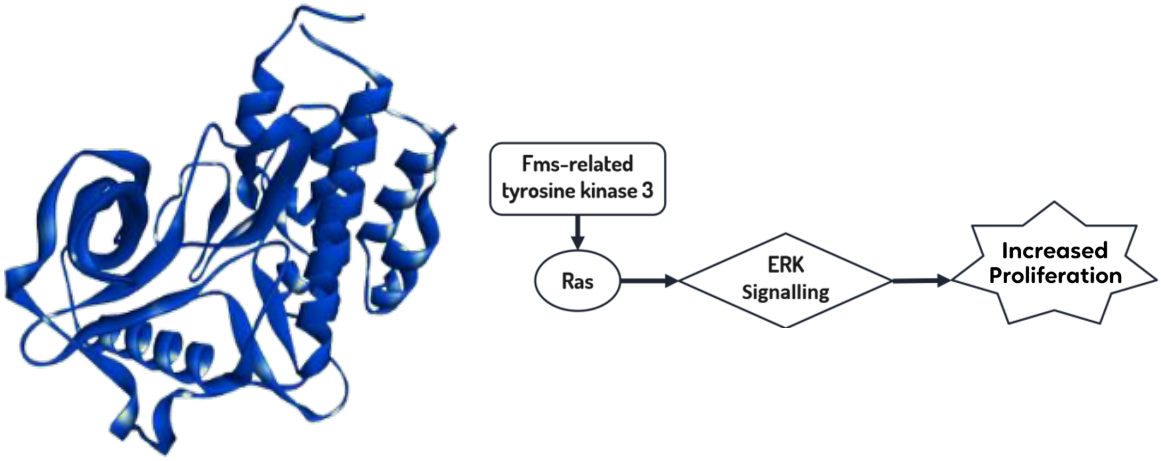
Figure 2. Visualization of the results of molecular binding between **(a)** Dibutyl phthalate, **(b)** Pyrazole, **(c)** Phytol, and **(d)** Stigmasterol with the target protein TGF-β receptor (TGFβR)

In the study of cell and molecular biology, all processes that occur in the body involve signaling and communication mechanisms. There are relay molecules and receptor proteins in the body that play a role during specific signaling and communication mechanisms. The role of these signaling molecules and receptor proteins is to transmit the signal message (signal transduction) they carry until the target cell or tissue can respond to the stimulus that has been received. The type of signaling molecule will vary depending on the response of the receptor protein that receives it. Every signal message received by a specific receptor protein is relayed by activating other relay molecules [9]. Functional proteins potentially involved in the development of leukemia include TGF-β receptor and Fms-related tyrosine kinase 3. These two types of proteins serve as target proteins for molecule binding. The TGF-β receptor (TGF-βR) plays a role in chronic leukemia, while the Fms-related tyrosine kinase 3 (FLT3) is involved in acute leukemia [13, 28]. Receptor protein pathway shown in **Fig. 3** and **Fig. 4**.



(a) **(b)**

Figure 3. (a) TGF-β receptor protein and **(b)** a simple diagram of the TGF-β receptor mechanism in the body.



(a) **(b)**

Figure 4. (a) Protein Fms-related tyrosine kinase 3 and **(b)** a simple diagram of the mechanism of Fms-related tyrosine kinase 3 in the body

4. Discussion

Based on the results of the binding assay of active compounds from water hyacinth leaves (*Eichhornia Crassipes*) against the target protein Fms-related Tyrosine Kinase 3 (FLT3), compared with reference compounds and control compounds presented in **Table 1**, three active compounds with the lowest binding affinity or most negative values were identified: stigmasterol, ethyl 9,12,15-octadecatrienoate, and phytol. The control compound used in the molecular binding of active compounds from water hyacinth leaves with the FLT3 protein was FF-10101, a synthetic inhibitor that covalently binds to the FLT3 protein in a selective manner. The binding characteristics of FF-10101 with FLT3 protein are characterized by binding to the cysteine residue at position 694 (CYS

