Jambura Medical and Health Science Journal, Vol.3 No.2 (August 2024)
p-ISSN 2830-0580 | e-ISSN 2830-4608

ORIGINAL ARTICLE **Open Access**

Phytochemical Screening of Ethyl Acetate Extract of Beta-beta Leaves (*Lunasia amara* Blanco) as Anticancer and Antimicrobial Based on Prediction of Activity Spectra for Substances (PASS) Online

Adriani Adriani[1,*]
[1] Faculty of Medicine, Universitas Muslim Indonesia, Makassar, Indonesia.

*Corresponding Author. Email: adriani.adriani@umi.ac.id, Telp: +6285255789306

ABSTRACT

Introduction: Beta-beta leaves (*Lunasia amara* Blanco) have anticancer and antibacterial activity, but the secondary metabolites involved are still not clearly known. The aim of this research is to screen secondary metabolites from beta-beta leaves that have potential anticancer and antibacterial properties using the Passonline server and determine potential compound target proteins using the Superpred online server.
Method: Extraction of beta-beta leaves was carried out using the maceration method using ethyl acetate and identification of secondary metabolites using Liquid Chromatography High-Resolution Mass Spectrometry (LC HRMS). Prediction of the anticancer, antibacterial and toxicity potential of secondary metabolites of beta-beta leaves using Prediction of Activity Spectra for Substances (PASS) Online. Analysis of similarity to drugs using Lipinski rule of five and prediction of target proteins using the online superpred server.
Results: There are 10 secondary metabolites each which have anticancer and antibacterial bioactivity. The compounds methyl cinnamate and 3,5-pyridinedicarboxylic acid are similar to drugs based on Lipisnki rule of five analysis and are non-toxic based on online PASS analysis. There are 3 target proteins for methyl cinnamate which are involved in anticancer and antibacterial activity, namely NFκβ P105, ADAM10 and Catephsin D.
Conclusion: Ethyl acetate extract from beta-beta leaves contains secondary metabolites as anticancer and antibacterial based on Passonline server analysis. Methyl cinnamate is a potential secondary metabolite candidate as an anticancer and antibacterial with 3 target proteins, namely NFκβ P105, ADAM10 and Catephsin D.

Key words: Anticancer, antibacterial, beta-beta, *Lunasia amara*, passonline, prediction

JMHSJ Jambura Medical and Health Science Journal

Published by:
Universitas Negeri Gorontalo

Address:
Jl. Jend. Sudirman No.6, Gorontalo City, Gorontalo, Indonesia

Mobile number:
+62852 3321 5280

Email:
jmhsj@ung.ac.id

Article History:
Received13 August 2024
Accepted 27 August 2024
Published 30 August 2024
DOI:
https://doi.org/10.37905/jmhsj.v3i2.27044

Introduction

Cancer and bacterial infections have now become major diseases that threaten physical and mental health worldwide. The number of patients that continues to increase every year is a particular concern because the mortality rate is also increasing. Chemotherapy treatment efforts for cancer patients are not always acceptable to patients or their families because of the side effects that cause a decrease in quality of life.[1,2] Treatment of infectious diseases with antibiotics is currently also starting to cause polemics because several species of bacteria are resistant to antibiotics. Therefore, it is necessary to develop new anticancer drugs that can selectively inhibit the growth of cancer cells, reduce chemoresistance, and cancer recurrence after treatment. Likewise with the development of antibiotics. One alternative effort that can be made is to use herbal plants in the surrounding environment. The use of medicinal plants as medicine is preferred for the treatment of diseases because it is efficient, easy to obtain, economical, and well tolerated by the body.[3] One of the Indonesian plants that has various bioactivities is Beta-beta (*Lunasia amara* Blanco).

