Jurnal Pertanian Terapan of JURNAL ROCE (AGROSCIENCE)
https://jurnal.rocewisdomaceh.com/index.php/roce *e-ISSN : 3032-4505*
Vol. 1 No.2 Thn. 2024

ANALISIS BIOAKTIVITAS ANTIOKSIDAN DAN ANTIKANKER TANAMAN GAMAL METODE IN SILICO DASAR

ANALYSIS OF THE ANTIOXIDANT AND ANTICANCER BIOACTIVITY OF GAMAL PLANTS WITH BASIC IN SILICO METHODS

Dodi Iskandar[1*]

[1]Integrated Plantation Product Processing, Agricultural Technology, Politeknik Negeri Pontianak

*email Koresponden: iskandar.dodi79@gmail.com

Article Info

Article history :
Received :
26 – 06 – 2024
Received in revised :
02 – 07 – 2024
Accepted :
10 – 07 – 2024
Availeble online :
15 – 07 – 2024

Abstract

In silico research has been carried out to analyze the antioxidant and anticancer bioactivity of the Gliricidiasepium plant. The software used includes knapsackfamily, pubchem, chemdraw, swissadme, passonline and MS excel. The result is that all compounds in the Gliricidia sepium plant have antioxidant and anticancer probability values above 0.500. Sepinol has the highest probability value of 0.873 for antioxidant, 0.869 for free radical scavenger, 0.784 for anticarcinogenic and 0.745 for chemopreventive. As for TP53, the strongest expression enhancer is robinetin with a probability value of 0.920.

Keywords **:** *antioxidant, anticancer, Gliricidiasepium, in silico*

Abstrak

Telah dilakukan penelitian in silico analisis bioaktivitas antioksidan dan antikanker tanaman Gliricidia sepium. Software yang digunakan meliputi knapsackfamily, pubchem, chemdraw, swissadme, passonline dan MS excel. Hasilnya yaitu semua senyawa dalam tanaman Gliricidia sepium memiliki nilai probabilitas antioksidan dan antikanker diatas 0,500. Sepinol memiliki nilai probabilitas tertinggi sebesar 0,873 untuk antioksidan, 0,869 untuk *Free radical scavenger*, 0,784 untuk anticarcinogenic dan 0,745 untuk chemopreventive. Adapun untuk TP53 expression enhancer terkuat pada robinetin dengan besar nilai probabilitasnya sebesar 0,920.

Kata Kunci : antioksidan, antikanker, Gliricidia sepium, in silico

INTRODUCTION

The Gliricidia sepium plant or known in Indonesian as Gamal is rarely used as a topic in research in West Kalimantan. This plant is number 22 in the plantation crop commodity group (Limpo, 2020). The taxonomy of this plant in order is kingdom (Plantae), division (magnoliophyta), class (magnoliopsida), order (fabales), family (fabaceae), genus (gliricidia) and species (Gliricidia sepium) (Alamu et al., 2023; Nartey et al., 2023). Several studies on this plant mention that part of this plant, namely the leaves, is used as an organic fertilizer material (Oviyanti, Fitri; Syarifah & Nurul, 2016), (Khairunanissa Khairunanissa, Akhmad Rizali, 2019).

Studies on the antioxidant and anticancer properties of this plant are still rare. While research on the anticancer medicinal properties of a plant requires a long and expensive stage (Singh et al., 2023). To approach cheap and fast research, bioinformatics is the solution (Ambrosino et al., 2019).

Several tools that can be used to analyze the anticancer effectiveness of a plant using a bioinformatics approach are knaspsackfamily (Nakamura et al., 2014), (Bhandari et al., 2022), chemdraw (Krasnov et al., 2024), pubchem (Kim et al., 2021), swissadme (Daina et al., 2017) and passonline (Christina et al., 2021). With this approach, the initial research as corroborating evidence or hypothesis in determining the stage of in vitro and in vivo research becomes solid. It is different if you depend on trial and error (Purna Singh et al., 2023).

RESEARCH METHODS

The bioinformatics method adopted in this research follows the steps of a previous study (Iskandar et al., 2022).

Materials

Materials and tools used in this study were gamal plant data extracts from the Knapsackfamily database (http://www.knapsackfamily.com/KNApSAcK_Family/).

Tools

The tools used in this research are laptop model AMD A4-9120e RADEON R3 4 COMPUTE CORES 2C+2G 1.50 GHz, Software used are chemdraw, pubchem (https://pubchem.ncbi.nlm.nih.gov), swissadme (http://www.swissadme.ch/) and passonline (https://www.way2drug.com/passonline/) and MS Excel. The flow of this research can be explained by Figure 1.

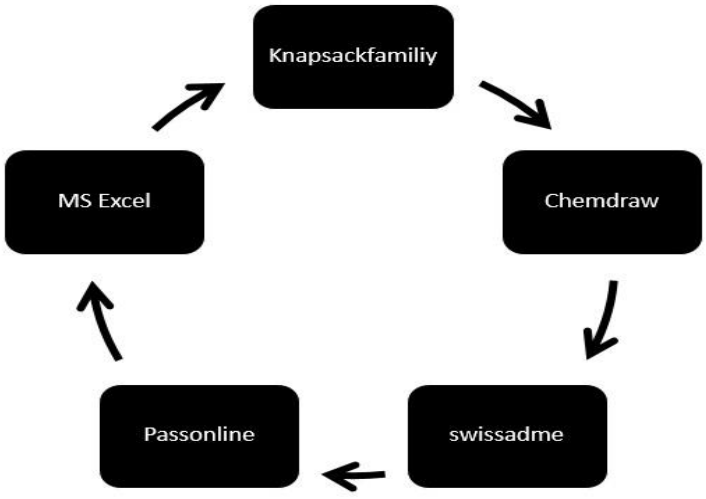
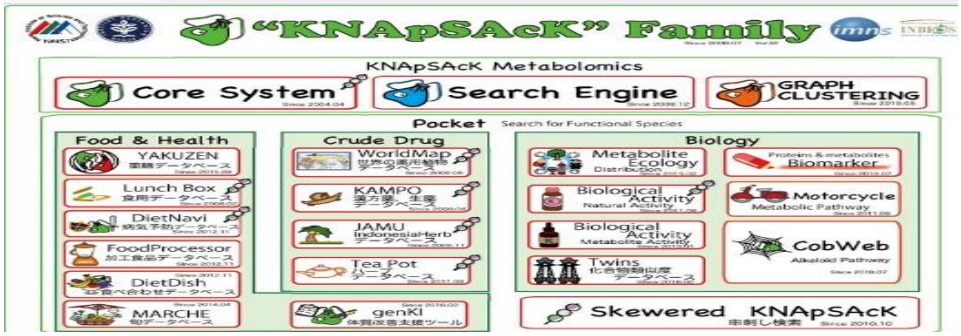