694) while maintaining its ability to bind to FLT3 protein in both active and inactive conformations [34]. The reference compound used in the binding assay of the active compounds from water hyacinth leaves with FLT3 protein is pyrazole. On the other hand, the binding assay results of the active compounds from water hyacinth leaves against the target protein TGF-β receptor type-1 (TGFβR1) identified three active compounds with the lowest binding affinity or most negative values, namely stigmasterol, dibutyl phthalate, and phytol. The control compound and the reference compound used in the binding of active compounds from water hyacinth leaves to the TGFβR1 protein are pyrazole, which is a similar reference compound in the binding activity of active compounds from water hyacinth leaves with the FLT3 protein. Pyrazole, as a control compound, binds to the TGFβR1 protein through covalent bonds, primarily at the lysine residue at position 232 (LYS 232) [35].

Pyrazole is one of the drugs that acts as an inhibitor and can effectively bind to the target proteins FLT3 and TGFβR1. Zhao et al. [26] stated in their study that pyrazole can act as an antibacterial, anticancer, anti-inflammatory, antioxidant, anti-TB, antiviral, and antihyperglycemic agent. However, the use of this drug is still considered concerning due to the risk of causing other disease symptoms such as leukopenia and agranulocytosis. Pyrazole as an antitumor agent plays a role in inducing apoptosis of cancer cells as part of the cytotoxic response of cancer cells [36]. Based on **Table 1**, it is known that pyrazole has a binding affinity value of -8.8 kcal/mol with the FLT3 protein and -11.2 kcal/mol with the TGFβR1 protein.

When examined based on the results of molecular binding visualization, **Fig. 1b** shows the molecular binding between pyrazole and the FLT3 protein, with a residue binding similarity of 33.33% compared to the control, as indicated in **Table 1**. The molecular binding formed between pyrazole and the FLT3 protein includes LEU 616, VAL 624, and PHE 830. The similarity in the binding positions of these molecules is very low compared to the control. This indicates that although pyrazole has a relatively high binding affinity, the researchers suspect that pyrazole treatment may be less effective for patients with acute leukemia mediated by FLT3 protein activity, as the similarity in the binding positions of amino acid residues with the control is still considered very low. The visualization results of the molecular binding between pyrazole and TGFβR1 protein presented in **Fig. 2b** show that the similarity in the binding positions of amino acid residues with the control is 100% because the control compound used is similar to the pyrazole used as the reference compound. This similarity in usage is due to the function of pyrazole as an anticancer agent targeting apoptosis induction, which inhibits the response mechanism mediated by the TGFβR1 protein. Pyrazole induces apoptosis, thereby eliminating cells with abnormal growth [12, 13]. The binding sites of pyrazole with the TGFβR1 protein include VAL 219, ALA 230, LYS 232, GLU 245, LEU 260, LEU 278, LYS 337, and LEU 340. Therefore, researchers speculate that pyrazole treatment may be effective for patients with chronic leukemia because one of its activities is mediated by TGFβR1 protein activity.

Molecular docking tests with increasingly negative affinity values and the number of bound amino acid residues indicate that the active compounds tested have the same potential as the reference compounds in influencing the activity of the target protein [23]. The more negative the binding affinity value, the stronger the bond formed, and vice versa [31]. Additionally, the larger or closer the similarity in the binding site location of the active compound to the control compound, the more stable the compound is likely to be in binding and influencing the target protein activity. Stigmasterol is an active compound found in water hyacinth leaves and has the lowest binding affinity value among all active compounds in water hyacinth leaves when tested for docking with both FLT3 and TGFβR1 proteins. Based on **Table 1**, stigmasterol has a binding affinity value of -10.2 kcal/mol and a residue binding site similarity value of 66.67% compared to the control for the FLT3 protein. The binding sites of stigmasterol with the FLT3 protein include LEU 616, VAL 624, ALA 642, LYS 644, PHE 691, LEU 818, CYS 828, and PHE 830 (**Fig. 1d**). There are six binding sites of stigmasterol with FLT3 protein that

correspond to the binding positions of the control compound, but none of the stigmasterol binding sites on FLT3 protein are located at the cysteine residue 694 (CYS 694), which is the key binding site of the control compound used.

