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In-silico ANALYSIS OF VERNONIOSIDE D AND VERNONIOSIDE E FROM *Vernonia amygdalina* Delile. LEAVES AS INHIBITOR OF EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) AND MAMMALIAN TARGET OF RAPAMYCIN (mTOR)

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ABSTRACT

Vernonia amygdalina Delile. Leaves contain cardiac glycosides, which are potential cardiotonic and anticancer. This study evaluated the activity of vernonioside D, and E inhibits the epidermal growth factor receptor (EGFR). The study of the mammalian target of rapamycin (mTOR) confirmed the activity of these glycosides. In silico docking using Autodock Vina PyRx 9.5 program and visualized by Ligplot 2.1. EGFR and mTOR structures were used as test receptors, binding pocket with the Protein Data Bank (PDB) code 1M17 and 3L16. To generate two and three dimensions of vernonioside D and E using the Marvin Sketch program. Both compounds and reference drugs (thienopyridine-2-il) aminopyridine and erlotinib) inhibited EGFR and mTOR with docking score -10.4; -8.6; -6.9 and -6.3; -6.6; -9.2 respectively. Vernonioside D and E are more potent in inhibit EGFR compare to the reference drug.

Keywords: Vernonioside D, Vernonioside E, *In-silico*, EGFR, mTOR

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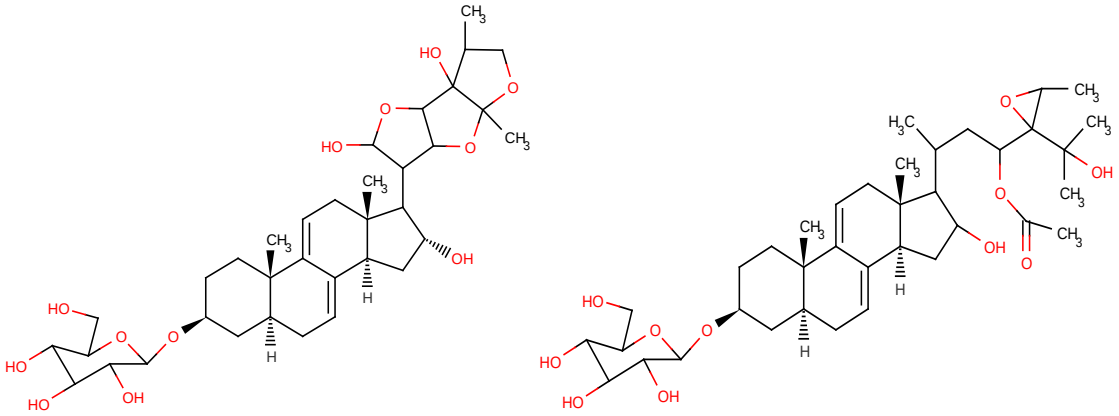
INTRODUCTION

Cancer can affect anyone, but this type of breast cancer only occurs in women.[1] The data states that breast cancer is ranked fifth as the type of cancer that causes the largest death cases in the world (522,000 deaths). In women, this type of cancer is a frightening threat (324,000 deaths, 14.3% of the total cases). Meanwhile, in strong and developed countries, breast cancer is second only to lung cancer-causing death (198,000 deaths, 15.4%).[2] The process of cellular survival of cancer cells is regulated by a variety of mechanisms, including EGFR and mTOR. EGFR is part of the HER transmembrane receptor. The inappropriate activity of the EGFR will have an impact on the formation of cancer cells.[3,4] Inhibition of EGFR activity will weaken cancer cells so that it is beneficial for the cancer therapy process.[5] Apart from EGFR, mTOR also has the same role in the process of cancer cell development, especially cell proliferation and growth. mTOR is in the PI3K / Akt / mTOR signaling pathway which is known play a role in the regulation of apoptosis, metastasis, and resistance of cancer cells to radiotherapy. In the last decade, the combination of PI3K/Akt/mTOR inhibitor with other therapy develop significant progress to overcome less effective treatment.[6-7]

The search for active compounds from plants to treat cancer continues. Active compounds such as cardiac glycosides are reported to inhibit cancer cell activity. Cardiac glycosides are steroid compounds with unsaturated α and β lactone rings. Cardiac glycosides are known as compounds that can affect cardiac activity through their influence on Na+ and K+ pumps.[8-10] *Vernonia amygdalina* has many pharmacological

effects including antimalarial, antidiabetic, anti-cancer, hepatoprotection, nephroprotection, analgesic, antibacterial, antioxidant and also has an inotropic effect on the heart. *Vernonia amygdalina* has contained various secondary metabolites including sesquiterpene lactone (vernolide, vernodalol, vernoamygdalin, vernolepin), Flavonoid (luteolin, luteolin 7-O-beta-glucoronoside dan luteolin 7-O-glucoside), and also contained cardiac glycosides (vernonioside D and E).[11-13] Based on this explanation, the vernonioside D and E activity testing will be carried out against the EGFR and mTOR receptors using the *in silico method.*



Vernonioside D Vernonioside E

Fig.-1: Chemical Structure of Vernonioside D and Vernonioside E

EXPERIMENTAL

Aspire Vivobook operated by Windows 7 Home Basic, Intel® CoreTM i5 (3.4 GHz), 64-bit, hard disc drive 320 GB and RAM 4 GB DDR3 L were used to run the molecular docking process. In silico docking using Autodock Vina PyRx 9.5 program and visualized by Ligplot 2.1. The model of three dimensions of enzyme structure used in this research was epidermal growth factor receptor (EGFR) and mammalian target of rapamycin (mTOR) binding pocket with the Protein Data Bank (PDB) code 1M17 and 3L16., which were obtained through from http://www.rscb.org/pdb. The Marvin sketch program generates the three-dimension conformation models of vernonioside D and E.[14-15]

RESULTS AND DISCUSSION

In-silico Analysis

Overexpression from EGFR and mTOR has long been found in the development of cancer cells, including breast cancer.[16] EGFR is part of the tyrosine kinase receptor. EGFR has an important role in physiological terms. EGFR development in epithelial tissue development, homeostasis and tumor cell development.[17] mTOR is an attractive protein used as a target for therapy in cancer. mTOR has distinctive functions such as convergence points for many growth stimuli and through downstream controlling cellular processes that contribute to cancer cell initiatives.[18]

Therefore, opposing EGFR and mTOR is very effective in finding therapies that inhibit the development of cancer cells. In this experiment the testing of the activity of natural compounds in silico against EGFR and mTOR. In silico docking between cardiac glycosides from *Vernonia amygdalina* Delile. Leaves (vernonioside D and E) into the 1M17 and 3L16 binding pocket result in the docking score in Tables-1 and 2.

