
ISSN: 0975-3575
ELSEVIER
PHARMACOGNOSY
JOURNAL
An Official Journal of Phcog.net
Volume 5 | Number 6 | November–December 2013
Phcog.Net

Pharmacognosy Journal (/)

An Open Access, Peer Reviewed Journal in the field of Pharmacognosy

Time to read
1 minute

Editorial Board (2020-21)

Share

(https://www.facebook.com/sharer/sharer.php?u=https%3A%2F%2Fwww.phcogj.com%2Feditorial-board-2020-21&t=Editorial+Board+%282020-21%29)

(https://plus.google.com/share?

About

Pharmacognosy Journal (Phcog J.) covers different topics in natural product drug discovery, and also publishes manuscripts that describe pharmacognostic investigations, evaluation reports, methods, techniques and applications of all forms of medicinal plant research

Distinctions: The most widely read, cited, and known Pharmacognosy journal and website is well browsed with all the articles published. More than 50,000 readers in nearly every country in the world each month

ISSN : 0975-3575 ; Frequency : Rapid at a time publication (6 issues/year)

Indexed and Abstracted in : SCOPUS, Scimago Journal Ranking, Chemical Abstracts, Excerpta Medica / EMBASE, Google Scholar, CABI Full Text, Index Copernicus, Ulrich's International Periodical Directory, ProQuest, Journalseek & Genamics, PhcogBase, EBSCOHost, Academic Search Complete, Open J-Gate, SciACCESS.

Rapid publication: Average time from submission to first decision is 30 days and from acceptance to In Press online publication is 45 days.

Open Access Journal: Pharmacognosy Journal is an open access journal, which allows authors to fund their article to be open access from publication.

Submit your Next Article

- Online submission
- Highly indexed and abstracted
- 10 years of successful publishing
- Wider visibility though open access
- Higher impact with wider visibility
- Prompt review

Submit your next article to Phcog J

and be a part of many successful authors.

Create free account (http://phcogj.info) / Login (https://www.phcogj.com/submissions/index.php/phcogj/index)

Pharmacognosy Journal, Vol 14, Issue 6, Nov-Dec, 2022

RECENT ARTICLES


(/article/1896)

Original Article

Preparation, Evaluation of Propolis Extract Gel and exploring its Antioxidant, Antimicrobial Activity (/article/1896)

Shahad Myasar Alfaris,Rasha Khalid Dhahir,Amina Mudhafar Al-Nima

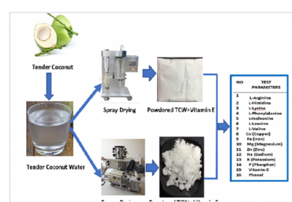
Pharmacognosy Journal,14(6):675-681
DOI: 10.5530/pj.2022.14.153
Published: Thu, 29-Dec-2022

Read More (/article/1896)

Original Article

Comparison of Powdered Active Compounds Made from Tender Coconut Water Fortified with Vitamin E, Processed by Spray Drying and Freeze Drying (/article/1897)

Siti Thomas Zulaikhah,Ratnawati Ratnawati,Atina Hussaana,Tjahja Muhandri

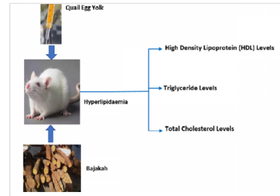

(/article/1897)

Pharmacognosy Journal,14(6):682-686
DOI: 10.5530/pj.2022.14.154
Published: Thu, 29-Dec-2022

Read More (/article/1897)

Original Article

Effect of Bajakah Tea Extract (Spatholobus littoralis Hassk) on High Density Lipoprotein, Triglyceride and Total Cholesterol Levels in Male Wistar Rats (/article/1898)



(/article/1898)

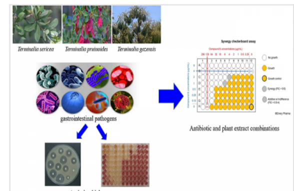
,Andin Putri Aulia,Eka Puji Liashari,Happy Hapsari,Syafrie Sahrul Gibran,Siti Thomas Zulaikhah

Pharmacognosy Journal,14(6):687-691
DOI: 10.5530/pj.2022.14.155
Published: Thu, 29-Dec-2022

Read More (/article/1898)

Original Article

The Interactive Antimicrobial Activities of Selected South African Terminalia spp. Extracts in Combination with Conventional Antibiotics against Gastrointestinal Pathogens (/article/1899)


(/article/1899)

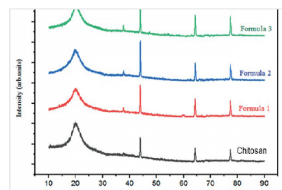
Muhammad Jawad Yous Zai,Matthew James Cheesman,Ian Edwin Cock

Pharmacognosy Journal,14(6):692-701
DOI: 10.5530/pj.2022.14.156
Published: Thu, 29-Dec-2022

Read More (/article/1899)

Original Article

Influence of Chitosan Concentration on Characteristic of Microspheres Delivery System Prepared from Eleutherine palmifolia (L.) Merr. Extract (/article/1900)



(/article/1900)

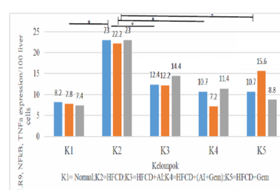
Roihatul Mutiah,Wirda Ardania,Arief Suryadinata,Dewi Sinta Megawati,Anik Listiyana,Abdul Wafi,Rahmi Annisa

Pharmacognosy Journal,14(6):702-709
DOI: 10.5530/pj.2022.14.157
Published: Thu, 29-Dec-2022

Read More (/article/1900)

Original Article

Effects of Acalypha indica L. Extract on Inflammatory Response in The Pathogenesis of Nonalcoholic Fatty Liver Disease: An Overview of TLR9, NFκB and TNFα Expression in Hepatocytes and Macrophages of Sprague-Dawley Rats (/article/1901)


(/article/1901)

Novianti Supriatna,Nurjati Chairani Siregar,Erni Hernawati Purwaningsih,Linda Erlina

Pharmacognosy Journal,14(6):710-719
DOI: 10.5530/pj.2022.14.158
Published: Tue, 3-Jan-2023

Read More (/article/1901)