On the other hand, in **Table 1**, stigmasterol has a binding affinity value of -9.4 kcal/mol and a residue binding site similarity value of 75% compared to the control for the TGFβR1 protein. The binding sites of stigmasterol with the TGFβR1 protein include VAL 219, LYS 232, LEU 260, LEU 278, LYS 337, LEU 340, and ALA 350 (**Fig. 2d**). There are six binding sites of stigmasterol with the TGFβR1 protein that correspond to the key binding sites of the control compound used, particularly the binding site of lysine 232 (LYS 232). Therefore, the researchers speculate that stigmasterol has the potential to serve as an active compound component for drugs targeting all types of leukemia, both acute and chronic, based on its significantly more negative binding affinity values compared to pyrazole in molecule binding with FLT3 protein, and its values approaching those of pyrazole in molecule binding with TGFβR1 protein. However, in terms of the similarity of the binding positions of the amino acid residues formed, stigmasterol cannot yet be considered suitable as a drug component, especially for acute leukemia, because the position of cysteine residue 694 (CYS 694), which is an important binding position for the control compound on FLT3, is not fulfilled or not formed when stigmasterol is bound to the FLT3 protein. These findings are consistent with Bae & Song [37] and Zhao et al. [26], who reported that stigmasterol has been proven to possess anticancer properties, such as inhibiting the growth of cholangiocarcinoma, increasing lipid peroxide levels, and damaging DNA by downregulating TNF-α I and VEGFR-2, increasing p53 protein expression, suppressing p21 and p27 protein expression, enhancing proapoptotic signaling (BAX and p53), while reducing antiapoptotic signaling, promoting the mitochondrial apoptosis signaling pathway, which includes the overexpression of caspase-8 and -9, increasing apoptosis, activating apoptosis proteins such as cytochrome c, caspase-3 cleavage, caspase-9, BAK, and BAX, and inhibiting angiogenesis.

Ethyl 9,12,15-octadecatrienoate is an active compound in water hyacinth leaves with the second-lowest binding affinity after binding with FLT3 protein. According to **Table 1**, this compound has a binding affinity of -7.2 kcal/mol and an amino acid residue binding similarity of 88.89% compared to the control. **Fig. 1a** shows the binding sites of these amino acid residues, including LEU 616, VAL 624, ALA 642, LYS 644, MET 665, VAL 675, PHE 691, CYS 694, LEU 818, CYS 828, and PHE 830. There are eight binding sites of ethyl 9,12,15-octadecatrienoate with the FLT3 protein, corresponding to the key binding sites of the control compound, one of which is the binding site of cysteine residue 694 (CYS 694). Ethyl 9,12,15-octadecatrienoate functions as a cell survival agent [6]. This agent is expected to assist in cell regulation, particularly during cell division. Therefore, the researchers speculate that ethyl 9,12,15-octadecatrienoate has the potential to become an active compound component for acute leukemia based on its binding affinity activity, which is close to the binding affinity of pyrazole in the binding of ethyl 9,12,15-octadecatrienoate with FLT3 protein, as well as the many similarities, particularly the important binding positions of residues, namely cysteine 694 (CYS 694) formed during the binding of ethyl 9,12,15-octadecatrienoate with the FLT3 protein.

The active compound from water hyacinth leaves with the second most negative binding affinity in the binding of molecules with TGFβR1 protein is dibutyl phthalate. Dibutyl phthalate has a binding affinity value of -7.2 kcal/mol and an amino acid residue binding similarity value with the control of 62.5% (**Table 1**). The binding sites of this compound with the TGFβR1 protein include VAL 219, LYS 232, LEU 260, LEU 278, SER 280, LEU 340, and ALA 350 (**Fig. 2a**). The position of lysine 232 (LYS 232), which is an important binding site for the control with the TGFβR1 protein, is also present at the binding site of dibutyl phthalate with the TGFβR1 protein, followed by four other amino acid residue binding sites. Previous studies that dibutyl phthalate is known to have an antitumor role. This compound has been shown to be active in significantly inhibiting tumor cell growth [20], [38]. Based on the binding affinity activity results, which are close to the pyrazole binding affinity values in the

binding of molecules with the TGFβR1 protein, and the significant number of binding site similarities compared to the control, particularly the formation of the important binding site of lysine 232 (LYS 232) in the binding results with the TGFβR1 protein, the researchers speculate that dibutyl phthalate has the potential to become a component active compound component for chronic leukemia.