Table-1: Docking Score between Vernonioside D and E in the Pocket of mTOR (3L16)

No	Compound	Binding Affinity (Kcal/mol)
1	Thienopyrimidin-2-yl-aminopyrimidines	-9.2
2	Vernonioside E	-6.6
3	Vernonioside D	-6.3

Table-1 showed docking score as a description mTOR inhibitory effect of Vernonioside D and E as natural compounds and Thienopyrimidin-2-yl-aminopyrimidines as comparison compound. Vernonioside D and E

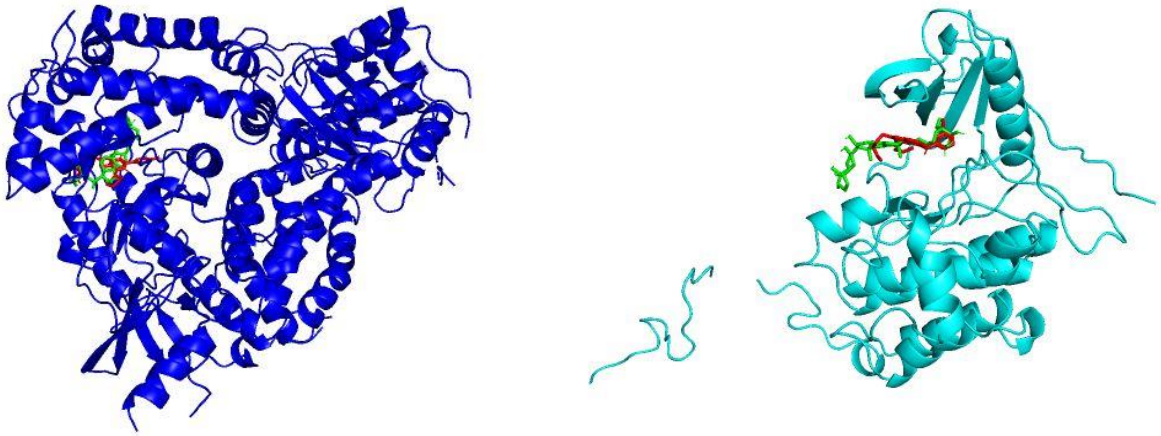
have an affinity binding value of -6.6 Kcal/mol and -6.3 Kcal/mol, while Thienopyrimidin-2-yl-aminopyrimidines was -9.2 Kcal/mol. The result showed Thienopyrimidin-2-yl-aminopyrimidines has a better activity in mTOR inhibited. However, Vernonioside D and E also can inhibit mTOR.

Table-2: Docking Score between Vernonioside D and E in the Pocket of EGFR (IM17)

No.	Compound	Binding Affinity (Kcal/mol)
1	Erlotinib	-6.9
2	Vernonioside E	-8.6
3	Vernonioside D	-10.4

EGFR Inhibitory activity of Vernonioside D and E was carried out by *In-silico* test. The result in Table-2 showed Vernoniosed D and E have an activity to inhibited EGFR with a docking score value of -10.4 Kcal/mol and -8.6 Kcal/mol. Erlotinib used as a comparison compound has an activity of -6.9 Kcal/mol docking score. Based on the result, Vernonioside D has a better activity to inhibited EGFR than Vernonioside E and Erlotinib. The lowest energy produced from the bond between the ligand and protein shows better inhibitory activity.[19]

The activity of the test material (ligands) binds to a receptor is influenced by many factors, one of which is the chemical bond formed between the test material (ligands) and amino acids at the receptor.[14] The binding of amino acid residues to ligands was showed in Table-3.



(a) (b)

Fig.-2: Three Dimentional Binding Form of (a) mTOR (control (red); Vernonioside E (green); (b) EGFR (control (red); Vernonioside D (green)

Table-3: Interaction of Vernonioside D and E to Amino Residues of EGFR and mTOR

Ligands	Amino Acids Involved	
	Hydrogen-Binding Interaction	Hydrophobic Interaction
Thienopyrimidin-2-yl-aminopyrimidines	Ile879, Leu838, Ile831, Ile881, Ala805, Met804, Lys890, Trp812, Tyr867	Asp841
Vernonioside E	Lys802, Thr886, Val882, Trp812, Ala885, Met804, Met953, Ile963, Ser806, Asp950, Lys807, Lys808, Ile963, Ile831, Thr887	Asn951, Asp964, Lys833
Erlotinib	Glu783, Met742, Lys721, Leu764, Thr766, Thr830, Leu694, Phe699	Asp831, Met769
Vernonioside D	His781, Phe771, Glu780, Tyr777, Leu820, Gly772, Ile720, Leu764, Asp831, Met742, Val702, Cys773, Asp776, Leu694	Lys721, Ala719, Thr776, Glu738, Thr830

Table-3 showed hydrogen-bonding interaction and hydrophobic interaction of ligands and amino acids. Based on the result showed that ligands bond to different amino acids. Thienopyrimidin-2-yl-aminopyrimidines have a hydrogen bond interaction with Ile879, Leu838, Ile831, Ile881, Ala805, Met804, Lys890, Trp 812, Tyr867 and hydrophobic interaction with Asp841. Vernonioside E and Vernonioside D

have a hydrogen bond interaction and hydrophobic interaction with their respective amino acids Lys802, Thr886, Val882, Trp812, Ala885, Met804, Met953, Ile963, Ser806, Asp950, Lys807, Lys808, Ile963, Ile831, Thr887 and Asn951, Asp964, Lys833 for Vernonioside E and His781, Phe771, Glu780, Tyr777, Leu820, Gly772, Ile720, Leu764, Asp831, Met742, Val702, Cys773, Asp776, Leu694 and Lys721, Ala719, Thr776, Glu738, Thr830 for Vernonioside D. Hydrogen bond and hydrophobic interaction occurred on Erlotinib as Glu783, Met742, Lys721, Leu764, Thr766, Thr830, Leu694, Phe699 and Asp831, Met769. The results of visualization of Vernoniosides D and Vernoniosides E to EGFR and mTOR using Ligplot 2.1 can see in Fig.-2 Differences in affinity between test compounds to receptors may occur due to differences in bonding between each test compound with amino acids and the type of bond that occurs.[20]

CONCLUSION

The results reveal that Vernonioside E and D are effective as anticancer through downregulation of EGFR and mTOR proteins.