Original Article

Efficacy of Combined Relaxed Deep-Breathing with Chest Mobilization Exercise and Vernonia cinerea-Hard Candy on Smoking Cessation and Oxidative Stress in Active Teenage Smokers (/article/1902)


(/article/1902)

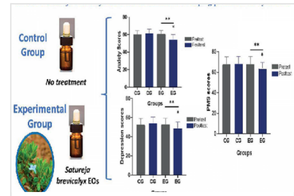
Rungtiwa Kanthain,Jirakrit Leelarungrayub,Surinporn Likhitsathian,Surapol Natakankitkul

Pharmacognosy Journal,14(6):720-727
DOI: 10.5530/pj.2022.14.159
Published: Thu, 29-Dec-2022

Read More (/article/1902)

Original Article

Effects of Satureja brevicalyx essential oil inhalation on coping premenstrual syndrome (/article/1903)



(/article/1903)

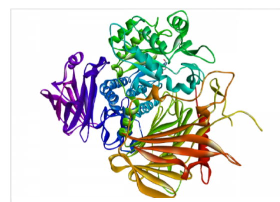
Paul Alan Arkin Alvarado-García,Marilú Roxana Soto-Vásquez,Francisco Mercedes I. Gomez,Yolanda Elizabeth de Guzmán,Taniht Lisseth Cu Romero,Natalia Mavila Guz Rodríguez,Olga Gessy Rodr Aguilar,Ana María Hon Alvarado,Elsa Rocío Var Díaz,Lesly Alexandra Cabrera,Klersy Almendra T. Román,Edwar Guido Bric Esquivel

Pharmacognosy Journal,14(6):728-735
DOI: 10.5530/pj.2022.14.160
Published: Thu, 29-Dec-2022

Read More (/article/1903)

Original Article

In Silico Analysis and ADMET Prediction of Flavonoid Compounds from Syzigium cumini var. album on α-Glucosidase Receptor for Searching Anti-Diabetic Drug Candidates (/article/1904)


(/article/1904)

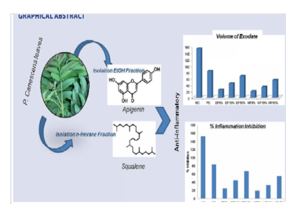
Yanu Andhiarto, ,Ersanda Nurma Praditapuspa,

Pharmacognosy Journal,14(6):736-743
DOI: 10.5530/pj.2022.14.161
Published: Tue, 10-Jan-2023

Read More (/article/1904)

Original Article

Isolation of a Flavone Apigenin and a Steroids Squalene from Peronema canescens Jack Leaves with Anti-Inflammatory Activities (/article/1905)


(/article/1905)

Indra Lasmana Tarigan, , ,Indah Pramana Sa Aini,Madyawati Latief

Pharmacognosy Journal,14(6):744-752
DOI: 10.5530/pj.2022.14.162
Published: Thu, 29-Dec-2022

Read More (/article/1905)

Original Article

Pharmacogn J. 2022; 14(6): 736-743
A Multifaceted Journal in the field of Natural Products and Pharmacognosy
www.phcogj.com

Original Article

In Silico Analysis and ADMET Prediction of Flavonoid Compounds from *Syzygium cumini* var. album on α-Glucosidase Receptor for Searching Anti-Diabetic Drug Candidates

Yanu Andhiarto[1], Suciati[2], Ersanda Nurma Praditapuspa[3], Sukardiman[2*]

ABSTRACT

Background: One of the causes of death is diabetes. Anti-diabetic drugs currently available do not work optimally because some have been reported to have side effect and resistance. **Objective:** This study aimed to flavonoid compounds from *Syzygium cumini* var. album with the greatest anti-diabetic activity and lower toxicity than acarbose. **Materials and Methods:** This research is an *in silico* study of nine flavonoid compounds from *Syzygium cumini* var. album, starting with PASS online was used to predict the activity spectrum of substances, drug-likeness prediction using DruLiTo, ADMET prediction (absorption, distribution, metabolism, excretion, and toxicity) using pkCSM online. Molecular docking was carried out by the AutoDock 4.2.6 program on α-glucosidase targeting. Visualization is done with the Discovery Studio Visualizer software. **Results:** From the data obtained, D-(+)-Catechin has a high affinity for α-glucosidase with a free energy of binding (ΔG) -5.94 kcal/mol and an inhibition constant (Ki) of 44270 nm. **Conclusion:** Based on the results of the study, it can be concluded that the flavonoid compounds from *Syzygium cumini* var. album has the potential as a promising anti-diabetic drug candidate, where the best candidate is D- (+)-Catechin. However, further studies of flavonoid compounds from *Syzygium cumini* var. album are needed.

Key words: α-glucosidase, Molecular docking, PASS, Pharmacokinetics, Flavonoid.

Yanu Andhiarto[1], Suciati[2], Ersanda Nurma Praditapuspa[3], Sukardiman[2*]

[1]*Doctoral Program, Faculty of Pharmacy, Airlangga University, Surabaya, INDONESIA.*

[2]*Department of Pharmaceutical Sciences, Faculty of Pharmacy, Airlangga University, Surabaya, INDONESIA.*

[3]*Department of Pharmaceutical Chemistry, Faculty of Medicine, Hang Tuah University, Surabaya, INDONESIA.*

Correspondence

Sukardiman

Department of Pharmaceutical Sciences, Faculty of Pharmacy, Airlangga University, Surabaya, INDONESIA.

E-mail: sukardiman@ff.unair.ac.id

History

- Submission Date: 23-08-2022;
- Review completed: 26-09-2022;
- Accepted Date: 05-10-2022.

DOI : 10.5530/pj.2022.14.

Article Available online 161

http://www.phcogj.com/v14/i6

INTRODUCTION

Pharmacotherapy of type 2 diabetes mellitus, there are six classes of oral antidiabetic drugs (OAD) with different mechanisms of action, one of which is α-glucosidase inhibitor (AGI). AGI drugs work by reducing the level of carbohydrate absorption in the body. The excess use of the AGI class of drugs is relatively safe because it does not produce insulin secretion so it does not cause hypoglycemic shock and does not cause weight gain, so it is certain, especially in obese and geriatric patients.[1,2] However, currently available AGI class of drugs cause unwanted side effects such as abdominal pain, diarrhea, flatulence, and distension.[3,4] Therefore, it is necessary to develop new natural AGI drugs with lower side effects than synthetic drugs.