Phytol is the compound with the third lowest binding affinity value after binding to both FLT3 and TGFβR1 proteins. This compound also produced a binding affinity value of -7.1 kcal/mol after binding with both target proteins, with amino acid residue binding similarity values compared to the control on each target protein of 66.67% for binding with FLT3 protein and 75% for binding with TGFβR1 protein (**Table 1**). **Fig. 1c** shows the binding sites of phytol with FLT3 protein, including LEU 616, VAL 624, ALA 642, VAL 675, PHE 691, TYR 693, LEU 818, CYS 828, PHE 830, and ARG 834. There are six binding sites of phytol with the FLT3 protein that correspond to the binding positions of the control compound, but none of the phytol binding sites on the FLT3 protein are located at the cysteine residue 694 (CYS 694), which is the critical binding site of the control compound used.

On the other hand, the binding sites of phytol with TGFβR1 protein include PHE 216, GLY 217, VAL 219, ALA 230, LYS 232, TYR 249, LEU 260, PHE 262, LEU 278, LEU 340, and ALA 350 (**Fig. 2c**). The binding sites of phytol with the TGFβR1 protein resulted in six positions similar to the binding sites of the control used against the TGFβR1 protein. One of the similarities in binding sites involves the position of lysine 232 (LYS 232). Phytol itself has been studied for its various activities, including anti-inflammatory, anti-allergenic, immunostimulatory, anti-nociceptive, antibacterial, and antioxidant properties. Additionally, this compound can induce mitochondrial membrane potential depolarization, induce apoptosis, and exhibit strong anti-angiogenic effects, making it a potential antiproliferative and anti-angiogenic agent [39], [40]. Based on the activities observed, researchers speculate that phytol has the potential to serve as an active compound component for drugs targeting all types of leukemia, both acute and chronic, due to its binding affinity values that are close to those of pyrazole when binding to both FLT3 and TGFβR1 proteins. However, in terms of the similarity of the binding positions of the amino acid residues formed, phytol has not yet been confirmed as suitable for use as a drug component, particularly for acute leukemia, because the important binding residue position of the control compound on FLT3, namely cysteine 694 (CYS 694), is not fulfilled or not formed when phytol is bound to the FLT3 protein.

Conclusion

Based on the results of exploration and computational testing that have been conducted, the conclusion obtained is that the results of the molecular docking study between the active compounds of water hyacinth leaves and the proteins FLT3 and TGFβR1 identified one active compound from water hyacinth leaves that has potential as a candidate drug for acute leukemia, namely ethyl 9,12,15-octadecatrienoate. On the other hand, three active compounds from water hyacinth leaves were also identified as potential candidates for chronic leukemia drugs, namely stigmasterol, dibutyl phthalate, and phytol. These compounds are predicted to be potential candidates for leukemia drugs based on the binding affinity values, which are more negative or closer to the binding affinity values of the reference compounds used. Additionally, the binding positions of these compounds with their target proteins can also determine the stability of their interactions. Both ethyl 9,12,15-octadecatrienoate, stigmasterol, dibutyl phthalate, and phytol form binding at binding sites consistent with the control compounds used for target protein, suggesting that these compounds have potential as candidate drugs for leukemia.

Reference

[1] H. Arifin *et al.*, “Analysis of Modifiable, Non-Modifiable, and Physiological Risk Factors of Non-Communicable Diseases in Indonesia: Evidence from the 2018 Indonesian Basic Health

Research," *J. Multidiscip. Healthc.*, vol. Volume 15, pp. 2203–2221, Sep. 2022, doi: 10.2147/JMDH.S382191.

[2] M. S. Chandraprasad, A. Dey, and M. K. Swamy, "Introduction to Cancer and Treatment Approaches," in *Paclitaxel*, Elsevier, 2022, pp. 1–27. doi: 10.1016/B978-0-323-90951-8.00010-2.