ACKNOWLEDGEMENT

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REFERENCES

1. A. Jemal, R. Siegel, E. Ward, Y. Hao, J. Xu, M. J. Thun, *CA: A Cancer Journal of Clinicians*, **59**, 225(2009), https://doi.org/10.3322/caac.20006
2. R. L. Siegel, K. D. Miller, A. Jemal, *CA: A Cancer Journal of Clinicians*, **65**, 5(2015), https://doi.org/10.3322/caac.21254
3. Y. Safdari, M. Khalili, M. A. Ebrahimzadeh, Y. Yazdani, and S. Farajnia, *Pharmacological Research*. **93**, 1(2015), https://doi.org/10.1016/j.phrs.2014.12.004
4. Y. Safdari, M. Khalili, S. Farajnia, M. Asgharzadeh, Y. Yazdani, M. Sadeghi, *Clinical Biochemistry*, **47**, 13(2014), https://doi.org/10.1016/j.clinbiochem.2014.05.066
5. T. M. Brand, and D. L. Wheeler, *Cancer Biology and Therapy*, **11**, 3(2011), https://doi.org/10.4161/cbt.11.3.14696
6. B. T. Hennessy, D. L. Smith, P. T. Ram, Y. Lu, and G. B. Mills, *Nature Reviews Drug Discovery*, **4**, 988(2005), https://doi.org/10.1038/nrd1902
7. A. Joshi, M. Gadhwal, and U. J. Joshi, *International Journal of Pharmacy and Pharmaceutical Sciences*, **7(6)**, 77(2015).
8. P. Erasto, D. S. Grierson, and A. J. Afolayan, *Food Chemistry*, **104(2)**, 636(2007), https://doi.org/10.1016/j.foodchem.2006.12.013
9. A. N. Magpusao, G. Omolloh, J. Johnson, J. Gascon, M. W. Pechzuh, and G. Fenteany, *Chemical Biology*, **10(2)**, 561(2015), https://doi.org/10.1021/cb500665r
10. A. M. Marzouk, and O. B. Abd Elhalim, *Natural Product Research*, **30(7)**, 741(2015), https://doi.org/10.1080/14786419.2015.1062004
11. Hajime Ohigashi,Mitsuo Jisaka,Teruyoshi Takagaki,Hiroshi Nozaki,Toshiji Tada,Michael A. Huffman,Toshisada Nishida,Mikio Kaji and Koichi Koshimizu, *Agricultural and Biological Chemistry*, **55(4)**, 1201(1991), https://doi.org/10.1080/00021369.1991.10870699
12. S. Patel, *Biomedicine & Pharmacotherapy*, **84**, 1036(2016), https://doi.org/10.1016/j.biopha.2016.10.030
13. Jing Wang, Hua Song, Xiaoxue Wu, Shuyi Zhang, Xuemin Gao, Funan Li, Xuan Zhu and Qing Chen, *Molecules*, **23(3)**, 579(2018), https://doi.org/10.3390/molecules23030579
14. R. A. Syahputra, U. Harahap, A. Dalimunthe, P. Nasution, G. Haro, Widodo, D. H. Utomo and D. Satria, *Rasayan Journal of Chemistry*, **13(2)**, 796(2020), https://doi.org/10.31788/RJC.2020.1325638
15. P. A. Z. Hasibuan, P. Sitorus, D. Satria, *Asian Journal of Pharmaceutical Clinical Research*, **10(5)**, 306(2017), https://doi.org/10.22159/ajpcr.2017.v10i5.16931
16. J. Wang, H. Ji, X. Niu, L.Yin, Y. Wang, Y. Gu, D. Li, H. Zhang, M. Lu, F. Zhang and Q. Zhang, *Disease Markers*, Article ID 6103542, 1-12(2020), https://doi.org/10.1155/2020/6103542

17. S. Sigismund, D. Avanzato and L. Lanzetti, *Molecular Oncology*, **12(1)**, 3(2018), https://doi.org/10.1002/1878-0261.12155
18. A. C. de Molo, E. Paulino and A. H. I. Garces, *Oxidative Medicine and Cellular Longevity*, Article ID 4809751, 1-8(2017), https://doi.org/10.1155/2017/4809751
19. Franklyn Nonso Iheagwam, Olubanke Olujoke Ogunlana, Oluseyi Ebenezer Ogunlana, Itunuoluwa Isewon, Jelili Oyelade, *Bioinformatics and Biology Inshights*, 13(2019), https://doi.org/10.1177/1177932218821371
20. J. L. Wang, L. Li, M .B. Hu, B. Wu, W. X. Fan, W. Peng, D. N. Wei, C. J. Wu, *Computational Biology and Chemistry*, **78**, 297(2019), https://doi.org/10.1016/j.compbiolchem.2018.12.021

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Kepada: weny@ung.ac.id

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FLAVONOID GLYCOSIDE COMPOUND FROM TOMBILI SEED (*Caesalpinia bonducella*) AND ITS ANTIOXIDANT ACTIVITY

Weny J. A. Musa[1,✉], Nurhayati Bialangi[1], Ahmad Kadir Kilo[1], C. J. Lamangantjo[2], Boima Situmeang[3] and Agus Malik Ibrahim[3]

[1]Department of Chemistry, Faculty of Mathematics and Natural Sain, Gorontalo State University, Gorontalo-96128, Indonesia

[2]Department of Biology, Faculty of Mathematics and Natural Sains, Gorontalo State University, Gorontalo-96128, Indonesia

[2]Department of Chemistry, Sekolah Tinggi Analis Kimia Cilegon, Banten-42161, Indonesia

✉Corresponding Author: wenymusa977@gmail.com

ABSTRACT

Caesalpinia bonducella, known as 'tombili' belongs to the family of *Fabaceae.* Tombili has been empirically used as traditional medicine. In a previous study, phytochemical screening showed that tombili seed contained alkaloid, flavonoid, terpenoid, and tannin compounds. This research aimed to isolate an antioxidant compound from tombili seed extract. Fractionated using *n*-hexane, ethyl acetate, and methanol as a solvent. All fractions were tested for their antioxidant potential. The ethyl acetate fraction gave a better antioxidant potential (IC_{50} 86.153±4.22 ppm) than it has purified. Characterization of an isolated compound using various spectroscopies data, including UV, FTIR, 1D-NMR, 2D-NMR, and LCMS/MS. The structure of the isolated compound was suggested as 7- (β-D-Glucopyranosyloxy) 5-hydroxy-2-(4-hydroxyphenyl)-6-methoxy-4H-1-benzopyran-4-one (homoplantaginin). The IC_{50} value of the isolated compound was 40.53 ±3.13 ppm, indicating the isolated compound has potent antioxidant activity.

Keywords: *Caesalpinia Bonducella,* Flavonoid, Homoplantaginin, and Tombili.

RASĀYAN*J. Chem.*, Vol. 15, No.4, 2022

INTRODUCTION

Caesalpinia bonducella known as tombili belongs to the family of *Fabaceae.*[1,2] Tombili can be found in Gorontalo province, Indonesia.[3] In Indonesia, *C. bonducella* is known as tombili and areuy.[4,5] Previous studies showed that seed extract of tombili contained alkaloids, flavonoids, terpenoids, and tannin compounds.[6-9] The seed kernel of tombili has traditionally been used by the community as a medicinal plant to treat cough, malaria, and anthelmintic diseases. The seed extract of tombili has several antioxidant, antidiabetic, and antibacterial activities. According to Esmaeili *et al*., 2015 tombili extract has a pharmacological activity that can decrease fasting glucose levels. In addition, tombili seed extract has an activity to reduce glucose levels.[10] Tombili seed methanol extract was also reported to have antihyperglycemic and hypolipidemic activity in induced diabetic rats.[11-12] The flavonoid compounds have the potential as natural antioxidants. In this study, isolated compounds using the chromatography method. Antioxidant content analysis from an isolated compound of tombili seed was evaluated. [13]Antioxidant activity *in vitro* method was used DPPH scavenging. Based on the previous study, this research aimed to isolate flavonoid glycoside compound from tombili seed extract as a natural antioxidant.[13]

EXPERIMENTAL

The materials used in this research are tombili seeds, collected from Bobohu villages, Gorontalo province, Indonesia. Tombili was identified at the Laboratory of Biology Department (plant taxonomy), Universitas Negeri Gorontalo, and Indonesia. The seed powder of tombili (1.0 kg) was macerated in methanol for 2 x 24 h. The methanol extract (210 g) was partitioned to obtain *n*-hexane, ethyl acetate, and methanol fractions. The total solvent used was 2.5 L, respectively. The fractions were obtained from *n*-hexane (29.5

g) and ethyl acetate (50.2 g), and methanol (70.2 g) extracts. All extracts test for antioxidant activity according to inhibition percentage. The higher antioxidant activity of ethyl acetate fraction then purification to give pure isolated antioxidant compound.