One of the plants that empirically reduces blood glucose levels is jamblang (*Syzygium cumini* (L.) Skeels.) from the Myrtaceae family. In general, there are three different varieties of jamblang, namely purple jamblang, white jamblang and marbled jamblang.[5] The white jamblang (*Syzygium cumini* var. album) is a rare type of jamblang and has the smallest distribution compared to other types of jamblang.[6] Based on research reported that the total phenolic and flavonoid levels from the jamlang leaf part were higher than the fruit and stem bark but have not been widely used by the community so that it can be developed pharmacologically.[7]

This jamblang plant is reported to contain chemical compounds including flavonoids, alkaloids, tannins and essential oils.[8] One of the compounds responsible for being antidiabetic is the flavonoid group. Quercetin and myricetin are one of the typical compounds of the flavonoid group found in jamblang plants. The activity of quercetin and myricetin as antidiabetic has been widely reported in recent years. Myricetin is possible to control hyperglycemia in diabetes mellitus through inhibition of alpha glucosidase activity.[9] In addition, the compounds quercetin and myricetin have a low IC_{50} value, so they may be future antidiabetic agents.[10] This study discusses the potential analysis of flavonoid compounds as antidiabetic from *Syzygium cumini* var. album which was obtained from UPLC-QToF-MS/MS through the mechanism of α-glucosidase inhibition using molecular docking.

MATERIALS AND METHODS

Hardware

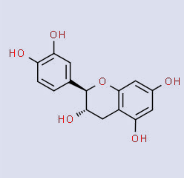
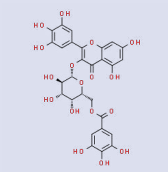
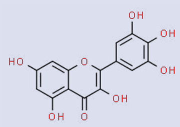
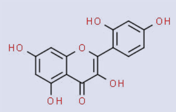
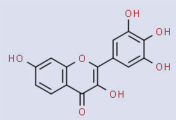
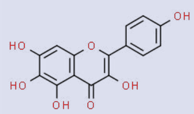
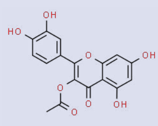
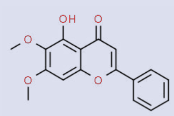
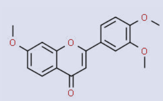
The specification of the computer that is used: Intel® Core™ i7 8565U@ 1.80 GHz processor (CPU), Nvidia® GeForce MX230 graphics processing unit (GPU), and 8 GB Random Access Memory (RAM) with Windows 10.

Compound test preparation

Flavonoid compounds from *Syzygium cumini* var. album were the results obtained using the UPLC-QToF-MS/MS instrument. The flavonoid compounds from *Syzygium cumini* var. album are as shown in figure 1 and table 1. The test compounds were made in 2D and 3D models, then optimized using the MMFF94 method on Chem3D 20.0. Then, the structure is translated into SMILES format using the Online SMILES Translator (https://cactus.nci.nih.gov/translate/).

Cite this article: Andhiarto Y, Suciati, Praditapuspa EN, Sukardiman. *In Silico* Analysis and ADMET Prediction of Flavonoid Compounds from *Syzigium cumini* var. album on α-Glucosidase Receptor for Searching Anti-Diabetic Drug Candidates. Pharmacogn J. 2022; 14(6): 736-743.

Table 1: The flavonoid compounds from *Syzygium cumini* var. album using the UPLC-QToF-MS/MS instrument.

No	Rt (Min)	Mass M/Z	Calculated M/Z	Formula	IUPAC	2D Models
1	4,42	291.0872	291. 0609	$C_{15}H_{14}O_6$	D-(+)-Catechin	
2	4.80	633.1070	633.1092	$C_{28}H_{24}O_{17}$	5,7-Dihydroxy-4-oxo-2-(3,4,5-trihydroxyphenyl)-4H-chromen-3-yl 6-O-(3,4,5-trihydroxybenzoyl)-β-D-galactopyranoside	
3	5,37	319.0464	319.0454	$C_{15}H_{10}O_8$	Myricetin	
4	6,13	353.0501	353.0505	$C_{15}H_{10}O_7$	Morin	
5	6,23	302.0426	302.2360	$C_{15}H_{10}O_7$	Robinetin	
6	6,13	302.236	302.0426	$C_{15}H_{10}O_7$	6-hydroxykaempferol	
7	7,02	345.0509	345.0610	$C_{17}H_{12}O_8$	Quercetin acetate	
8	11,56	299.0927	299.0911	$C_{17}H_{14}O_5$	Mosloflavone	
9	11,91	313.1093	313.1076	$C_{18}H_{16}O_5$	Fasciculiferin	