[3] World Health Organization, "World Health Organization. Cancer no. 2020 country profile." Accessed: Jan. 10, 2026. [Online]. Available: https://www.who.int/publications/m/item/cancer-idn-2020

[4] S. Sembill *et al.*, "Management of Children and Adolescents with Chronic Myeloid Leukemia in Blast Phase: International Pediatric CML Expert Panel Recommendations," *Leukemia*, vol. 37, no. 3, pp. 505–517, Mar. 2023, doi: 10.1038/s41375-023-01822-2.

[5] M. Shadman, "Diagnosis and Treatment of Chronic Lymphocytic Leukemia," *JAMA*, vol. 329, no. 11, p. 918, Mar. 2023, doi: 10.1001/jama.2023.1946.

[6] J. H. Chang, M. M. Poppe, C. Hua, K. J. Marcus, and N. Esiashvili, "Acute Lymphoblastic Leukemia," *Pediatr. Blood Cancer*, vol. 68, no. S2, May 2021, doi: 10.1002/pbc.28371.

[7] I. M. van der Sluis *et al.*, "Blinatumomab Added to Chemotherapy in Infant Lymphoblastic Leukemia," *N. Engl. J. Med.*, vol. 388, no. 17, pp. 1572–1581, Apr. 2023, doi: 10.1056/NEJMoa2214171.

[8] Brianna and S. H. Lee, "Chemotherapy: How to Reduce Its Adverse Effects while Maintaining the Potency?," *Med. Oncol.*, vol. 40, no. 3, p. 88, Feb. 2023, doi: 10.1007/s12032-023-01954-6.

[9] A. S. M. Mosa, A. M. Hossain, B. J. Lavoie, and I. Yoo, "Patient-Related Risk Factors for Chemotherapy-Induced Nausea and Vomiting: A Systematic Review," *Front. Pharmacol.*, vol. 11, Apr. 2020, doi: 10.3389/fphar.2020.00329.

[10] Y.-Q. Liu, X.-L. Wang, D.-H. He, and Y.-X. Cheng, "Protection Against Chemotherapy- and Radiotherapy-Induced Side Effects: A Review Based on the Mechanisms and Therapeutic Opportunities of Phytochemicals," *Phytomedicine*, vol. 80, p. 153402, Jan. 2021, doi: 10.1016/j.phymed.2020.153402.

[11] N. Behranvand *et al.*, "Chemotherapy: A Double-Edged Sword in Cancer Treatment," *Cancer Immunol. Immunother.*, vol. 71, no. 3, pp. 507–526, Mar. 2022, doi: 10.1007/s00262-021-03013-3.

[12] V. R. Minciacchi, R. Kumar, and D. S. Krause, "Chronic Myeloid Leukemia: A Model Disease of the Past, Present and Future," *Cells*, vol. 10, no. 1, p. 117, Jan. 2021, doi: 10.3390/cells10010117.

[13] A. I. Antar, Z. K. Otrock, E. Jabbour, M. Mohty, and A. Bazarbachi, "FLT3 Inhibitors in Acute Myeloid Leukemia: Ten Frequently Asked Questions," *Leukemia*, vol. 34, no. 3, pp. 682–696, Mar. 2020, doi: 10.1038/s41375-019-0694-3.

[14] F. Amalina, A. S. A. Razak, S. Krishnan, A. W. Zularisam, and M. Nasrullah, "Water Hyacinth (Eichhornia crassipes) for Organic Contaminants Removal in Water – A Review," *J. Hazard. Mater. Adv.*, vol. 7, p. 100092, Aug. 2022, doi: 10.1016/j.hazadv.2022.100092.

[15] A. Abba and S. Sankarannair, "Global Impact of Water Hyacinth (Eichhornia crassipes) on Rural Communities and Mitigation Strategies: A Systematic Review," *Environ. Sci. Pollut. Res.*, vol. 31, no. 31, pp. 43616–43632, Jun. 2024, doi: 10.1007/s11356-024-33905-7.

[16] I. Harun, H. Pushiri, A. J. Amirul-Aiman, and Z. Zulkeflee, "Invasive Water Hyacinth: Ecology, Impacts and Prospects for the Rural Economy," *Plants*, vol. 10, no. 8, p. 1613, Aug. 2021, doi: 10.3390/plants10081613.