Beta-beta is an endemic plant in Indonesia that has medicinal properties. Traditional uses of beta-beta include increasing stamina, reducing swelling, cleaning the eyes, treating snake bites, and as an antidiabetic.[4] Several research results have shown that Beta-beta leaf and bark powder have aphrodisiac effects. [5,6] Beta-beta crude extract is reported to have bioactivity as an anti-inflammatory,[7,8] antiparasitic,[9] antioxidant,[10,11,12] anticancer,[12,13] and antidiabetic.[14] Recent research has successfully proven that the ethanol extract of beta-beta leaves *Staphylococcus aureus, E. coli, Klebsiella pneumonia, Pseudomonas aeroginosa*, and *Salmonella typhimurium*.[15,16]

Although it is known to have antibacterial effects, the types of secondary metabolites from beta-beta leaves and the receptor proteins involved are still unclear because they have never been reported. Through this study, beta-beta leaves will be extracted using LCHR-MS, screening their potential secondary metabolites as anticancer and antibacterial along with the target proteins involved. Thus, the purpose of this study is to screen secondary metabolites from beta-beta leaves that have the potential as anticancer and antibacterial using the Passonline server and determine the target proteins of potential compounds using the Superpred online server.

Methods

Extraction and identification of secondary metabolites from leaves Beta-beta

A total of 250 grams of beta-beta leaf powder was extracted using the maceration

method using ethyl acetate solvent. The extract obtained was then identified for its secondary metabolite content using LCHRMS based on previous research.[14,17]

Prediction of anticancer and antibacterial activity of secondary metabolite from beta-beta leaves

Secondary metabolites contained in the ethyl acetate extract of Beta-beta leaves were predicted for their potential as antibacterial, anticancer, and toxicity using the passonline server (https://www.way2drug.com/passonline/predict.php). Canonical smiles of each secondary metabolite were obtained from Pubchem (https://pubchem.ncbi.nlm.nih.gov/) then entered into the passonline server and then run to obtain bioactivity data from secondary metabolites.

Drug-likeness Prediction

Canonical smiles of each secondary metabolite were obtained from Pubchem (https://pubchem.ncbi.nlm.nih.gov/) then entered into the http://www.scfbio-iitd.res.in/software/drugdesign/lipinski.jsp and then run to obtain bioactivity data from secondary metabolites.

Prediction of LD50 activity of secondary metabolite from leaves beta-beta

The canonical smile of each secondary metabolite was obtained from Pubchem and inputted into Protox II (https://tox-new.charite.de/protox_II/) to obtain data on the cytotoxic activity of each secondary metabolite.

Prediction of protein targets from potential secondary metabolites

To find out the target proteins from potential secondary metabolites, the Canonical smile of each compound is inputted into SuperPred (https://prediction.charite.de/).

Result

Metabolite secondary from beta-beta leaves

Based on the results of LCHR-MS analysis, it is known that there are 139 secondary metabolites contained in the ethyl acetate extract of beta-beta leaves (Figure 1). All of these secondary metabolites were then screened using the Passonline server to see their anticancer and antibacterial activity.

Result of screening secondary metabolites from ethyl acetate extract Beta-beta leaves as anticancer and antibacterial.

Based on the screening results using Passonline, it is known that there are 10 secondary metabolites that have the potential as anticancer and 10 secondary metabolites that have the

potential as antibacterial (Pa value > 0.7). The types of secondary metabolites that have the potential as anticancer and antibacterial are shown in Table 1.