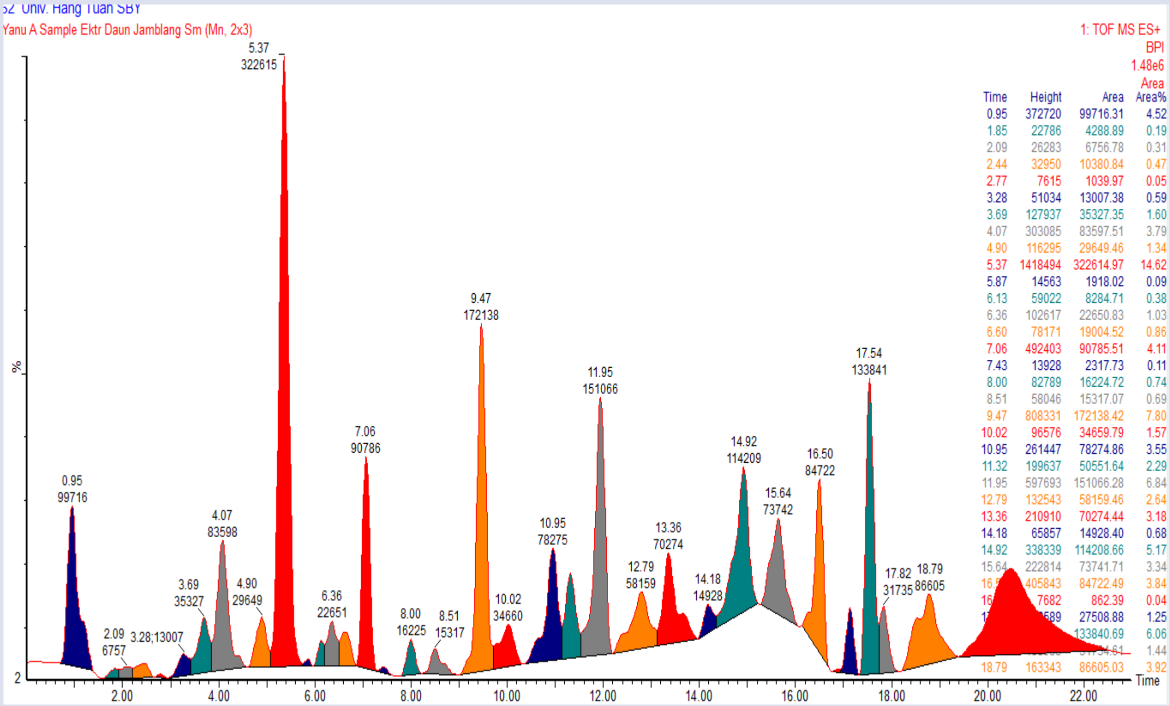


Figure 1: UPLC-QToF-MS/MS chromatogram.

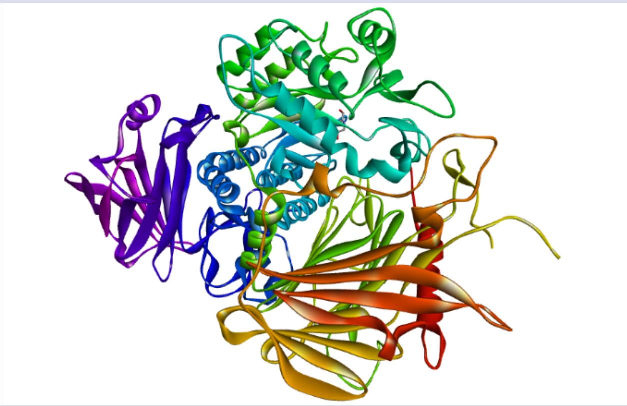


Figure 2: Structure of α-glucosidase (PDB ID: 5DKY).

PASS prediction

To validate compounds as suitable drug candidates, prediction of activity spectra for substances (PASS) (http://www.pharmaexpert.ru/passonline/) is used to predict the possible pharmacological effects of a compound based on structural information by looking at the Pa score (probability " to be active") and Pi (probability "to be inactive") by entering the SMILES format.[11]

Drug-likeness prediction

Three filters of the DruLiTo program (Lipinski's rule, Veber rule, and Ghose filter) were used to predict the drug-likeness of the test compound by entering *sdf file format.[12-14]

ADMET prediction

Prediction of pharmacokinetics (ADME) and toxicity of the flavonoid compounds from *Syzygium cumini* var. album was done by the pkCSM website (http://biosig.unimelb.edu.au/pkcsm/prediction) with the SMILES format.[15]

Molecular docking

The structure of the α-glucosidase target receptor (PDB ID: 5DKY) obtained from the Protein Data Bank (https://www.rcsb.org/) and containing the native ligand (1-deoxynojirimycin) that is shown in figure 2. As for a comparison ligand, Acarbose is also used.

Molecular docking is done using AutoDockTools 4.2.6 program. Starting with the validation process, the redocking method uses the extracted cocrystal ligand from the receptor as the test ligand and the location of the cocrystal ligand as the binding site.[16] The validation results are indicated by the Root Mean Square Deviation (RMSD) value.[17] Center the grid box using a grid box (40 × 40 × 40). The binding site coordinates are x = 16,353; y = 49,298; z = 22,353 with spacing per unit 0.375 angstrom. AutoDockTools 4.2.6 program run with the specified parameters: number generation algorithm 27,000, calculate 2,500,000 times (Medium), population 150, and the implementation of running GA as much as 10 times. Visualization analysis of protein-ligand interactions was performed with Discovery Studio Visualizer v.19.1.0.18287 from BIOVIA.

RESULTS

Flavonoid compound from *Syzygium cumini* var. album (Figure 1).

PASS prediction

The prediction results of the Pa and Pi scores of flavonoid compounds from *Syzygium cumini* var. album are shown in table 2.

Drug-likeness prediction

Prediction results of drug-likeness of flavonoid compounds from *Syzygium cumini* var. album are shown in table 3.

ADMET prediction

The prediction results of the ADMET of flavonoid compounds from *Syzygium cumini* var. album are shown in table 4.