Figure 1. Flow of Bioinformatics Methods

RESULTS AND DISCUSSION

Knapsackfamily

Data on the extraction of compounds from gamal plants can be accessed through http://www.knapsackfamily.com/KNApSAcK_Family/. An illustration of using this tool can be seen in Figure 2.



Number of matched data :18

C_ID	CAS ID	Metabolite	Molecular formula	Mw	Organism or InChIKey etc.
C00000945	492-14-8	Butin	C15H12O5	272.06847349	Gliricidia sepium
C00001092	490-31-3	Robinetin	C15H10O7	302.04265268	Gliricidia sepium
C00002507	550-79-8	Afformosin	C17H14O5	298.08412356	Gliricidia sepium
C00002525	485-72-3	Formononetin	C16H12O4	268.07355887	Gliricidia sepium
C00002547	32383-76-9	(-)-Medicarpin	C16H14O4	270.08920894	Gliricidia sepium
C00002728	458-36-6	Coniferaldehyde	C10H10O3	178.06299419	Gliricidia sepium
C00002749	583-17-5	2-Hydroxycinnamic acid	C9H8O3	164.04734412	Gliricidia sepium
C00007952	72061-66-6	Gliricidol	C16H16O7	320.08960287	Gliricidia sepium
C00008587	72061-63-3	Sepinol	C16H14O7	318.0739528	Gliricidia sepium
C00009402	72061-64-4	Gliricidin	C16H12O6	300.06338812	Gliricidia sepium
C00009709	63631-42-5	Isovestitol	C16H16O4	272.104859	Gliricidia sepium
C00009714	64474-51-7	Isomucronulatol	C17H18O5	302.11542369	Gliricidia sepium
C00009750	60434-16-4	Sepiol	C16H14O5	286.08412356	Gliricidia sepium
C00009752	62078-14-2	2'-O-Methylsepiol	C17H16O5	300.09977362	Gliricidia sepium
C00018862	202345-78-6	7,4'-Dihydroxy-3'-methoxyisoflavan	C16H16O4	272.104859	Gliricidia sepium
C00020091	528-53-0	Delphinidin chloride	C15H11ClO7.Cl	372.98818313	Gliricidia sepium
C00049077	220386-02-7	2-Methoxygliricidol	C18H16O7	344.08960287	Gliricidia sepium
C00049078	56866-29-6	2'-O-Methylvestitol	C17H18O4	286.12050906	Gliricidia sepium

Figure 2. Knapsackfamily Result

A list of their names, CIDs, formulas and molecular weights can be seen in Table 1.

Table 1. List of Compounds in Gamal Plant

C_ID	Metabolite	Molecular formula	Mw
C00000945	Butin	C15H12O5	27.206.847.349
C00001092	Robinetin	C15H10O7	30.204.265.268
C00002507	Afrormosin	C17H14O5	29.808.412.356
C00002525	Formononetin	C16H12O4	26.807.355.887
C00002547	(-)-Medicarpin	C16H14O4	27.008.920.894
C00002728	Coniferaldehyde	C10H10O3	17.806.299.419
C00002729	2-Hydroxycinnamic acid	C9H8O3	16.404.734.412
C00007952	Gliricidol	C16H16O7	32.008.960.287
C00008587	Sepinol	C16H14O7	3.180.739.528
C00009402	Gliricidin	C16H12O6	30.006.338.812
C00009709	Isovestitol	C16H16O4	272.104.859
C00009714	Isomucronulatol	C17H18O5	30.211.542.369
C00009750	Sepiol	C16H14O5	28.608.412.356
C00009752	2'-O-Methylsepiol	C17H16O5	30.009.977.362
C00018862	7,4'-Dihydroxy-3'-methoxyisoflavan	C16H16O4	272.104.859
C00020091	Delphinidin chloride	C15H11ClO7.Cl	37.298.818.313
C00049077	2-Methoxygliricidol	C18H16O7	34.408.960.287
C00049078	2'-O-Methylvestitol	C17H18O4	28.612.050.906

Chemdraw

The list of compound names from the Knapsackfamily database is then searched for two-dimensional images of each compound by pressing the CID code. For example, the first order compound is butin with its International Union of Pure and Applied Chemistry (IUPAC) name 7,3',4'-Trihydroxyflavanone obtained from the pubchem database. Furthermore, the IUPAC name is copied to the chemdraw program to get the entire two-dimensional image of the compound and the results can be seen in Figures 3 to 18.