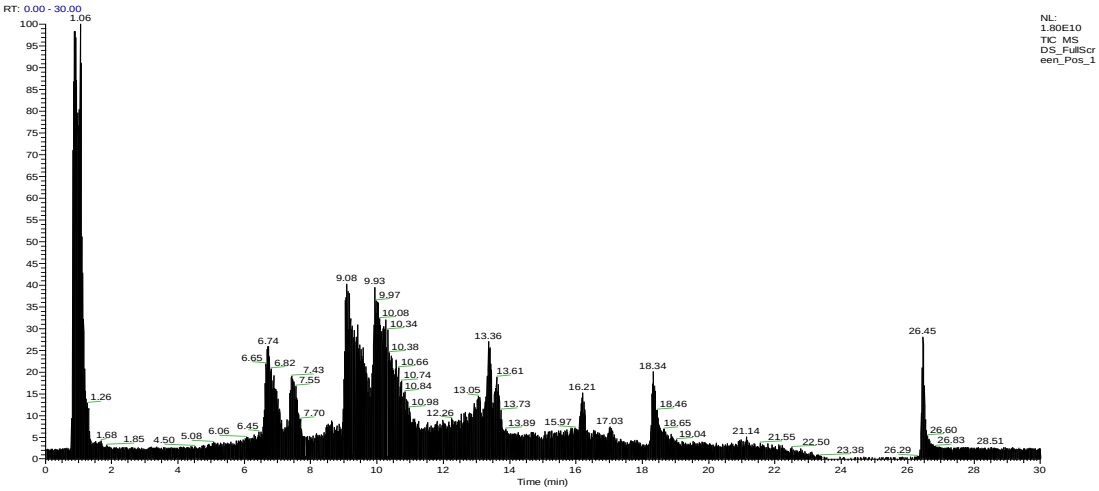

Figure 1. Chromatogram of secondary metabolites from Beta-beta leaves

Table 1. Anticancer and antibacterial activity prediction of secondary metabolites from Beta-beta leaves

No	Secondary metabolites	Structure	Mass weight	Anticancer activity(Pa value)	Antibacterial activity (Pa value)
1	Giberelic acid (diterpenoid)	C19H22O6	363	0.95	
2	Dextrorphan	C17H23NO	257	0.92	
3	Tangeritin	C20H20O7	372	0.82	0.89
4	Schaftoside	C26H28O14	564	0.85	
5	Nobiletin	C21H22O8	402	0.85	0.91
6	2,2,6,6-Tetramethyl-1-piperidinol (TEMPO)	C9H19NO	157	0.85	
7	Stanolone	C19H30O2	290	0.81	0.88
8	-(-) Caryophyllene oxide	C15H24O	220	0.95	
9	Galaxolidone	C18H24O2	272	0.81	
10	Corymboside	C26H28O14	564	0.85	
11	Dibutyl phthlate	C16H22O4	278		0.827
12	3,5-Pyridinedicarboxylic acid	C14H21NO4	289		0.83
13	Trietylene glicol monobutyl eter	C10H22O4	206		0.8
14	Metyl cinnamate	C10H10O2	162		0.81
15	Scopoletin	C10H8O4	192		0.82
16	Chlorogenic acid	C16H18NO2	354		0.86
17	Benzyl butyl phthalate	C19H20O4	312		0.81

Pa : *prediction activity*

Publisher: Universitas Negeri Gorontalo

Result of similarity with drugs (lipinski rule of five) , LD50 and toxicity

From the results of the similarity analysis with drugs (Table 2), it is known that schaftoside does not meet the Lipinski rule of five. Based on the results of the toxicity analysis using passonline, 2 compounds were obtained that were not toxic (Pa> 0.7), namely 3,5-pyridinedicarboxylic acid and methyl cinnamate. The results of analysis using protox 2 stated that the LD50 dose for methyl cinnamate was 1910 mm/kg and was categorized as level IV toxicity. While the LD50 dose for 3,5-pyridinedicarboxylic acid was 3720 mm/kg and was categorized as level V toxicity. The structures of the two compounds are shown in Figure 2.

Table 2. Result of screening secondary metabolites similarity with Lipinski rule of five, LD50 value and toxicity

No	Secondary Metabolites	Mass mol.	H accept	H donor	Log P	Molar refrac-Tibity	Predict LD50 (mm/kg)	Toxicity
1	Dibutyl phthlate	278	4	0	3,6	77	3474	Toxic
2	3,5-pyridinedicarboxylic acid	167	5	2	0,4	38	3720	Non toxic
3	Trietyleneglicol monobutyleter	206	4	1	0,8	54	3900	Toxic
4	Methyl cinnamate	162	2	0	1,8	47	1910	Non toxic
5	Tangeritin	371	7	0	3,3	98	5000	Toxic
6	Nobiletin	402	8	0	3,3	105	5000	Toxic
7	Androstanolone	290	2	1	3,9	82	3000	Toxic
8	Scopoletin	192	4	1	1,3	49	3800	Toxic
9	Chlorogenic acid	354	9	6	-0,6	82	5000	Toxic
10	Benzyl butyl phthlate	312	4	0	4	87	2330	Toxic
11	Giberellic acid	346	6	3	1	85	6300	Toxic
12	Dextrorphan	257	2	1	2,8	75	-	Toxic
13	Schaftoside	564	14	10	-1,9	130	823	Toxic
14	2,2,6,6-tetramethyl-1-piperidinol (TEMPO)	157	2	1	2,3	45	139	Toxic
15	-(-) caryophyllene oxide-	220	1	0	3,9	66	5000	Toxic
16	Galaxolidone	272	2	0	3,9	79	3200	Toxic
17	Corymboside							Toxic