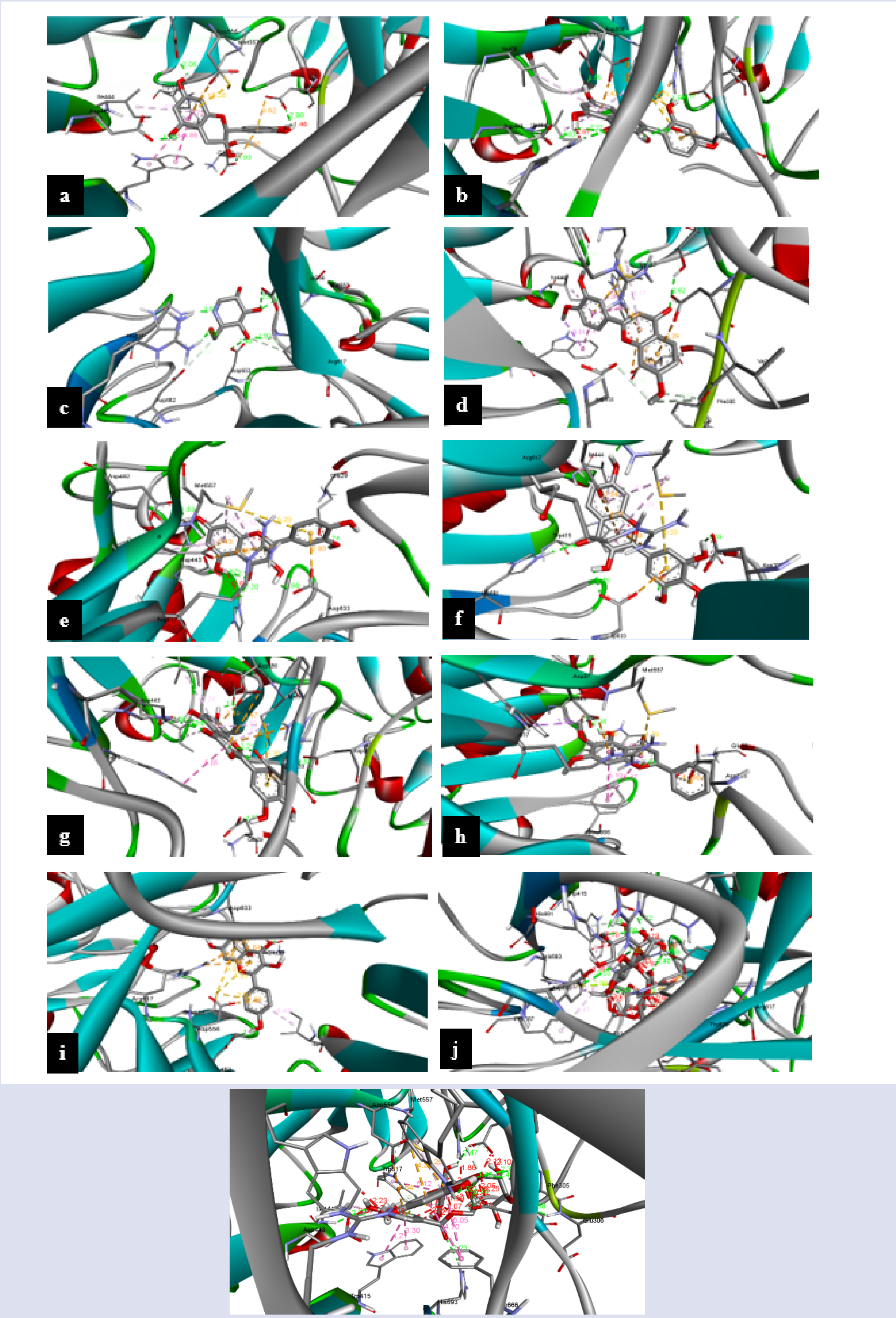


Figure 3: Visualization of D-(+)-Catechin (a) morin, (b) native ligand, (c) fasciculiferin, (d) quercetin acetate, (e) robinetin, (f) myricetin, (g) mosloflavone, (h) 6-hydroxykaempferol, (i) acarbose, (j) 5,7-Dihydroxy-4-oxo-2-(3,4,5-trihydroxyphenyl)-4H-chromen-3-yl 6-O-(3,4,5-trihydroxybenzoyl)-β-D-galactopyranoside, (k) bound to the active sites of α-glucosidase.

Table 2: The PASS result.

Code	Compound Name	Alpha glucosidase inhibitor	
		Pa	Pi
S1	D-(+)-Catechin	0.300	0.003
S2	5,7-Dihydroxy-4-oxo-2-(3,4,5-trihydroxyphenyl)-4H-chromen-3-yl 6-O-(3,4,5-trihydroxybenzoyl)-β-D-galactopyranoside	0.811	0.001
S3	Myricetin	0.321	0.003
S4	Morin	0.245	0.004
S5	Robinetin	0.245	0.004
S6	6-hydroxykaempferol	0.281	0.004
S7	Quercetin acetate	0.273	0.004
S8	Mosloflavone	0.165	0.008
S9	Fasciculiferin	0.139	0.013

Table 3: Prediction of Druglikeness with DruLiTo program.

Kode	MW	logP	HBA	HBD	TPSA	AMR	nRB	nAtom	Lipinski's Rule	Ghose Filter	Veber Rule
S1	290.08	0.852	6	5	110.38	81.07	1	35	1	1	1
S2	632.1	1.802	17	11	293.59	156.02	7	69	0	0	0
S3	318.04	2.182	8	6	147.68	85.04	1	33	0	1	0
S4	302.04	1.405	7	5	127.45	83.44	1	32	1	1	1
S5	312.1	2.101	5	0	53.99	95.27	4	39	1	1	1
S6	302.04	2.263	7	5	127.45	83.44	1	32	1	1	1
S7	302.04	1.834	7	5	127.45	83.44	1	32	1	1	1
S8	298.08	2.413	5	1	64.99	90.23	3	36	1	1	1
S9	312.1	2.101	5	0	53.99	95.27	4	39	1	1	1

MW: Molecular weight, LogP: Partition coefficient, HBA: H-Bond Acceptor, HBD: H-Bond Donor, TPSA: Total polar surface area, AMR: Atom molar refractivity, nRB: Number of rotatable bond, nAtom: Number of atoms. 1 compound follows the rule; 0 compound does not follow the rule.

Table 4: Prediction of ADMET.

Code	Intestinal absorption (human)	Skin Permeability	VDss (human)	BBB permeability	CYP2D6 substrate	CYP2D6 inhibitior	Total Clearance	Renal OCT2 substrate	Ames toxicity	Hepatotoxicity
S1	72.06	-2.739	0.141	-1.159	No	No	0.234	No	No	No
S2	31.11	-2.735	-0.131	-3.199	No	No	0.561	No	Yes	No
S3	67.06	-2.735	-0.201	-1.825	No	No	0.521	No	Yes	No
S4	74.62	-2.735	-0.239	-1.478	No	No	0.561	No	Yes	No
S5	77.01	-2.735	-0.282	-1.559	No	No	0.483	No	No	No
S6	66.78	-2.735	-0.112	-1.608	No	No	0.489	No	Yes	No
S7	74.08	-2.735	-0.124	-1.490	No	No	0.523	No	Yes	No
S8	94.93	-2.807	-0.236	-0.364	No	No	0.381	No	No	No
S9	100	-2.660	0.265	-0.024	No	No	0.784	Yes	No	No

Table 5: Molecular docking binding affinity of flavonoid compounds from Syzygium cumini var. album, ranked by the lowest free energy of binding (ΔG) and inhibition constant (Ki).