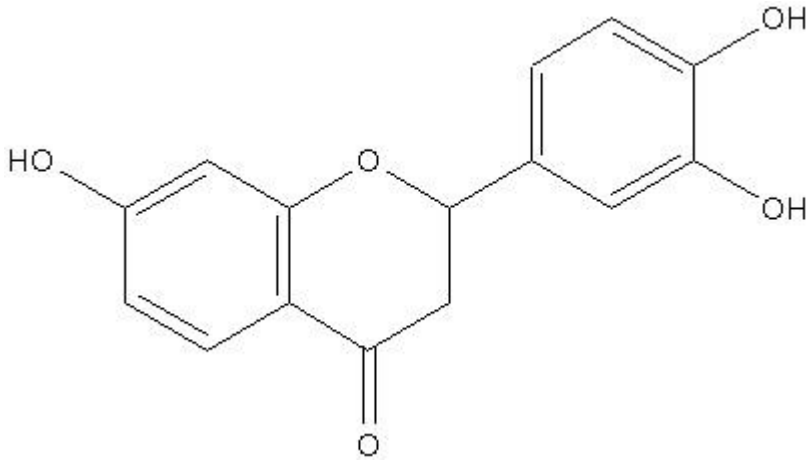


Figure 3. Butin (first order compound name)