Molecule mass < 500 Da; LogP < 5; H donor < 5; H acceptor < 10; molar refractivity 40-130.

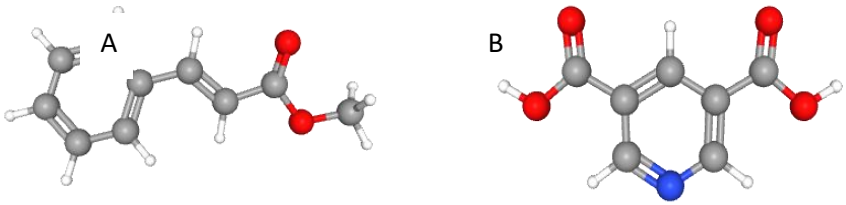

Figure 2. 3D Structure of methyl cinnamate(A) dan 3,5-pyridinedicarboxylic acid (B)

Result of screening protein target for potentially secondary metabolites from beta-beta leaves

Methyl cinnamate has 3 anti-ancer and antibacterial target proteins, namely NFκβ P105, ADAM 10, Catephsin. D For 3,5-pyridinedicarboxylic acid, no target proteins were found for anticancer and antibacterial. The results of the target protein screening are shown in Table 3.

Table 3. Result of target protein from methyl cinnmate and 3,5-pyridinedicarboxylic acid

Secondary metabolites	Super pred
Methyl cinnamate	NFκβ P105
	ADAM10
	Catephsin D
	-

Discussion

The use of beta-beta leaves in treating diseases has not been maximized. This is because the potential of beta-beta leaves is not widely known. Not only that, traditional medicine has used more beta-beta stems and roots because they are believed to have better benefits than leaves. Based on the results of the study, it was found that the leaves of the beta-beta plant contain various secondary metabolites that are pharmacologically important. The results of screening using LCHR-MS showed that beta-beta leaves contain 139 secondary metabolites, especially from the steroid, ester, flavonoid, coumarin, alkaloid, and terpenoid groups (Figure 1). There are 10 secondary metabolites each that have the potential as anticancer and antibacterial based on screening using Passonline (Pa> 0.7). Secondary metabolites with the highest activity as anticancer are gibberellic acid and (-) caryophyllene oxide (Pa = 0.95) while the highest activity as an antibacterial is shown by nobiletin (Pa = 0.91).

Passonline is a tool that can predict the bioactivity of a compound using the QSAR principle, namely the quantitative relationship between structure and compound.[18] Currently, passonline has been able to predict thousands of activities of secondary metabolites with an

accuracy level of more than 95% (https://www.way2drug.com/passonline/predict.php). This is certainly very useful in the search for natural-based drugs because it can save time, energy and costs. The results of Passonline analysis are expressed in predicted activity (Pa). A high Pa value (> 0.7) describes the bioactivity of a secondary metabolite based on the results of experimental tests. The higher the Pa value of a secondary metabolite, the higher its bioactivity value. However, if the Pa value <0.7, it can be ascertained that the secondary metabolite has a low probability of pharmacological activity However, not all potential secondary metabolites from beta-beta leaves have similarities to drugs and are safe for the body.