Antioxidant Activity Test

DPPH Solution Preparation Crystalline DPPH was weighed and dissolved in ethanol at a concentration of 0,004 %. This solution was freshly prepared every time and kept under low temperature and light. The antioxidant test was performed following Gurning *et al.* (2021).[13] Extract (1.2 mL) was added to 0.3 m DPPH solution to obtain a 1.5 mL mixture, then incubated the mixture of sample, methanol, and DPPH for 30 minutes. The amount of unreacted DPPH was determined using UV-Vis at 515 nm. A similar procedure was applied to the blank solution (DPPH without sample). The following formula calculated the percentage of free radical inhibition by the sample:

$$\%\ \text{Inhibition} = \frac{absorbance\ control - absorbance\ sample}{absorbance\ control}\ x\ 100\%$$

The antioxidant activity data were analyzed using probit analysis to obtain the IC_{50}. The experiment was performed in triplicate.

RESULTS AND DISCUSSION

Antioxidant, Isolation, and Determination of Isolated Compound

The highest antioxidant activity of all fractions was the ethyl acetate fraction (Tabel-1). Bioactivity-guided chromatography isolated the flavonoid glycoside compound from ethyl acetate fraction of tombili seed. TLC checked the purification of the isolated compound on Silica G60 F254 with observed on UV at λ 254 and 365 nm. The isolated compound reacted with the coloring reagent of $FeCl_3$ to give amorphous yellow spots. Then the structure of the isolated compound was elucidated by analysis of various spectroscopies data (UV, FT-IR, NMR, and LCMS).

Table-1: Antioxidant Activity Test of Fractions of Tombili Seed

fractions	IC_{50} value replicated			IC_{50} average ± SD
	1	2	3	
n-Hexane	100.798	99.505	102.495	100.933± 1.50
Ethyl acetate	88.499	81.286	88.675	86.153±4.22
Methanol	93.551	95.890	92.718	94.053±1.64

The isolated compound from ethyl acetate fraction (20 mg) was obtained in yellow amorphous form. The isolated compound was soluble in methanol solvent. The IR spectra of the isolated compounds showed an absorptions peak at 3360 $cm^{-1}$for hydroxyl group (-OH). Absorptions peaks at 1658,33 and 1326,42 cm^{-1} for carbonyl (C=O) and olefinic (C=C) functional groups. Absorptions peaks at 2941,33 $cm^{-1}$for (C-H) group. [14-16] LCMS spectra data showed that isolated compounds were $C_{22}H_{22}O_{11}$ (m/z 463.1222) $[M+H]^+$. The ^{1}H-NMR spectrum (500 MHz, methanol D-4): showed proton signal at δH 11.91ppm (1H, s, 5-OH), δH 7.46 ppm (2H, d, H-2', 6'), δH 6.92 ppm (1H, s, H-8), δH 6.94 ppm (2H, d, H-3', 5'), δH 6.83 ppm (1H, s, H-3), δH 5.11ppm (1H, d, H-1"), δH 3.77 ppm (3H, s, 6-OCH3), δH 3.35 ppm (1H, brd, H-6"a), δH 3.19-3.42 ppm (5H, H-2", 3", 4", 5", 6b"). The ^{13}C-NMR spectra (125 MHz, methanol D-4): δC 178.31 ppm (C-4) belongs to carbonyl group (C=O), δC 163.25 (C-2) belongs to olefinic compound, δC 160.45 (C-4'), δC 149.21 (C-7), δC 147.76 (C-9), δC 145.12 (C-5), δC 131.49 (C-6), δC 127.56 (C-2', 6'), δC 118.89 (C-1'), 116.08 (C-3', 5'), 105.73 (C-10) belongs to methin hydroxy group (CH-OH), 102.64 (C-3), 100.22 (C-1"), 92.42 (C-8), 77.26 (C-3"), 76.29 (C-5"), δC 73.12 (C-2"), δC 69.32 (C-4"), δC 59.49 (C-6"), δC 60.59 (6-OCH_3) belong to methoxy group (Table-2).

Table-2: The NMR Data of Isolated Compound (Homoplantaginin)

Carbon position	δC (ppm)	δH (Ppm)
C4	178.31	11.91 (1H, s, 5-OH)
C2	163.25	7.46 (2H, d, H-2', 6')
C4'	160.45	6.92 (1H, s, H-8)
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C9	147.76	6.83 (1H, s, H-3)
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C6	131.49	3.77 (3H, s, 6-OCH3)
C2', C6'	127.56	3.35 (1H, H-6")
C1	118.89	3.19-3.42 (5H, H-2", 3", 4", 5", 6")
C3', C5'	116.08	6.65 (1H, s, H-3)
C10	105.73	
C3	102.64	
C1"	100.22	
C8	92.42	
C3"	77.26	
C5"	76.29	
C2"	73.12	
C4"	69.32	
C6"	59.49	
C6	60.59 OCH_3	

The ^{13}C-NMR, DEPT 135°, and ^{1}H-NMR showed that the isolated compound contained 22 signals of carbons (Table-2). The ^{13}C-NMR spectra (Fig.-1) of the isolated compound indicated signals for twenty-two carbons, including one methoxy signal (-OCH_3), one methylene (CH_2), and eleven sp^2 methynes (-CH), and nine quaternary carbons. Chemical sift at δc 60.59 ppm indicated the isolated compound contained methoxy group (-OCH_3).[17] The chemical sift at δc 59,49-77.26 ppm means the isolated compound had glucose groups.[18] The glucose group was confirmed by the HMBC spectra data by correlation of H-1" connected with δC C-7 (149.21 ppm). Therefore the isolated compound was suggested as 7- (β-D-Glucopyranosyloxy) 5-hydroxy-2-(4-hydroxyphenyl)-6-methoxy-4H-1-benzopyran-4-one (homoplantaginin).[19-20] According to a previous study from various literature, the isolation of homoplantaginin compound from ethyl acetate fraction of tombili seed was first reported.