Code	Compound name	ΔG (kcal/mol)	Ki (nM)
S1	D-(+)-Catechin	-5.94	44270
S4	Morin	-5.63	75000
NOJ	Native ligand	-4.86	239900
S9	Fasciculiferin	-4.23	273700
S7	Quercetin acetate	-4.04	1100000
S5	Robinetin	-3.87	1450000
S3	Myricetin	-3.26	4100000
S8	Mosloflavone	-3.24	4200000
S6	6-hydroxykaempferol	-3.24	4230000
A	Acarbose (standard drug)	-3.00	4556000
S2	5,7-Dihydroxy-4-oxo-2-(3,4,5-trihydroxyphenyl)-4H-chromen-3-yl 6-O-(3,4,5-trihydroxybenzoyl)-β-D-galactopyranoside	-2.94	4652000

Molecular docking

The results of docking validation are indicated by the RMSD value of 1.588, so it can be concluded that the docking protocol can be declared valid because the RMSD value is < 2.[17] Based on the docking results, six flavonoid compounds from *Syzygium cumini* var. album obtained more negative ΔG scores than Acarbose (Table 5). The more negative the ΔG score and the smaller the Ki value, it indicates a very strong complex formed between the ligand and standard. While the visualization of ligands and comparisons can be seen in figure 3 and table 5.

DISCUSSION

The Pa value is the possibility of a compound being active in carrying out biological activities in laboratory experiments, while the Pi value is the opposite. If a compound has a value of Pa > Pi, then the compound has the potential to have this activity. In Table 1, 5,7-Dihydroxy-4-oxo-2-(3,4,5-trihydroxyphenyl)-4H-chromen-3-yl 6-O-(3,4,5-trihydroxybenzoyl)-β-D-galactopyranoside has strong potential on a laboratory scale because the Pa value > 0.7, while its flavonoid compound have under activity because the Pa value is Pa<0.5.[18] Because these compounds have not been studied on a laboratory scale, further research is needed.

The prediction results of physicochemical properties based on several drug-likeness rules (Table 3) showed that one flavonoid compound from *Syzygium cumini* var. album did not comply with Lipinski's rule, Ghose's filter and Veber's rule ((5,7-Dihydroxy-4-oxo-2-(3,4,4)). 5-trihydroxyphenyl)-4H-chromen-3-yl 6-O-(3,4,5-trihydroxybenzoyl)-β-D-galactopyranoside). However, there is one compound that does not comply with Lipinski's rule and Veber's rule, Myricetin (HBD 6). It does not mean that Myricetin is unable to penetrate cell membranes because the drug can penetrate cell membranes if it complies with at least 2 of Lipinski's rules.[19]

ADMET prediction can be seen from (Table 4). Where the prediction of absorption is expressed by the value of intestinal absorption, the distribution is expressed by the value of VDss and BBB permeability, metabolism is expressed by CYP2D6 substrate and inhibitor, excretion is expressed by the value of total clearance, and toxicity is expressed by hepatotoxicity and LD50. It can be seen that the intestinal absorption (human) value of the tested compounds is around 31.11% - 100%, so it can be predicted that the nine compounds will be absorbed well in the human intestine. The VDss is a steady-state volume of distribution that predicts the value total dose of the drug would need to be uniformly distributed to give the same concentration as in blood plasma. The test compounds VDss are range from -0.55 to 0.01 (log L/kg)[15], the predicted results showed VDss relatively low. The BBB (Blood Brain Barrier) values of nine compounds above -1,[15] which means that they can penetrate the BBB moderately. In the table, it can be seen that none of the seven compounds act as substrates or inhibitors of CYP2D6, so it can be predicted that all test compounds to be metabolized by the enzyme cytochrome P450. The total Clearance value of the test compounds ranges from 0.205 to 0.784, and from these values it can be predicted the compound's excretion. OCT2 in the kidney plays an important role in the disposition and clearance of endogenous drugs and compounds.[15] There is one compounds (Fasciculiferin) affecting the OCT2 substrate so that adverse effects or contraindications are predicted. From the results Table 4 shows that five compounds (Myricetin, 5,7-Dihydroxy-4-oxo-2-(3,4,5-trihydroxyphenyl)-4H-chromen-3-yl 6-O-(3,4,5-trihydroxybenzoyl)-β-D-galactopyranoside, Myricetin, Morin, 6-hydroxykaempferol, and quercetin acetate) are predicted to be active to cause mutagenic effects and all flavonoid compounds from *Syzygium cumini* var. album are non-hepatotoxic.

Molecular docking is computational modeling research that aims to detect the interaction of ligands with receptors. Bond energy is influenced by Gibbs free energy (ΔG), a reaction that takes place spontaneously will have a negative Gibbs free energy at temperature and constant temperature. Bond energy is affected by several components which are expressed by the following equation: ΔG〛_Hatanic = ΔG〛_Gauss + 〚ΔG〛_Repulsion + ΔG〛_HBond + ΔG〛_Hydrophobic +ΔG〛_Torsion. The more energy components contribute, the smaller the "ΔG" value (becomes negative), the bond impact will be stronger and cause high affinity.[20] From the results of the study [Table 5], it is known that D-(+)-Catechin has a stronger inhibitory activity than acarbose, marked by ΔG of -5.94 kcal/mol and acarbose -3.00 kcal/mol. So that ΔG is very negative, it can be ascertained that the reaction will be proceed spontaneously and lead to high affinity. The Ki values of these compounds are 44270 and 4556000 nM. The Ki value is not only used to indicate the affinity of a ligand; it is also used to predict *in vitro* analysis processes. In this study, the presence of the D-(+)-Catechin had a significant effect on the affinity of the flavonoid compounds from *Syzygium cumini* var. album for the α-glucosidase target receptor. Thus, all flavonoid compounds from *Syzygium cumini* var. album have greater activity against target receptors than acarbose, except 5,7-Dihydroxy-4-oxo-2-(3,4,5-trihydroxyphenyl)-4H-chromen-3-yl 6-O-(3,4,5-trihydroxybenzoyl)-β-D-galactopyranoside.

CONCLUSION

The development of anti-diabetic drugs with greater therapeutic activity and fewer side effects is an urgent need. This study evaluates the anti-diabetic activity of flavonoid compounds from *Syzygium cumini* var. album targeting α-glucosidase. Therefore, it can be concluded that the flavonoid compounds from *Syzygium cumini* var. album has the potential as a promising anti-diabetic drug candidate, where the best candidate is D- (+)-Catechin. However, further studies of flavonoid compounds from *Syzygium cumini* var. album are needed.