The results of the analysis using Lipinski's rule of five found that schaftoside had no similarities to drugs. This is because the properties of schaftoside do not comply with the Lipisnki rule of five, namely molecular mass> 500 Da, H acceptor> 10, H donor> 5. The size of the molecular mass> 500 Da causes the ligand to be impermeable to penetrate the lipid bilayer in the digestive tract and the blood-brain barrier.[19] Likewise, the number of H donors and H acceptors that are too many makes it difficult for the ligand to pass through the cell membrane.[20,21] This of course inhibits the absorption process of the ligand in the digestive tract. Based on the results of the toxicity prediction, only 3,5-pyridine dicarboxylic acid and methyl cinnamate were declared safe and non-toxic. To be used as a drug ingredient, it is necessary to search for target proteins from 3,5-pyridine dicarboxylic acid and methyl cinnamate.

Other target proteins owned by methyl cinnamate are NFκβ P105, ADAM10, and Catephsin D. NFκβ is one of the proteins involved in the process of cell transcription, stimulating cell proliferation, preventing apoptosis and increasing tumor angiogenesis and metastasis.[22] One of the subunits of NFKb is NFκβ P105 which is a transcription factor in the development of canine oral melanoma cells. The ADAM 10 protein is reported to support cancer cell growth by mediating cell division on several substrates that can promote the growth of malignant tumors.[23] In addition, ADAM10 is also involved in the development and chemoresistance of triple-negative breast cancer (TNBC),[24] and prostate cancer metastasis.[25] In cancer patients, exosomal ADAM10 expression increased so that ADAM10 can be used as a potential biomarker to detect cancer. Not only in cancer, ADAM 10 is also related to *Staphylococcus aureus* infection. When *Staphylococcus aureus* infection occurs, ADAM10 becomes a receptor for the cytotoxin α-hemolysin (Hla) which triggers the body's immune response. Currently, ADAM10 is used as a candidate target protein in antibiotic treatment due to *Staphylococcus aureus* infection. Cathepsin D is a protein found in

lysosomes and is involved in angiogenesis, proliferation, carcinogenesis, and pathogenesis of several types of cancer (breast, ovarian, and gastric). Recent studies have found that the mechanism of cathepsin D in promoting macrophage polarization and tumor-related metastasis is through TGFBI-CCL20 signaling.[26]

Methyl cinnamate and its derivatives are derivatives of cinnamic acid which has been known for its bioactivity as a potential anticancer and antimicrobial. Previous studies have found that methyl cinnamate is cytotoxic to RAW264.7 cells.[27] Based on in vitro studies, it is known that cinnamic acid derivatives, namely phenyl amide cinnamate, have strong cytotoxic activity against the MCF-7 cell line.[28] The anticancer ability of cinnamic acid and its derivatives is likely due to the presence of α,β-unsaturated bonds in its chemical structure.[29] As an antimicrobial, methyl cinnamate has been reported to be able to inhibit biofilm formation, thereby inhibiting the growth of *Staphylococcus aureus, Staphylococcus epidermidis, Pseudomonas aeroginosa, Heliobacter pylori* and *Candida albicans* colonies.[30, 31,32] Through this research, valuable insights were obtained regarding the anticancer and antibacterial potential of secondary metabolites from beta-beta leaves which have not yet been revealed. By knowing the activity of methyl cinnamate, we can further explore its potential therapeutic benefits and identify it as a source of valuable potential bioactive compounds. In the next stage, it is necessary to conduct in vitro activity tests of beta-beta leaf extracts to see the extent of the antimicrobial and anticancer effects caused.

Conclusion

Ethyl acetate extract from beta-beta leaves contains secondary metabolites that are anticancer and antibacterial based on Passonline server analysis. Methyl cinnamate is a potential secondary metabolite as an anticancer and antibacterial with target proteins such as NFκβ P105, ADAM10, and Catephsin D.