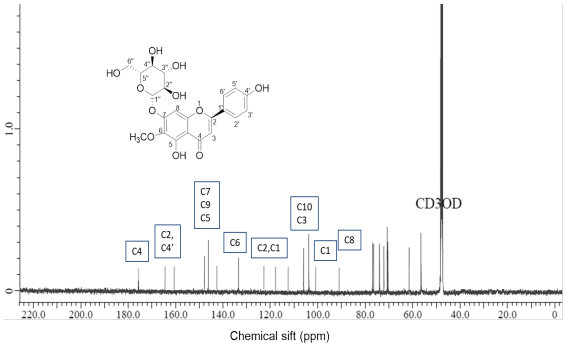

Fig.-1: The ^{13}C-NMR Spectrum of the Isolated Compound (Homoplantaginin)

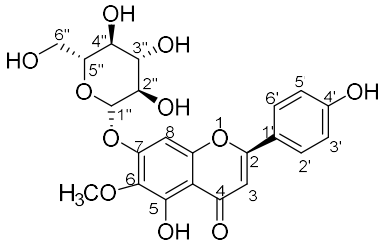

Fig.-2: The Chemical Structure of Isolated Compound 7- (β-D-Glucopyranosyloxy) 5-hydroxy-2-(4-hydroxyphenyl)-6-methoxy-4H-1-benzopyran-4-one (Homoplantaginin)

The LCMS/MS showed the molecular formula of the isolated compound was $C_{22}H_{22}O_{11}$ with LCMS-MS: m/z 463.1222 [M+H]+ (Fig.-3). The retention time of the isolated compound was 7.16 min (Fig.-4). Homoplantaginin compounds have been isolated by Kil et al., 2020 from *Salvia plebeia* using HPLC.

Jang et al., 2017 and lee et al., 2010 have isolated homoplantaginin compounds from *Salvia plebeian*. According to Meng et al., 2022 homoplantaginin has an activity to protect VECs by activating Nrf2 and thus inhibited atherosclerosis in apoE-/- mice.[18-21]

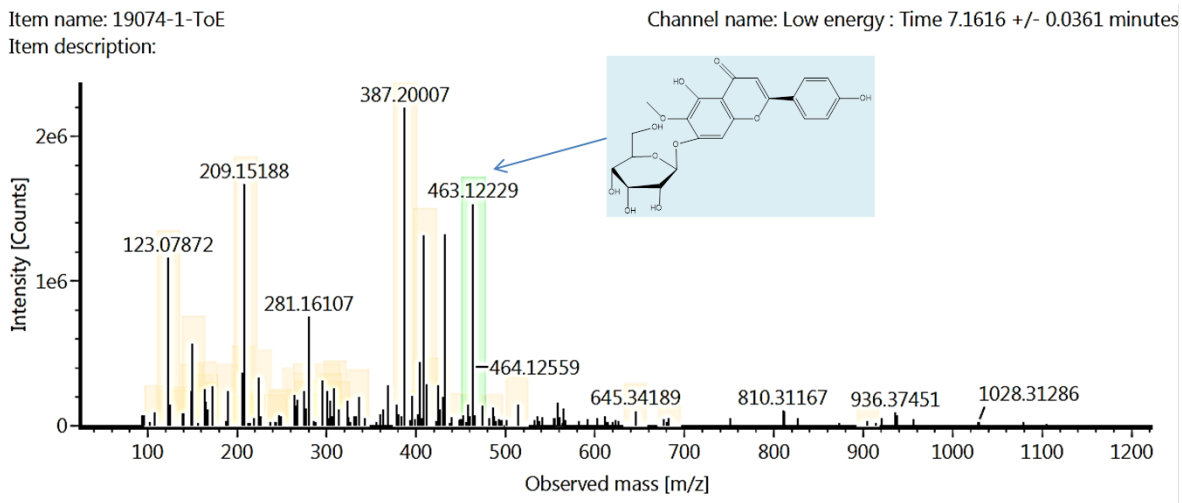

Fig.-3: The LCMS/MS Mass Spectra of the Isolated Compound

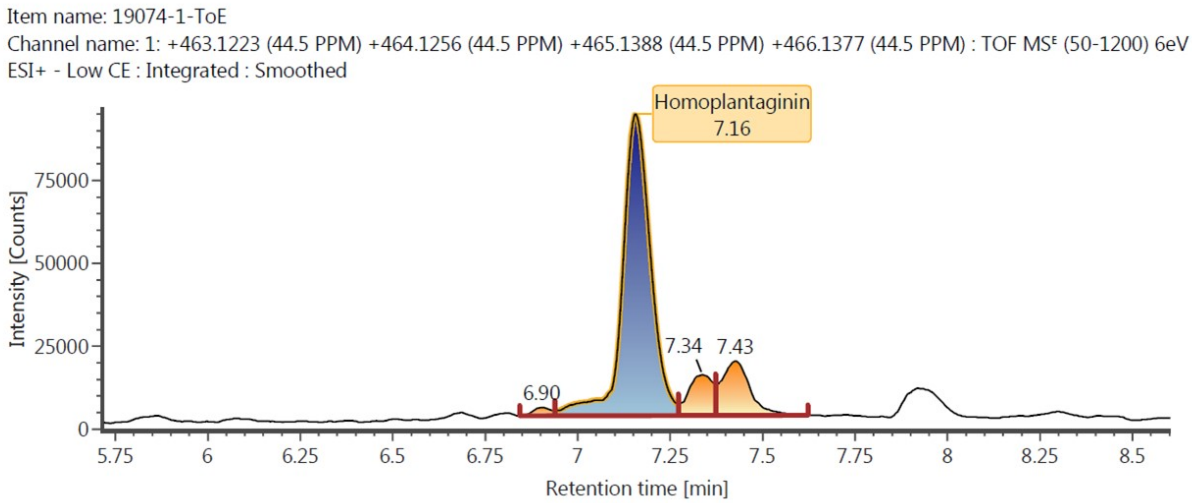

Fig.-4: The Retention Time (Min) of the Isolated Compound

Antioxidant Activity of 7- (β-D-Glucopyranosyloxy) 5-hydroxy-2-(4-hydroxyphenyl)-6-methoxy-4H-1-benzopyran-4-one (homoplantaginin)

Antioxidant activity of isolated compound using DPPH method shown in Table-3. The concentration and inhibition percentage curve was constructed, and the linear regression equation obtained from the curve was used to calculate the IC_{50}. The IC_{50} value of the isolated compound was 40.53 ±3.13 ppm. This result indicated that the isolated compound has potent antioxidant activity.

Table-3: Absorbance and Inhibition Percentage of the Isolated Compound

Concentration (ppm)	Absorbance replicated		% Inhibition replicated	
	1	2	1	n 2
0	0.601	0.612	0	0
20	0.397	0.411	33.94	32.84
40	0.258	0.244	57.07	60.13
60	0.126	0.133	79.03	78.27
80	0.068	0.073	88.68	88.07