ACKNOWLEDGMENTS:

The Directorate General of Higher Education, Research, and Technology of the Ministry of Education, Culture, Research, and Technology has provided funding for this research through the Program of Doctoral Research Scheme , Contract Number 085/E5/PG.02.00.PT /2022

REFERENCES

1. Kazi AA, Blonde L. Classification of diabetes mellitus. Clin Lab Med. 2001;21(1):1-3.
2. Riddle MC. Diabetes Care in 2020: Following and leading the stories of diabetes. Diabetes Care. 2020;43(1):3-4.
3. Sheliya MA, Rayhana B, Ali A, Pillai KK, Aeri V, Sharma M, *et al.* Inhibition of α-glucosidase by new prenylated flavonoids from Euphorbia hirta L. herb. J Ethnopharmacol. 2015;176:1-8.
4. Salehi B, Ata A, Anil KN, Sharopov F, Ramírez-Alarcón K, Ruiz-Ortega A, *et al.* Antidiabetic potential of medicinal plants and their active components. Biomolecules. 2019;9(10):551.
5. Palmolina M, Fauziyah E. Konstruksi kearifan lokal masyarakat petani hutan rakyat dalam pemanfaatan duwet *(Syzygium cumini* Linn). J Penelitian Sosial dan Ekonomi Kehutanan. 2018;15(1):1-3.
6. Kusumawati A, Putri NE, Azhar NO, Swasti E. Karakterisasi plasma nutfah buah lokal di Kabupaten Lima Puluh Kota dan Kota Solok. J Agrosains dan Teknologi. 2018;3(1):19-29.
7. Putri VA, Rahayu SE, Dharmawan A. Komposisi senyawa aktif ekstrak daun jamblang (*Syzygium cumini* L.) dan pengaruhnya terhadap perilaku larva *aedes aegypti* composition of the active compound of *Syzygium cumini* L. leaf extract and their effect on the behavior of *Aedes aegypti* Larvae. InProsiding Seminar Nasional Kesehatan, Sains dan Pembelajaran. 2021;1(1):723-31.

8. Alam MR, Rahman AB, Moniruzzaman M, Kadir MF, Haque MA, Alvi MR, *et al*. Evaluation of antidiabetic phytochemicals in *Syzygium cumini* (L.) Skeels (Family: Myrtaceae). J Appl Pharm Sci. 2012;2(10):94-8.

9. Kang SJ, Park JH, Choi HN, Kim JI. α-glucosidase inhibitory activities of myricetin in animal models of diabetes mellitus. Food Sci Biotechnol. 2015;24(5):1897-900.

10. Tadera K, Minami Y, Takamatsu K, Matsuoka T. Inhibition of α-glucosidase and α-amylase by flavonoids. J Nutr Sci Vitaminol. 2006;52(2):149-53.

11. Filimonov DA, Lagunin AA, Gloriozova TA, Rudik AV, Druzhilovskii DS, Pogodin PV, *et al*. Prediction of the biological activity spectra of organic compounds using the PASS online web resource. Chem Heterocycl Compounds. 2014;50(3):444-57.

12. Lipinski CA, Lombardo F, Dominy BW, Feeney PJ. Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. Adv Drug Delivery Rev. 1997;23(1-3):3-25.

13. Veber DF, Johnson SR, Cheng HY, Smith BR, Ward KW, Kopple KD. Molecular properties that influence the oral bioavailability of drug candidates. J Med Chem. 2002;45(12):2615-23.

14. Ghose AK, Viswanadhan VN, Wendoloski JJ. A knowledge-based approach in designing combinatorial or medicinal chemistry libraries for drug discovery. 1. A qualitative and quantitative characterization of known drug databases. J Combinatorial Chem. 1999;1(1):55-68.

15. Pires DE, Blundell TL, Ascher DB. pkCSM: Predicting small molecule pharmacokinetic and toxicity properties using graph-based signatures. J Med Chem. 2015;58(9):4066-72.

16. Megantara S, Iwo MI, Levita J, Ibrahim S. Determination of ligand position in aspartic proteases by correlating tanimoto coefficient and binding affinity with root mean square deviation. J Appl Pharm Sci. 2016;6(1):125-9.

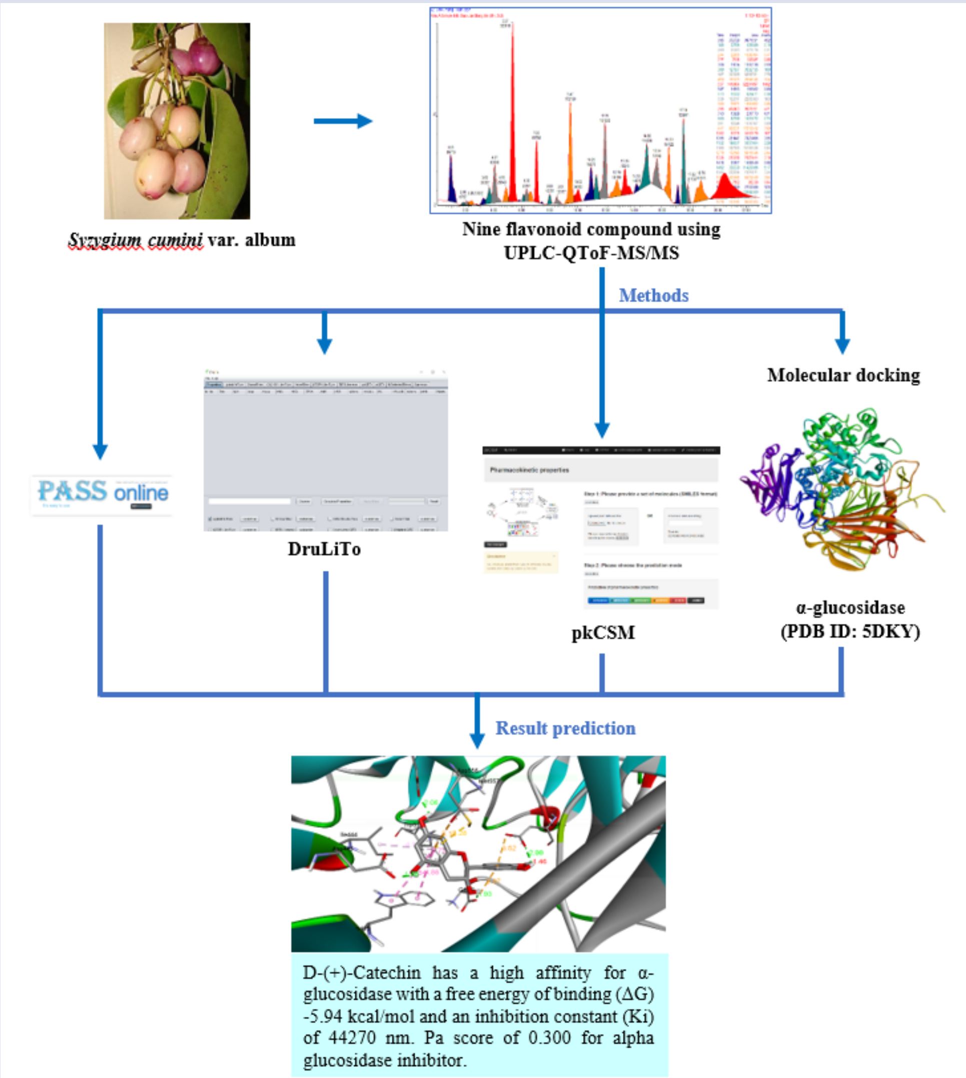
17. Pagadala NS, Syed K, Tuszynski J. Software for molecular docking: A review. Biophys Rev. 2017;9(2):91-102.