Conflicts of Interest

We have no conflicts of interest to disclose

Funding sources

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors

Acknowledgments

Nothing to declare

References

1. Nurgali K, Jagoe RT, Abalo R. Editorial : Adverse Effects of Cancer Chemotherapy : Anything New to Improve Tolerance and Reduce Sequelae ?. *Front Pharmacol* 2018;9:245.
2. Batra A, Kalyani CV, Romilla KK. Incidence and severity of self - reported chemotherapy side - effects in patients with hematolymphoid malignancies : A cross - sectional study. *Cancer Res Stat Treat.* 2020;3:736–41.
3. Al-Rimawi F, Khalid M, Salah Z, Zawahreh MAA, Alnasser SM, Alshammari SO, Wedian F, Karimulla S, Almutairi A, Alanazi FIB, Alanazi HO, Al-Mazaideh GM, Nafidi HA, Salamatullah AM, Mekonnen AB, Bourhia M. Anticancer, antioxidant, and antibacterial activity of chemically fingerprinted extract from Cyclamen persicum Mill. *Sci Rep.* 2024;14(1):8488.
4. Macabeo APG, Aguinaldo AM. Chemical and Phytomedicinal Investigations in Lunasia amara. *Phcog Rev.* 2008;2(4):317-325.
5. Zumrotun, Masyud B, Thohari AM. The Role Of Sanrego (Lunasia Amara Blanco) to Increasing Libido Sexual of Male Timor Deer (Cervus Timorensis De Bla). *Media Konserv.* 2006;Xi(September 2005):72–6.
6. Hasan H, Akuba J, Nathania B. Efek Afrodisiaka Ekstrak Kulit Batang Sanrego (Lunasia Amara Blanco) Terhadap Mencit Jantan (Mus musculus). *Indonesian J Pharm Edu* 2021;1(3):152–7.
7. Adriani A. Prediksi Senyawa Bioaktif Dari Tanaman Sanrego (Lunasia amara Blanco) Sebagai Inhibitor Enzim Siklooksigenase-2 (COX-2) Melalui Pendekatan Molekular Docking. *J Ilmiah Pena* 2018;1:6–11.
8. Hasnaeni, Sudarsono, Nurrochmad A, Widyarini S. Identification of active anti-inflammatory principles of beta- beta wood (Lunasia amara Blanco) from Siawung Barru- South Sulawesi , Indonesia. *Trop J Pharm Res* 2017;16(January):161–4.
9. Lallo S, Ariani F, Syamsu R, ANTI- Plasmodium Berghei EKSTRAK DAUN DAN KAYU Lunasia amara Blanco. *Majalah Farmasi dan Farmakologi* 2017;21(3):55–8.
10. Hasnaeni H, Aminah A. Uji Aktivitas Antioksidan dan Profil Fitokimia Ekstrak Kayu Beta-beta (Lunasia amara Blanco .). *Galenika J Pharm* 2019;5(1):101–7.
11. Latu S, Rame O. Uji Aktivitas Antioksidan Terhadap Hasil Fraksinasi N-Heksan Batang Sanrego (Lunasia Amara Blanco) Dengan Metode DPPH. *Inhealth J* 2023;2(2):170–80.