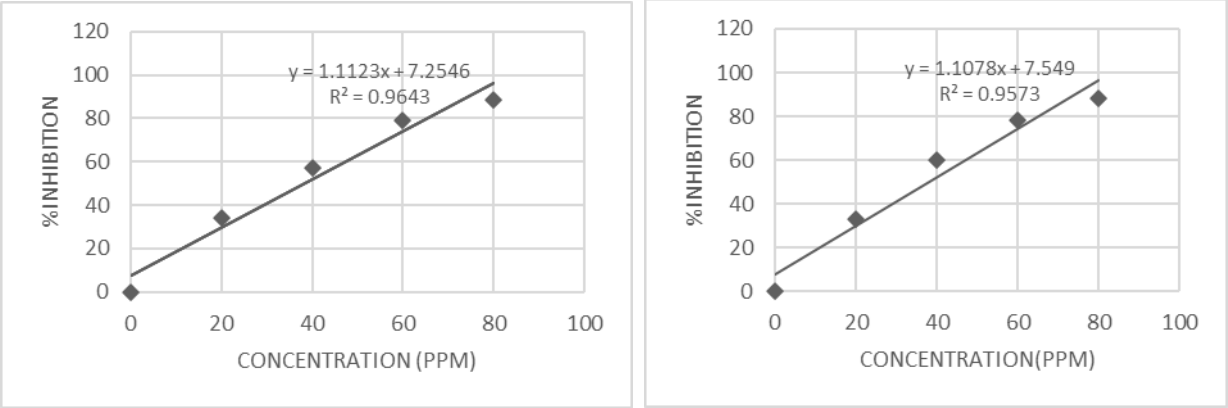

Fig.-5: Linear Regression of an Antioxidant of the Isolated Compound

CONCLUSION

The isolated compound was suggested as 7- (β-D-Glucopyranosyloxy) 5-hydroxy-2-(4-hydroxyphenyl)-6-methoxy-4H-1-benzopyran-4-one (homoplantaginin). The IC_{50} value of the isolated compound was 40.53 ±3.13 ppm, indicating that the isolated compound has potent antioxidant activity.

REFERENCES

1. W.J.A. Musa, S. Duengo, A.K. Kilo and B. Situmeang, *Jurnal Pendidikan Kimia*, **12**, 3 (2020) https://doi.org/10.24114/jpkim.v12i3.21165
2. P.D. Khandagale, A.V. Puri, Y.N. Ansari and R.Y. Patil, *International Journal of Pharmacy and Biological Sciences,* **8**, 3 (2018)
3. V.P. Vadlakonda and S.G. Chaudhari, *Indo American Journal of Pharmaceutical Research.* **9**, 12 (2019)
4. S. Shukla, A. Mehta, J. John, S. Singh, P. Mehta and S.P. Vyas, *Food and Chemical Toxicology,* **47**, (2009) https://doi.org/10.1016/j.fct.2009.04.040
5. E.N. Sembiring, B. Elya and R. Sauriasari, *Pharmacogn Journal,* **10**, 1 (2018) https://doi.org/10.5530/pj.2018.1.22
6. T. Liu, X. Li, Z. Ning, S. Qi and H. Gao, *Natural Product Research,* (2021) https://doi.org/10.1080/14786419.2021.1896511
7. F.N. Iheagwam, O.O. Ogunlana, O.E. Ogunlana, I. Isewon and J. Oyelade, *Bioinformatics and Biology Insights,* **13**, (2018) https://doi.org/10.1177/1177932218821371
8. A. Iftikhar, B. Aslam, M. Iftikhar, W. Majeed, M. Batool, B. Zahoor, N. Amna, H. Gohar and I. Latif, *Hindawi Oxidative Medicine and Cellular Longevity,* (2020) https://doi.org/10.1155/2020/9020219
9. M. Sindete, A. Gbankoto, R. Osseni, N.D. Tossavi, S. Azonbakin, L.B. Moussa, and A. Laley, *Hindawi Evidence-Based Complementary and Alternative Medicine,* (2021) https://doi.org/10.1155/2021/6620026
10. V. Larasati, W. Pangkahila and A.A.G. Budhiarta, *Jurnal kedokteran dan kesehatan*, **3**, 2 (2016)
11. M. Modak, P. Dixit, J. Londhe, S. Ghaskadbi, and T.P.A. Devasagayam. *Journal of Clinical Biochemistry and Nutrition* , **40**, 3 (2006) https://doi.org/10.3164/jcbn.40.163
12. N.K. Kakade, S.S. Pingale and M.G. Chaskar, *International research journal of pharmacy*, **7**, 12 (2016) https://doi.org/10.7897/2230-8407.0712139
13. K. Gurning, W. Haryadi and H. Sastrohamidjojo, *Rasayan Journal of Chemistry*, **14**, 1 (2021), https://doi.org/10.31788/RJC.2021.1416077
14. M.H Satari, B. Situmeang, I.P Yuda and D. Kurnia, *Jurnal Kimia Valensi*, **2**, 5 (2019), https://doi.org/10.15408/jkv.v5i2.8864
15. T. Okselni, A. Santoni, A. Dharma, and M. Efdi, *Rasayan Journal of Chemistry*, 12(1), 146(2019), https://doi.org/10.31788/RJC.2019.1215019

16. H.W. Kil, T. Rho, Y.J. Seo, A. Yu and K.D. Yoon, *Natural Product Sciences*, 26, 3 (2020) https://doi.org/10.20307/nps.2020.26.3.236
17. H.J. Jang, S.J. Lee, C.Y. Kim, J.T. Hwang, J.H. Choi, J.H. Park, S.W. Lee and M.C. Rho, *Molecules*, 22, 1279 (2017) http://dx.doi.org/10.3390/molecules22081279
18. X. Jin, J. Qian and Y. Lu, *Journal of Medicinal Plants Research*, 5, 9 (2011) http://www.academicjournals.org/JMPR
19. N. Meng, K. Chen, Y. Wang, J. Hou, W. Chu, S. Xie, F. Yang and C. Sun, *Molecules*, 27, 1990 (2022) https://doi.org/10.3390/molecules27061990
20. G.T. Lee, C.H. Duan, J.N. Lee, K.S. Lee, J.T. Hong and K.K. Lee, *Natural Product Sciences*, 16, 4 (2010)
21. T. Okselni, A. Santoni, A. Dharma, and M. Efendi, *Rasayan Journal of Chemistry*, 12(1), 146(2019), https://doi.org/10.31788/RJC.2019.1215019

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FLAVONOID GLYCOSIDE COMPOUND FROM TOMBILI SEED (*Caesalpinia bonducella*) AND ITS ANTIOXIDANT ACTIVITY

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ABSTRACT

Caesalpinia bonducella, known as 'tombili' belongs to the family of *Fabaceae*. Tombili has been empirically used as traditional medicine. In a previous study, phytochemical screening showed that tombili seed contained alkaloid, flavonoid, terpenoid, and tannin compounds. This research aimed to isolate an antioxidant compound from tombili seed extract. Fractionated using *n*-hexane, ethyl acetate, and methanol as a solvent. All fractions were tested for their antioxidant potential. The ethyl acetate fraction gave a better antioxidant potential (IC_{50} 86.153±4.22 ppm) than it has purified. Characterization of an isolated compound using various spectroscopies data, including UV, FTIR, 1D-NMR, 2D-NMR, and LCMS/MS. The structure of the isolated compound was suggested as 7- (β-D-Glucopyranosyloxy) 5-hydroxy-2-(4-hydroxyphenyl)-6-methoxy-4H-1-benzopyran-4-one (homoplantaginin). The IC_{50} value of the isolated compound was 40.53 ±3.13 ppm, indicating the isolated compound has potent antioxidant activity.

Keywords: *Caesalpinia Bonducella*, Flavonoid, Homoplantaginin, and Tombili.