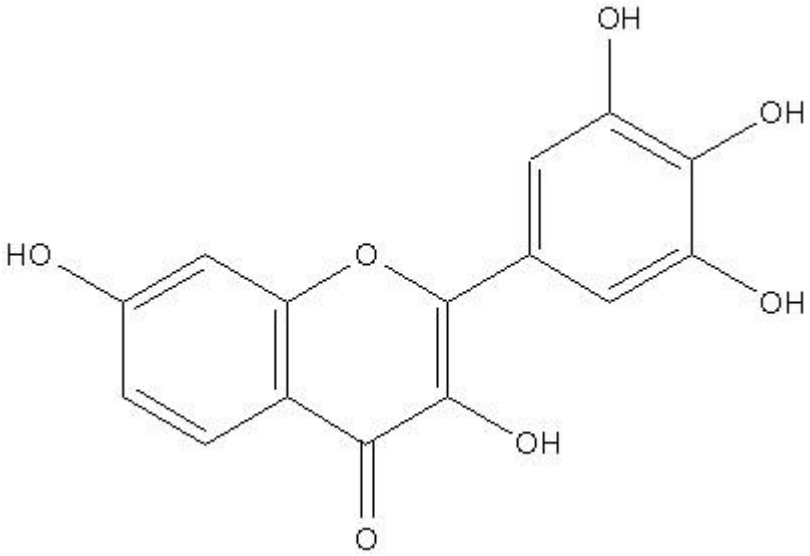


Figure 4. Robinetin

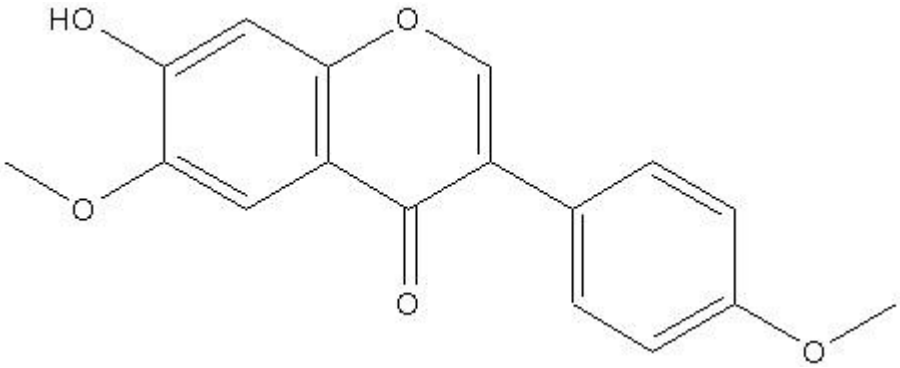


Figure 5. Afrormosin

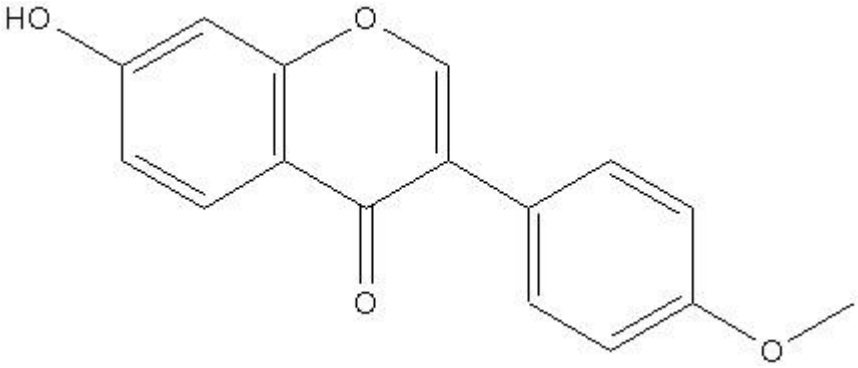


Figure 6. Formononetin

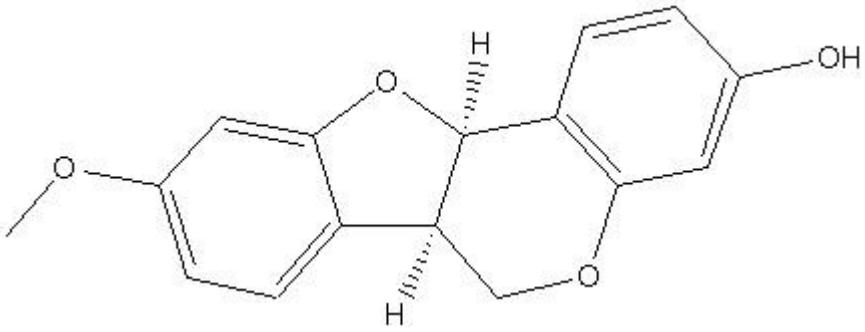


Figure 7. Medicarpin

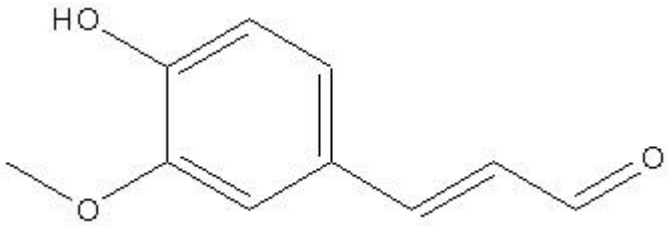


Figure 8. Coniferaldehyde

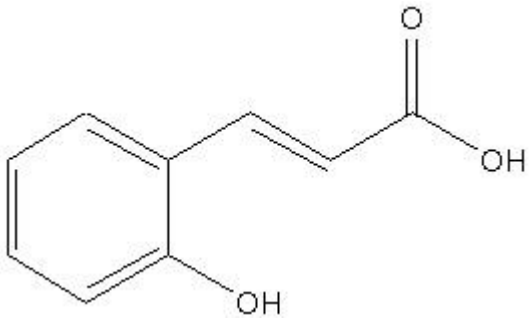


Figure 9. 2-Hydroxycinnamic acid

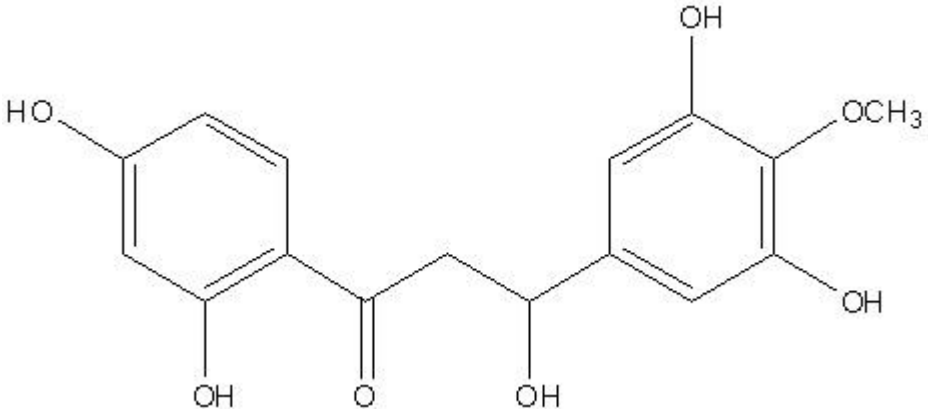


Figure 10. Gliricidol

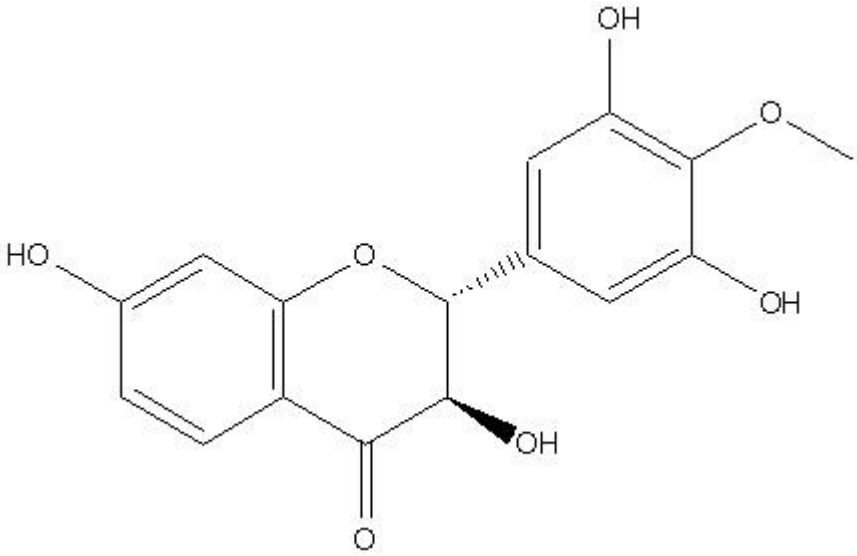