12. Saputra A, Laut MM, Ndaong NA. Aktivitas Antioksidan dan Antibakteri Ekstrak Etanol Kulit Batang Lunasia amara. *J Kaj Vet* 2024;12(1):113–21.
13. Zubair MS, Anam S, Lallo S. Cytotoxic activity and phytochemical standardization of Lunasia amara Blanco wood extract. *Asian Pac J Trop Biomed.* 2016;6(11):962–6.
14. Adriani A, Noorhamdani N, Ardyati T, Winarsih S. Non-targeted screening with LC-HRMS and In-Silico Study on Diabetic activity of ethyl acetate extract of Sanrego (Lunasia amara Blanco). *Res J Pharm Technol.* 2022;15(3):1077–84.
15. Totaan ID V, Calma ZD, Nicdao MAC. Antioxidant , Antibacterial and Anti-Clastogenic Activities of Lunasia amara , Blanco Leaf Extract. *Int J Adv Sci Tech Res* 2018; 1(8):111-125.
16. Dasor AYC, Sanam MUE, Ndaong NA. Uji Potensi Antibakteri Ekstrak Etanol Daun Kayu Metang (Lunasia Amara Blanco) Terhadap Staphylococcus aureus. *J Kaji Vet*. 2021;9(3):157–63.
17. Adriani A. Prediksi Kandidat Protein Target Antikanker Derivate Kumarin Asal. *Biol Educ J*. 2022;2(2):55–64.
18. Widyananda MH, Fatchiyah F, Muflikhah L, Ulfa SM, Widodo N. Computational examination to reveal Kaempferol as the most potent active compound from Euphorbia hirta against breast cancer by targeting AKT1 and ER α. *Egypt J Basic Appl Sci* 2023;10(1):753–67.
19. Tilaqza A, Herbani M. Studi In silico Potensi Anti Hipertensi dan Prediksi Profil Farmakokinetika Daun Jati Belanda (Guazuma ulmifolia . Lamk). *J Kesehat Islam.* 2021;10:45–52.
20. Adriani, Noorhamdani, Winarsih S, Ardyati T. Molecular Docking Study from Lunacridine, Scopoletin and Skimmianine as Antidiabetes through α-Glucosidase Inhibitor. *J Phys Conf Ser*. 2019;1374(1).
21. Zafar M, Khan H, Rauf A, Khan A, Lodhi MA. In silico study of alkaloids as α-glucosidase inhibitors: Hope for the discovery of effective lead compounds. *Front Endocrinol (Lausanne)*. 2016;7(DEC):1–17.
22. Kaltschmidt B, Greiner JFW, Kadhim HM, Kaltschmidt C. Subunit-Specific Role of NF-κB in Cancer. *Biomedicines.* 2018;6(2):44.
23. J Smith TM Jr, Tharakan A, Martin RK. Targeting ADAM10 in Cancer and Autoimmunity. *Front Immunol.* 2020;11:499.
24. Cheng Y, Lin L, Li X, Lu A, Hou C, Wu Q, et al. ADAM10 is involved in the oncogenic process and chemo - resistance of triple - negative breast cancer via

regulating Notch1 signaling pathway , CD44 and PrPc. *Cancer Cell Int*. 2021;1–15.

25. Cai C, Zhang M, Liu L. ADAM10-cleaved ephrin-A5 contributes to prostate cancer metastasis. *Cell Death Dis* 2022; 13:453.
26. Lee SG, Woo SM, Seo SU, Lee CH, Baek MC, Jang SH, Park ZY, Yook S, Nam JO, Kwon TK. Cathepsin D promotes polarization of tumor-associated macrophages and metastasis through TGFBI-CCL20 signaling. *Exp Mol Med.* 2024;56(2):383-394.
27. Murakami Y, Kawata A, Suzuki S, Fujisawa S. Properties of Cinnamates , Acrylates and Methacrylates Against RAW264 . 7 *Cells.* 2018;1321:1309–21.
28. Ernawati T, Artanti N, Kurniawan YD. In silico and in vitro anti-cancer activity against breast cancer cell line MCF-7 of amide cinnamate derivatives. *J Appl Pharm Sci* 2024;14(03):102–7.
29. Wang R, Yang W, Fan Y, Dehaen W, Li Y, Li H, et al. Bioorganic Chemistry Design and synthesis of the novel oleanolic acid-cinnamic acid ester derivatives and glycyrrhetinic acid-cinnamic acid ester derivatives with cytotoxic properties. *Bioorg Chem* 2019;88(April):102951.
30. Vita D De, Simonetti G, Pandolfi F, Costi R, Di R, Diodata F, et al. Bioorganic & Medicinal Chemistry Letters Exploring the anti-biofilm activity of cinnamic acid derivatives in Candida albicans. *Bioorg Med Chem Lett* 2016;12–4.
31. Prasetya YA, Nisyak K, Amanda ER, Prasetya YA, Nisyak K, Amanda ER. Aktivitas Antibakteri Nanoemulsi Minyak Lengkuas (Alpinia galanga L . Willd) dalam Menghambat Pertumbuhan Helicobacter pylori Antibacterial Activity of Galangal (Alpinia galanga L . Willd) Oil Nanoemulsion in Inhibiting the Growth of Helicobacter pylori. *Biotropika: J Trop Biol* 2019;7(3):136–42.
32. de Morais MC, de Oliveira Lima E, Perez-Castillo Y, de Sousa DP. Synthetic Cinnamides and Cinnamates: Antimicrobial Activity, Mechanism of Action, and In Silico Study. *Molecules.* 2023;28(4):1918.