[17] O. P. Ilo, M. D. Simatele, S. L. Nkomo, N. M. Mkhize, and N. G. Prabhu, "The Benefits of Water Hyacinth (Eichhornia crassipes) for Southern Africa: A Review," *Sustainability*, vol. 12, no. 21, p. 9222, Nov. 2020, doi: 10.3390/su12219222.

[18] W. Ben Bakrim *et al.*, "Eichhornia crassipes (Mart.) Solms: A Comprehensive Review of Its Chemical Composition, Traditional Use, and Value-Added Products," *Front. Pharmacol.*, vol. 13, Mar. 2022, doi: 10.3389/fphar.2022.842511.

[19] H. Hasnat *et al.*, "Unveiling the Therapeutic Potentials of Water Hyacinth (Eichhornia crassipes

(Mart.) Solms) Flower against Oxidative Stress, Inflammation and Depressive Disorders: GC-MS/MS, In Vitro, In Vivo and In Silico Approaches," *Chem. Biodivers.*, vol. 21, no. 12, Dec. 2024, doi: 10.1002/cbdv.202401268.

[20] P. Banakar and M. Jayaraj, "Gc-Ms Analysis of Bioactive Compounds from Ethanolic Leaf Extract of Waltheria Indica Linn. and Their Pharmacological Activities," *Int. J. Pharm. Sci. Res.*, vol. 9, no. 5, pp. 2005–2010, 2018, doi: 10.13040/IJPSR.0975-8232.9(5).2005-10.

[21] A. R. Syita, I. Shofiyah, Y. E. Putri, and M. R. Afnani, "Pengembangan E-Modul Bioinformatika Berbasis Program Based Learning (PBL) Tentang Prediksi Interaksi Senyawa Aktif Daun Pepaya Sebagai Kandidat Obat Kanker Paru-Paru," *Otus Educ. J. Biol. dan Pendidik. Biol.*, vol. 3, no. 1, pp. 1–12, Apr. 2025, doi: 10.62588/otusedu.2025.v3i1.0243.

[22] M. A. Anggarani *et al.*, "In silico Study of Ruminant Feed Wafer Formulation with Empon-Empon as Health Support Food," *Trop. J. Nat. Prod. Res.*, vol. 9, no. 8, pp. 3695–3703, Aug. 2025, doi: 10.26538/tjnpr/v9i8.28.

[23] M. R. Afnani, N. F. Emilia, A. E. Damayanti, C. N. Rabbani, and E. R. Purnama, "Potency of Active Compounds Extract of Soursop Leaves (Annona muricata) As A Candidate for Cervical Cancer Drug in Silico," *E3S Web Conf.*, vol. 513, p. 03005, Apr. 2024, doi: 10.1051/e3sconf/202451303005.

[24] A. A. Theodosiou and R. C. Read, "Artificial intelligence, Machine Learning and Deep Learning: Potential Resources for the Infection Clinician," *J. Infect.*, vol. 87, no. 4, pp. 287–294, 2023, doi: 10.1016/j.jinf.2023.07.006.

[25] Z. Barriga and J. C. Borj Ecleo, "In-Silico Pipelined Medical Compound Generation for Neglected Tropical Diseases," *Int. Conf. Inf. Commun. Technol. ICOIACT*, no. 2024, pp. 85–90, 2024, doi: 10.1109/ICOIACT64819.2024.10912975.

[26] Z. Zhao *et al.*, "Pyrazolone Structural Motif in Medicinal Chemistry: Retrospect and Prospect," *Eur. J. Med. Chem.*, vol. 186, p. 111893, Jan. 2020, doi: 10.1016/j.ejmech.2019.111893.

[27] S. K. Kondapuram, S. Sarvagalla, and M. S. Coumar, "Docking-Based Virtual Screening Using PyRx Tool: Autophagy Target Vps34 as a Case Study," in *Molecular Docking for Computer-Aided Drug Design*, Elsevier, 2021, pp. 463–477. doi: 10.1016/B978-0-12-822312-3.00019-9.