Figure 11. Sepinol

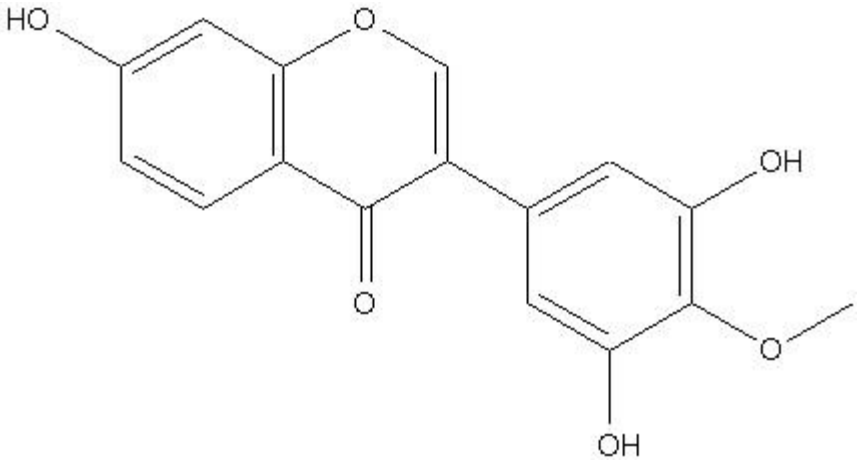


Figure 12. Gliricidin

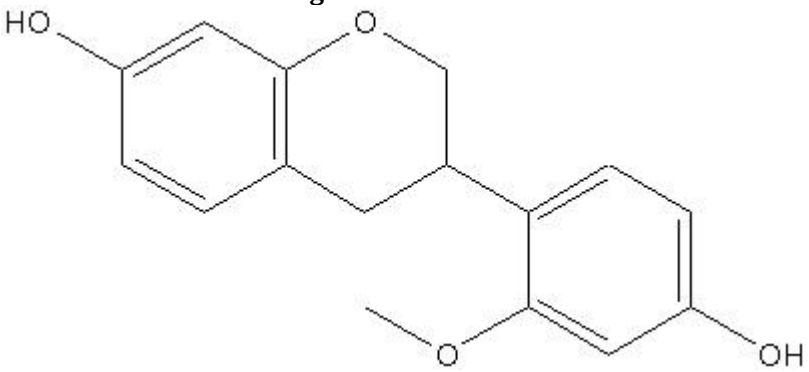


Figure 13. Isovestitol

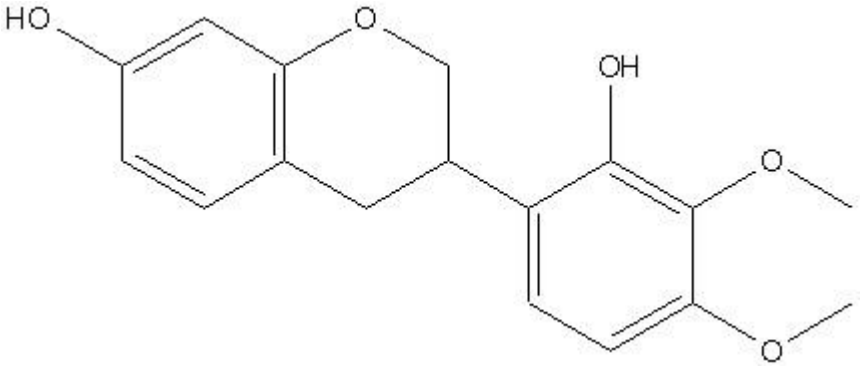


Figure 14. Isomucronulatol

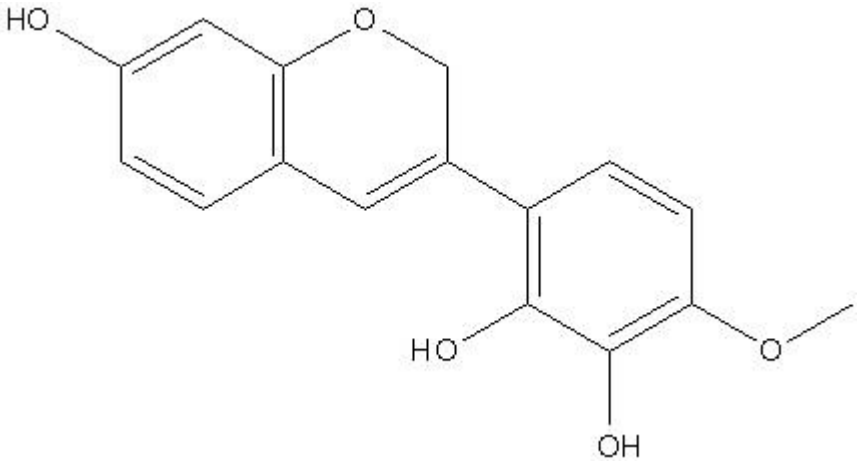


Figure 15. Sepiol

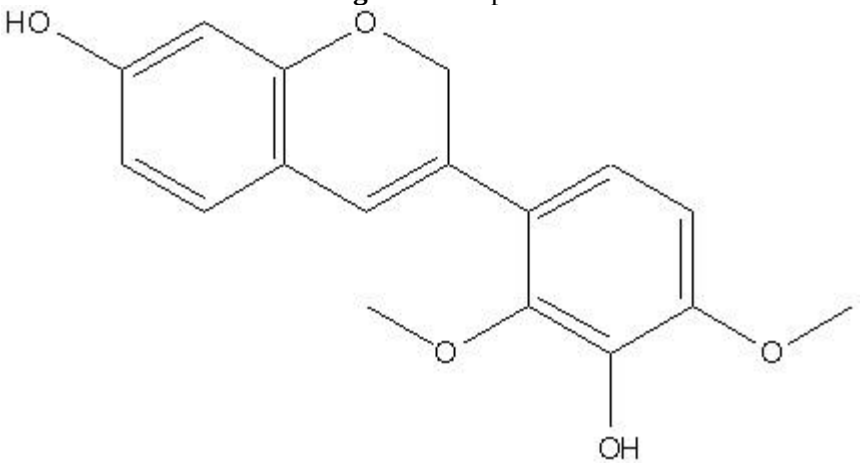


Figure 16. 2'-O-Methylsepiol

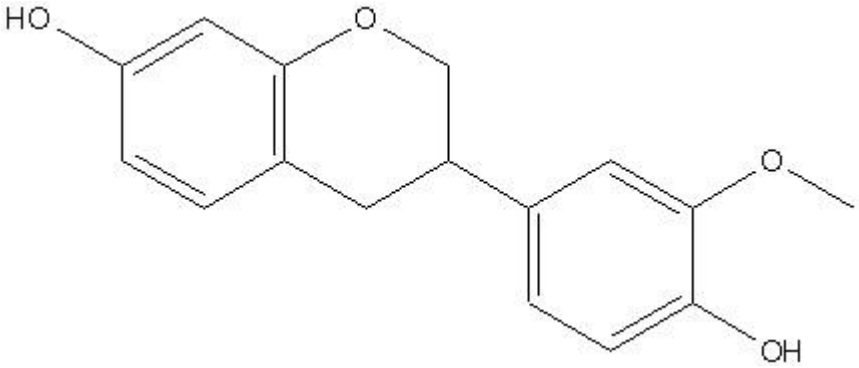


Figure 17. 7,4'-Dihydroxy-3'-methoxyisoflavan

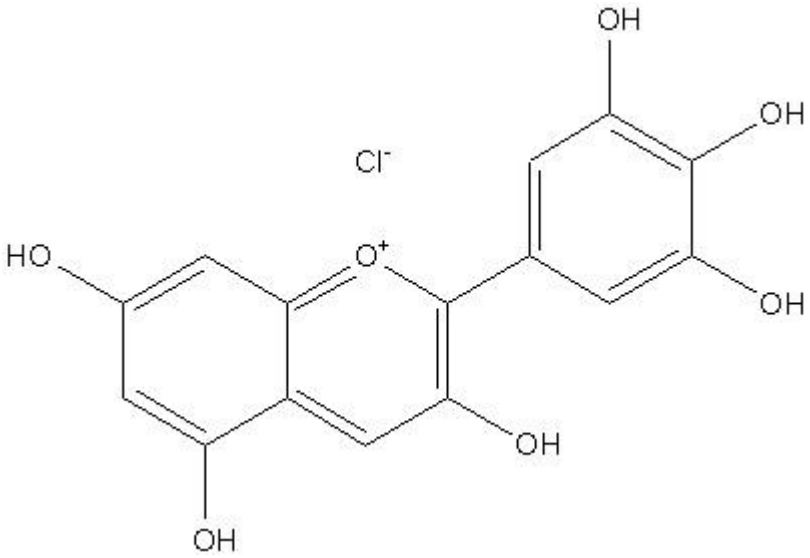