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C6	60.59 OCH_3	

The ^{13}C-NMR, DEPT 135°, and ^{1}H-NMR showed that the isolated compound contained 22 signals of carbons (Table-2). The ^{13}C-NMR spectra (Fig.-1) of the isolated compound indicated signals for twenty-two carbons, including one methoxy signal (-OCH_3), one methylene (CH_2), and eleven sp^2 methynes (-CH), and nine quaternary carbons. Chemical sift at δc 60.59 ppm indicated the isolated compound contained methoxy group (-OCH_3).[17] The chemical sift at δc 59,49-77.26 ppm means the isolated compound had glucose groups.[18] The glucose group was confirmed by the HMBC spectra data by correlation of H-1" connected with δC C-7 (149.21 ppm). Therefore the isolated compound was suggested as 7- (β-D-Glucopyranosyloxy) 5-hydroxy-2-(4-hydroxyphenyl)-6-methoxy-4H-1-benzopyran-4-one (homoplantaginin).[19-20] According to a previous study from various literature, the isolation of homoplantaginin compound from ethyl acetate fraction of tombili seed was first reported.

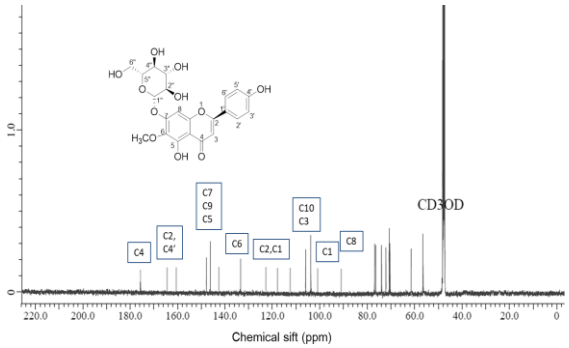

Fig.-1: The ^{13}C-NMR Spectrum of the Isolated Compound (Homoplantaginin)

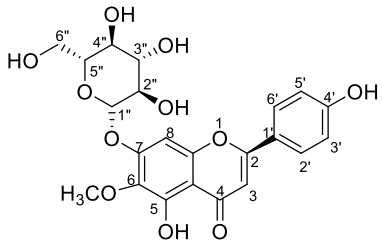

Fig.-2: The Chemical Structure of Isolated Compound 7- (β-D-Glucopyranosyloxy) 5-hydroxy-2-(4-hydroxyphenyl)-6-methoxy-4H-1-benzopyran-4-one (Homoplantaginin)

The LCMS/MS showed the molecular formula of the isolated compound was $C_{22}H_{22}O_{11}$ with LCMS-MS: m/z 463.1222 [M+H]+ (Fig.-3). The retention time of the isolated compound was 7.16 min (Fig.-4).

Homoplantaginin compounds have been isolated by Kil et al., 2020 from *Salvia plebeia* using HPLC. Jang et al., 2017 and lee et al., 2010 have isolated homoplantaginin compounds from *Salvia plebeian*. According to Meng et al., 2022 homoplantaginin has an activity to protect VECs by activating Nrf2 and thus inhibited atherosclerosis in apoE-/- mice.[18-21]

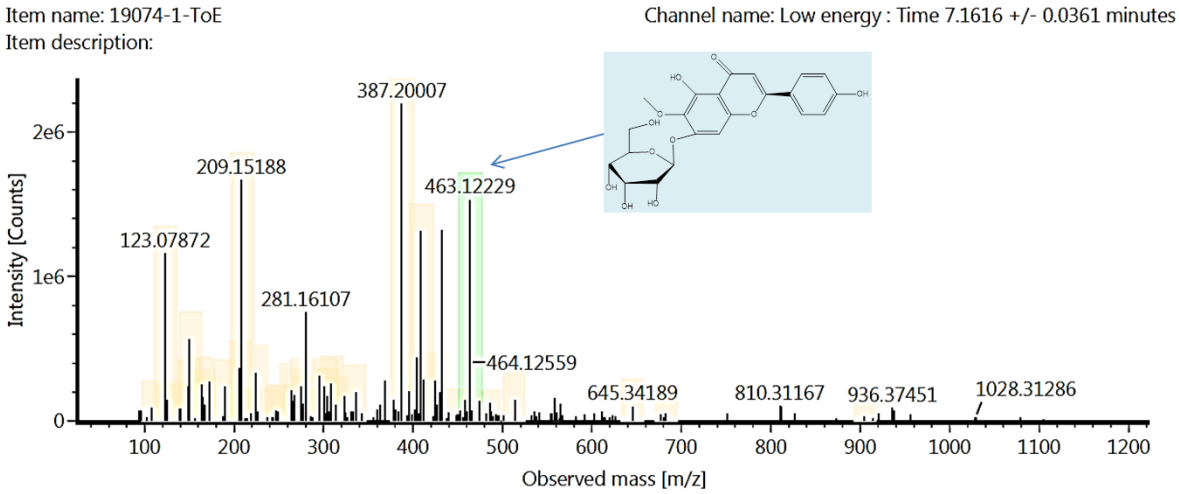

Fig.-3: The LCMS/MS Mass Spectra of the Isolated Compound

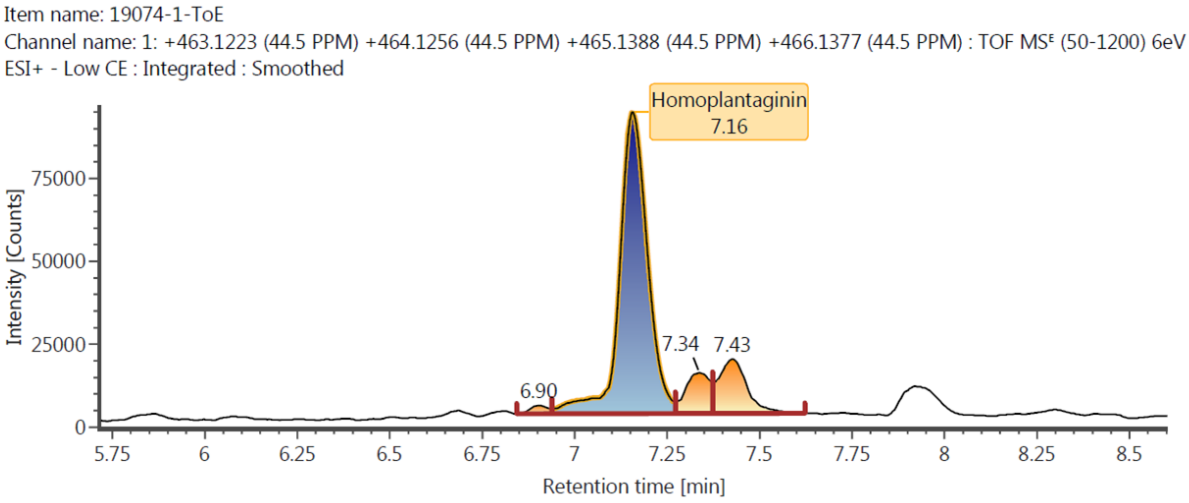

Fig.-4: The Retention Time (Min) of the Isolated Compound

Antioxidant Activity of 7- (β-D-Glucopyranosyloxy) 5-hydroxy-2-(4-hydroxyphenyl)-6-methoxy-4H-1-benzopyran-4-one (homoplantaginin)

Antioxidant activity of isolated compound using DPPH method shown in Table-3. The concentration and inhibition percentage curve was constructed, and the linear regression equation obtained from the curve was used to calculate the IC_{50}. The IC_{50} value of the isolated compound was 40.53 ±3.13 ppm. This result indicated that the isolated compound has potent antioxidant activity.