[28] D. S. Goodsell *et al.*, "RCSB Protein Data Bank: Enabling Biomedical Research and Drug Discovery," *Protein Sci.*, vol. 29, no. 1, pp. 52–65, Jan. 2020, doi: 10.1002/pro.3730.

[29] M. T. Muhammed and E. Aki-Yalcin, "Molecular Docking: Principles, Advances, and Its Applications in Drug Discovery," *Lett. Drug Des. Discov.*, vol. 21, no. 3, pp. 480–495, Mar. 2024, doi: 10.2174/1570180819666220922103109.

[30] R. Jakhar, M. Dangi, A. Khichi, and A. K. Chhillar, "Relevance of Molecular Docking Studies in Drug Designing," *Curr. Bioinform.*, vol. 15, no. 4, pp. 270–278, Jun. 2020, doi: 10.2174/1574893615666191219094216.

[31] S. Singh, Q. Bani Baker, and D. B. Singh, "Molecular Docking and Molecular Dynamics Simulation," in *Bioinformatics*, Elsevier, 2022, pp. 291–304. doi: 10.1016/B978-0-323-89775-4.00014-6.

[32] U. Baroroh, Z. S. Muscifa, W. Destiarani, F. G. Rohmatullah, and M. Yusuf, "Molecular Interaction Analysis and Visualization of Protein-Ligand Docking using Biovia Discovery Studio Visualizer," *Indones. J. Comput. Biol.*, vol. 2, no. 1, p. 22, Jul. 2023, doi: 10.24198/ijcb.v2i1.46322.

[33] B. H. M. Mooers, "Shortcuts for Faster Image Creation in PyMOL," *Protein Sci.*, vol. 29, no. 1, pp. 268–276, Jan. 2020, doi: 10.1002/pro.3781.

[34] T. Yamaura *et al.*, "A Novel Irreversible FLT3 Inhibitor, FF-10101, Shows Excellent Efficacy Against AML Cells with FLT3 Mutations," *Blood*, vol. 131, no. 4, pp. 426–438, Jan. 2018, doi: 10.1182/blood-2017-05-786657.

[35] K. Guckian *et al.*, "Pyrazolone Based TGFβR1 Kinase Inhibitors," *Bioorg. Med. Chem. Lett.*, vol. 20, no. 1, pp. 326–329, Jan. 2010, doi: 10.1016/j.bmcl.2009.10.108.

[36] M. Ashourpour *et al.*, "Pyrazole Derivatives Induce Apoptosis via ROS Generation in the Triple Negative Breast Cancer Cells, MDA-MB-468," *Asian Pacific J. Cancer Prev.*, vol. 22, no. 7, pp.

2079–2087, Jul. 2021, doi: 10.31557/APJCP.2021.22.7.2079.

[37] H. Bae, G. Song, and W. Lim, "Stigmasterol Causes Ovarian Cancer Cell Apoptosis by Inducing Endoplasmic Reticulum and Mitochondrial Dysfunction," *Pharmaceutics*, vol. 12, no. 6, p. 488, May 2020, doi: 10.3390/pharmaceutics12060488.

[38] Z. Wu, K. Ameer, and G. Jiang, "Isolation and Characterization of Anti-Tumor Compounds from Ethyl Acetate Extract of Rumex japonicus Houtt Roots and their Cytotoxic Effects," *Food Sci. Technol.*, vol. 42, 2022, doi: 10.1590/fst.05421.

[39] B. Pejin, V. Kojic, and G. Bogdanovic, "An Insight Into the Cytotoxic Activity of Phytol at in Vitro Conditions," *Nat. Prod. Res.*, vol. 28, no. 22, pp. 2053–2056, Nov. 2014, doi: 10.1080/14786419.2014.921686.

[40] R. Sakthivel, D. S. Malar, and K. P. Devi, "Phytol Shows Anti-Angiogenic Activity and Induces Apoptosis in A549 Cells by Depolarizing the Mitochondrial Membrane Potential," *Biomed. Pharmacother.*, vol. 105, pp. 742–752, Sep. 2018, doi: 10.1016/j.biopha.2018.06.035.