Figure 18. Delphinidin chloride

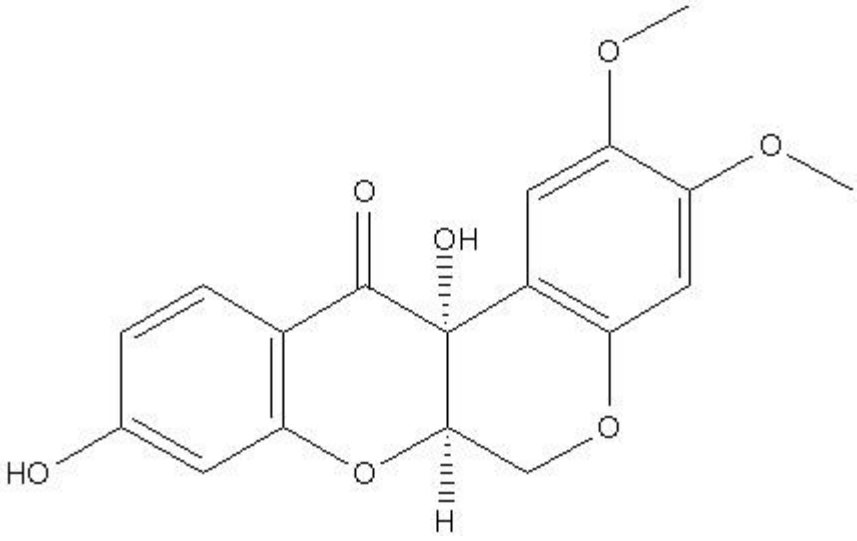


Figure 19. 2-Methoxygliricidol

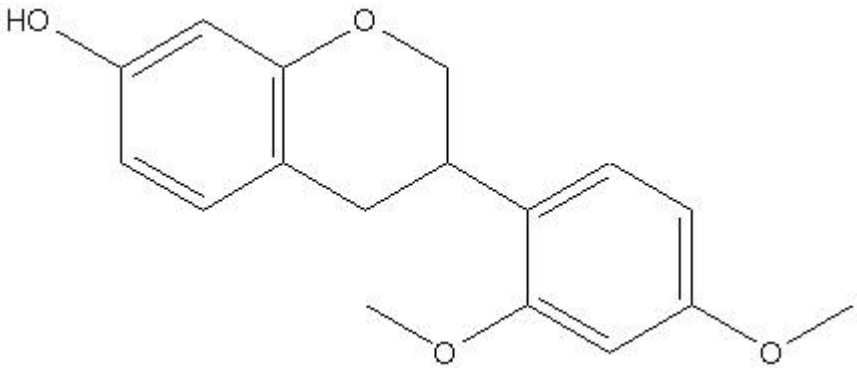


Figure 20. 2'-O-Methylvestitol

Swissadme

All chemical compound structure images are saved as files with cdx extension format. Furthermore, it is converted using swissadme (http://www.swissadme.ch/) to get a smile code (Simplified Molecular Input Line Entry). For example, butin compounds are converted into smile codes as shown in Figure 21.