Table-3: Absorbance and Inhibition Percentage of the Isolated Compound

Concentration (ppm)	Absorbance replicated		% Inhibition replicated	
	1	2	1	n 2
0	0.601	0.612	0	0
20	0.397	0.411	33.94	32.84
40	0.258	0.244	57.07	60.13

60	0.126	0.133	79.03	78.27
80	0.068	0.073	88.68	88.07

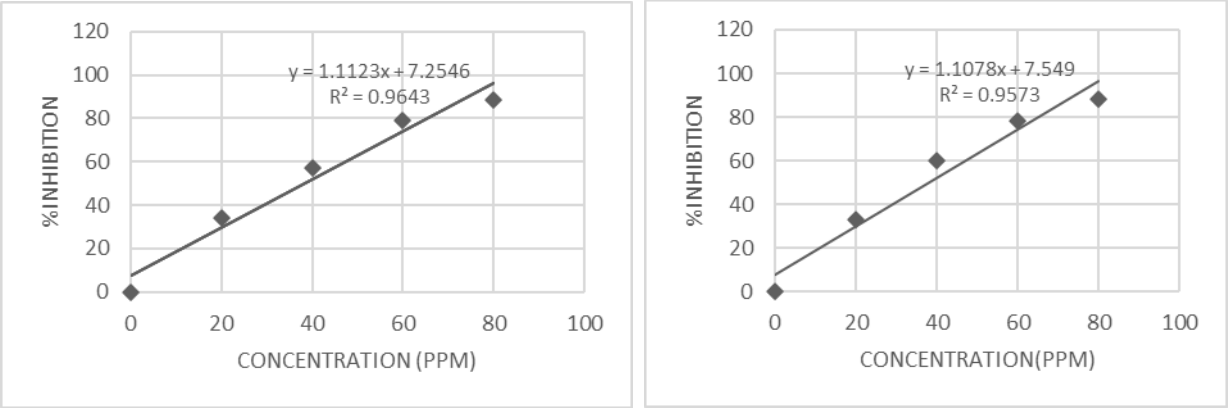

Fig.-5: Linear Regression of an Antioxidant of the Isolated Compound

CONCLUSION

The isolated compound was suggested as 7- (β-D-Glucopyranosyloxy) 5-hydroxy-2-(4-hydroxyphenyl)-6-methoxy-4H-1-benzopyran-4-one (homoplantaginin). The IC_{50} value of the isolated compound was 40.53 ±3.13 ppm, indicating that the isolated compound has potent antioxidant activity.

REFERENCES

1. W.J.A. Musa, S. Duengo, A.K. Kilo and B. Situmeang, *Jurnal Pendidikan Kimia*, **12**, 3 (2020) https://doi.org/10.24114/jpkim.v12i3.21165
2. P.D. Khandagale, A.V. Puri, Y.N. Ansari and R.Y. Patil, *International Journal of Pharmacy and Biological Sciences*, **8**, 3 (2018)
3. V.P. Vadlakonda and S.G. Chaudhari, *Indo American Journal of Pharmaceutical Research*. **9**, 12 (2019)
4. S. Shukla, A. Mehta, J. John, S. Singh, P. Mehta and S.P. Vyas, *Food and Chemical Toxicology*, **47**, (2009) https://doi.org/10.1016/j.fct.2009.04.040
5. E.N. Sembiring, B. Elya and R. Sauriasari, *Pharmacogn Journal*, **10**, 1 (2018) https://doi.org/10.5530/pj.2018.1.22
6. T. Liu, X. Li, Z. Ning, S. Qi and H. Gao, *Natural Product Research*, (2021) https://doi.org/10.1080/14786419.2021.1896511
7. F.N. Iheagwam, O.O. Ogunlana, O.E. Ogunlana, I. Isewon and J. Oyelade, *Bioinformatics and Biology Insights*, **13**, (2018) https://doi.org/10.1177/1177932218821371
8. A. Iftikhar, B. Aslam, M. Iftikhar, W. Majeed, M. Batool, B. Zahoor, N. Amna, H. Gohar and I. Latif, *Hindawi Oxidative Medicine and Cellular Longevity*, (2020) https://doi.org/10.1155/2020/9020219
9. M. Sindete, A. Gbankoto, R. Osseni, N.D. Tossavi, S. Azonbakin, L.B. Moussa, and A. Laley, *Hindawi Evidence-Based Complementary and Alternative Medicine*, (2021) https://doi.org/10.1155/2021/6620026
10. V. Larasati, W. Pangkahila and A.A.G. Budhiarta, *Jurnal kedokteran dan kesehatan*, **3**, 2 (2016)
11. M. Modak, P. Dixit, J. Londhe, S. Ghaskadbi, and T.P.A. Devasagayam. *Journal of Clinical Biochemistry and Nutrition* , **40**, 3 (2006) https://doi.org/10.3164/jcbn.40.163
12. N.K. Kakade, S.S. Pingale and M.G. Chaskar, *International research journal of pharmacy*, **7**, 12 (2016) https://doi.org/10.7897/2230-8407.0712139
13. K. Gurning, W. Haryadi and H. Sastrohamidjojo, *Rasayan Journal of Chemistry*, **14**, 1 (2021), https://doi.org/10.31788/RJC.2021.1416077
14. M.H Satari, B. Situmeang, I.P Yuda and D. Kurnia, *Jurnal Kimia Valensi*, **2**, 5 (2019), https://doi.org/10.15408/jkv.v5i2.8864

15. T. Okselni, A. Santoni, A. Dharma, and M. Efdi, *Rasayan Journal of Chemistry*, 12(1), 146(2019), https://doi.org/10.31788/RJC.2019.1215019
16. H.W. Kil, T. Rho, Y.J. Seo, A. Yu and K.D. Yoon, *Natural Product Sciences*, 26, 3 (2020) https://doi.org/10.20307/nps.2020.26.3.236
17. H.J. Jang, S.J. Lee, C.Y. Kim, J.T. Hwang, J.H. Choi, J.H. Park, S.W. Lee and M.C. Rho, *Molecules*, 22, 1279 (2017) http://dx.doi.org/10.3390/molecules22081279
18. X. Jin, J. Qian and Y. Lu, *Journal of Medicinal Plants Research*, 5, 9 (2011) http://www.academicjournals.org/JMPR
19. N. Meng, K. Chen, Y. Wang, J. Hou, W. Chu, S. Xie, F. Yang and C. Sun, *Molecules*, 27, 1990 (2022) https://doi.org/10.3390/molecules27061990
20. G.T. Lee, C.H. Duan, J.N. Lee, K.S. Lee, J.T. Hong and K.K. Lee, *Natural Product Sciences*, 16, 4 (2010)
21. T. Okselni, A. Santoni, A. Dharma, and M. Efendi, *Rasayan Journal of Chemistry*, 12(1), 146(2019), https://doi.org/10.31788/RJC.2019.1215019

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