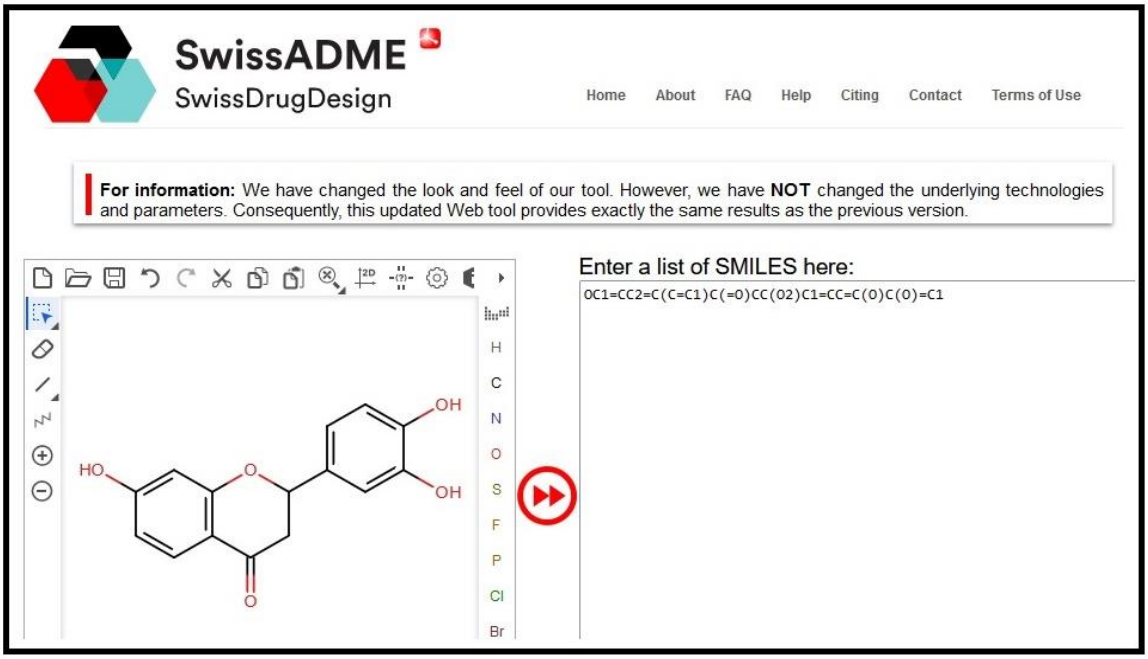


Figure 21. Butin Compound Smile Code

With the same procedure, all smile codes are collected in Table 2.

Table 2. Smile Codes of Compounds in Gamal Plant

No	Metabolite	Kode Smile
1	Butin	OC1=CC2=C(C=C1)C(=O)CC(O2)C1=CC=C(O)C(O)=C1
2	Robinetin	c1(ccc2c(c1)oc(c(c2=O)O)c1cc(c(c(c1)O)O)O)O
3	Afrormosin	c1(c(cc2c(c1)occ(c2=O)c1ccc(cc1)OC)OC)O
4	Formononetin	c1(ccc2c(c1)occ(c2=O)c1ccc(cc1)OC)O
5	(-)-Medicarpin	c1(ccc2c(c1)OC[C@@H]1[C@H]2Oc2c1ccc(c2)OC)O
6	Coniferaldehyde	c1(c(ccc(c1)/C=C/C=O)O)OC
7	2-Hydroxycinnamic acid	c1ccc(c(c1)/C=C/C(=O)O)O
8	Gliricidol	c1(cc(c(cc1)C(=O)C[C@H](c1cc(c(c(c1)O)OC)O)O)O)O
9	Sepinol	c1cc2c(cc1O)O[C@@H]([C@@H](C2=O)O)c1cc(c(c(c1)O)OC)O
10	Gliricidin	c1(ccc2c(c1)occ(c2=O)c1cc(c(c(c1)O)OC)O)O
11	Isovestitol	c1(ccc2c(c1)OC[C@H](C2)c1c(cc(cc1)O)OC)O
12	Isomucronulatol	c1(ccc2c(c1)OC[C@@H](C2)c1c(c(c(cc1)OC)OC)O)O
13	Sepiol	c1(ccc2c(c1)OCC(=C2)c1c(c(c(cc1)OC)O)O)O
14	2'-O-Methylsepiol	c1(ccc2c(c1)OCC(=C2)c1c(c(c(cc1)OC)O)OC)O
15	7,4'-Dihydroxy-3'-methoxyisoflavan	c1(ccc2c(c1)OC[C@@H](C2)c1ccc(c(c1)OC)O)O
16	Delphinidin chloride	c1(cc(c2c(c1)[o+]c(c(c2)O)c1cc(c(c(c1)O)O)O)O)O
17	2-Methoxygliricidol	c12c(O[C@H]3[C@@](C1=O)(c1c(OC3)cc(c(c1)OC)OC)O)cc(cc2)O
18	2'-O-Methylvestitol	c1(ccc2c(c1)OC[C@H](C2)c1c(cc(cc1)OC)OC)O

Passonline

Each smile code was entered into passonline software for bioactivity analysis. Bioactivity is displayed with the probability value of activeness with a value range of 0.000-1.000. The results of antioxidant and anticancer bioactivity analysis can be seen in Table 3.

Table 3. Probability of Antioxidant and Anticancer Bioactivity of Gamal Plant

No.	Biological Agents	Antioxidants		Anticancer		
		Antioxidants	*Free radical scavenger*	TP53 expression enhancer	Anticarcinogenic	Chemopreventive
1	Butin	0,721	0,748	0,786	0,704	0,706
2	Robinetin	0,842	0,778	0,920	0,719	0,687
3	Afrormosin	0,591	0,478	0,775	0,682	0,663
4	Formononetin	0,557	0,42	0,77	0,644	0,612
5	(-)-Medicarpin	0,408	0,572	0,774	0,429	0,636
6	Coniferaldehyde	0,353	0,487	0,83	0,498	0,706
7	2-Hydroxycinnamic acid	0,523	0,613	0,714	0,46	0,535
8	Gliricidol	0,384	0,466	0,636	0,416	0,463
9	Sepinol	0,873	0,869	0,952	0,784	0,745
10	Gliricidin	0,617	0,504	0,793	0,712	0,69
11	Isovestitol	0,472	0,622	0,68	0,511	0,631
12	Isomucronulatol	0,495	0,693	0,681	0,528	0,68
13	Sepiol	0,434	0,534	0,849	0,547	0,529
14	2'-O-Methylsepiol	0,417	0,531	0,797	0,53	0,528
15	7,4'-Dihydroxy-3'-methoxyisoflavan	0,495	0,637	0,701	0,584	0,633
16	Delphinidin chloride	0,332	0,198	0,508	0,420	0,369
17	2-Methoxygliricidol	0,377	0,548	0,791	0,441	0,608
18	2'-O-Methylvestitol	0,46	0,625	0,67	0,508	0,638
	Average	0,519	0,573	0,757	0,562	0,614

Among the compounds in Gamal plant, sepinol has the highest probability value of 0.873 for antioxidant, 0.869 for free radical scavenger, 0.784 for anticarcinogenic and 0.745 for chemopreventive. The strongest TP53 expression enhancer was robinetin with a probability value of 0.920.

CONCLUSION

Based on the results of Passonline analysis, all compounds in Gamal plants have potential as antioxidants and anticancer with probability values above 0.500.

REFERENCES

Alamu, E., Adesokan, M., Fawole, S., Maziya-Dixon, B., Mehreteab, T., & Chikoye, D. (2023). Gliricidia sepium (Jacq.) Walp Applications for Enhancing Soil Fertility and Crop Nutritional Qualities: A Review. *Forests*, *14*, 635. https://doi.org/10.3390/f14030635.

Ambrosino, L., Tangherlini, M., Colantuono, C., Esposito, A., Sangiovanni, M., Miralto, M., Sansone, C., & Chiusano, M. L. (2019). Bioinformatics for Marine Products: An Overview of Resources, Bottlenecks, and Perspectives. In *Marine Drugs* (Vol. 17, Issue 10). https://doi.org/10.3390/md17100576.

Bhandari, A., Kalotra, S., Bajaj, P., Sunkaria, A., & Kaur, G. (2022). Dietary intervention with Tinospora cordifolia improved aging-related decline in locomotor coordination and cerebellar cell survival and plasticity in female rats. *Biogerontology*, *23*(6), 809–824. https://doi.org/10.1007/s10522-022-09975-w.

Christina, Y., Nafisah, W., Fitri Atho'illah, M., Rifa'i, M., Widodo, N., Djati, M., & Garrido, G. (2021). Anti-breast cancer potential activity of Phaleria macrocarpa (Scheff.) Boerl. leaf extract through in silico studies. *Journal of Pharmacy & Pharmacognosy Research*, *9*, 824–845. https://doi.org/10.56499/jppres21.1092_9.6.824.

Daina, A., Michielin, O., & Zoete, V. (2017). SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. *Scientific Reports*, *7*(1), 42717. https://doi.org/10.1038/srep42717.

Iskandar, D., Widodo, N., Warsito, W., Masruri, M., Rollando, R., Warsidah, W., & Antang, Y. P. P. (2022). Proposed Functional Activity of Bioactive Compounds from Spatholobus littoralis Hassk in LC-MS-MS and Silico Studies. *Materials Science Forum*, *1061*, 181–186. https://doi.org/10.4028/p-0uei8m.

Khairunanissa Khairunanissa, Akhmad Rizali, N. K. (2019). Aplikasi Pupuk Organik Cair Daun Gamal Menggunakan Trichoderma Harzianum Terhadap Pertumbuhan Dan Hasil Tanaman Terung Ungu. *Agroekotek View*, *2*(3), 24–29. https://doi.org/https://doi.org/10.20527/agtview.v2i3.1215.

Kim, S., Chen, J., Cheng, T., Gindulyte, A., He, J., He, S., Li, Q., Shoemaker, B. A., Thiessen, P. A., Yu, B., Zaslavsky, L., Zhang, J., & Bolton, E. E. (2021). PubChem in 2021: new data content and improved web interfaces. *Nucleic Acids Research*, *49*(D1), D1388–D1395. https://doi.org/10.1093/nar/gkaa971.

Krasnov, A., Barnabas, S. J., Boehme, T., Boyer, S. K., & Weber, L. (2024). Comparing software tools for optical chemical structure recognition. *Digital Discovery*. https://doi.org/10.1039/D3DD00228D.

Limpo, S. Y. (2020). *Keputusan Menteri Pertanian Republik Indonesia*. https://hortikultura.pertanian.go.id/wp-content/uploads/2020/06/Kepmentan-104-tahun-2020-komoditas-Binaan-Kementan.pdf.

Nakamura, Y., Mochamad Afendi, F., Kawsar Parvin, A., Ono, N., Tanaka, K., Hirai Morita, A., Sato, T., Sugiura, T., Altaf-Ul-Amin, M., & Kanaya, S. (2014). KNApSAcK Metabolite Activity Database for Retrieving the Relationships Between Metabolites and Biological Activities. *Plant and Cell Physiology*, *55*(1), e7–e7. https://doi.org/10.1093/pcp/pct176.

Nartey, E., Addai, F., Arthur, S., & Bawah, E. (2023). Effect of Gliricidia Sepium Leafy Biomass And Npk (15:15:15) Fertiliser On The Growth And Yield Of Tomato, Solanum Lycopersicum (L.). *Journal of Applied Life Sciences and Environment*, *56*, 273–288. https://doi.org/10.46909/alse-562100.

Oviyanti, Fitri ; Syarifah, S. H., & Nurul. (2016). Pengaruh Pemberian Pupuk Organik Cair Daun Gamal (Gliricidia Sepium (Jacq.) Kunth Ex Walp.) Terhadap Pertumbuhan Tanaman Sawi (Brassica Juncea L.). *Jurnal Biota*, *2*(1), 61–67. https://jurnal.radenfatah.ac.id/index.php/biota/article/view/531.

Purna Singh, A., Vadakedath, S., & Kandi, V. (2023). Clinical Research: A Review of Study Designs, Hypotheses, Errors, Sampling Types, Ethics, and Informed Consent. *Cureus*, *15*(1), e33374. https://doi.org/10.7759/cureus.33374.

Singh, N., Vayer, P., Tanwar, S., Poyet, J.-L., Tsaioun, K., & Villoutreix, B. O. (2023). Drug discovery and development: introduction to the general public and patient groups. *Frontiers in Drug Discovery*, *3*. https://doi.org/10.3389/fddsv.2023.1201419.