18. Chelliah DA. Biological activity prediction of an ethno medicinal plant *Cinnamomum camphora* through bio-informatics. Ethnobot leafl. 2008;12:181-90.

19. Jadhav PB, Yadav AR, Gore MG. Concept of drug likeness in pharmaceutical research. Int J Pharm Biol Sci. 2015;6:142-54.

20. Kharisma VD, Septiadi L, Syafrudin S. Prediction of novel bioactive compound from *zingiber officinale* as non-nucleoside reverse transcriptase inhibitors (NNRTIs) of HIV-1 through computational study. Biomed Res J. 2018;1(2):49-55.

GRAPHICAL ABSTRACT



ABOUT AUTHORS

Yanu Andhiarto is a doctoral student at Faculty of Pharmacy Airlangga University. He obtained his bachelor's and master's degree at Faculty of Pharmacy, Airlangga University. His research is focuses on drug discovery for antidiabetic from bioactive natural products.

Sukardiman is a professor from the Department of Pharmaceutical Sciences at Airlangga University. He has a lot of research experience in the field of herbal plant activities as anticancer, antidiabetic, biochemical, toxicity and herbal medicine standardization. He is a member of the national commission for herbal medicine in Indonesia and has done many national and international publications.

Suciati is a lecturer from the Pharmaceutical Science Department, Faculty of Pharmacy, Airlangga University. She obtained her bachelor's degree at Faculty of Pharmacy, Airlangga University. She was further pursued her master's and doctoral degree at the University of Queensland, Australia. Her research Interest on Chemistry and Bioactivity of Marine Natural Products and Terretrial Natural Products.

Ersanda Nurma Praditapuspa is lecturer from the Department of Pharmaceutical Chemistry, Faculty of Medicine, Hang Tuah University. She obtained her bachelor degree in Pharmacy at Faculty of Medicine, Hang Tuah University. She was further pursued her Master's degree at the Faculty of Pharmacy, Airlangga University. Her research is focuses on drug design and drug development from bioactive natural products for anti-breast cancer drugs.

Cite this article: Andhiarto Y, Sukardiman, Suciati, Praditapuspa EN. *In Silico* Analysis and ADMET Prediction of Flavonoid Compounds from *Syzygium cumini* var. album on α-Glucosidase Receptor for Searching Anti-Diabetic Drug Candidates. Pharmacogn J. 2022;14(6): 736-743.

Source details

Pharmacognosy Journal

Scopus coverage years: from 2009 to 2022

Publisher: Pharmacognosy Network Worldwide

ISSN: 0975-3575

Subject area: Pharmacology, Toxicology and Pharmaceutics: Pharmacology

Pharmacology, Toxicology and Pharmaceutics: Drug Discovery

Source type: Journal

View all documents > Set document alert Save to source list

CiteScore 2021
1.9

SJR 2021
0.258

SNIP 2021
0.718

CiteScore   CiteScore rank & trend   Scopus content coverage

i Improved CiteScore methodology

CiteScore 2021 counts the citations received in 2018-2021 to articles, reviews, conference papers, book chapters and data papers published in 2018-2021, and divides this by the number of publications published in 2018-2021. Learn more >

CiteScore 2021

1.9 = 1,760 Citations 2018 - 2021 / 946 Documents 2018 - 2021

Calculated on 05 May, 2022

CiteScoreTracker 2022

1.9 = 1,653 Citations to date / 867 Documents to date

Last updated on 05 March, 2023 • Updated monthly

CiteScore rank 2021

Category	Rank	Percentile
Pharmacology, Toxicology and Pharmaceutics — Pharmacology	#219/303	27th
Pharmacology, Toxicology and Pharmaceutics — Drug Discovery	#116/154	25th

View CiteScore methodology > CiteScore FAQ > Add CiteScore to your site

Minimum documents

Citescore highest quartile

- [ ] Show only titles in top 10 percent
- [ ] 1st quartile
- [ ] 2nd quartile
- [x] 3rd quartile
- [ ] 4th quartile

Source type

- [x] Journals
- [ ] Book Series
- [ ] Conference Proceedings
- [ ] Trade Publications

Apply   Clear filters

				Pharmaceutical Science			
[x]	3	Pharmacognosy Journal	1.9	27% 219/303 Pharmacology	1,760	946	56
[ ]	4	Turkish Journal of Pharmaceutical Sciences	1.5	40% 102/171 Pharmaceutical Science	455	311	55
[ ]	5	Journal of Research in Pharmacy	1.3	43% 42/74 General Pharmacology, Toxicology and Pharmaceutics	476	373	49
[ ]	6	Vitae *Open Access*	0.6	41% 18/30 Pharmacology, Toxicology and Pharmaceutics (miscellaneous)	26	45	31

Pharmacognosy Journal

COUNTRY

India

Universities and research institutions in India

Media Ranking in India

SUBJECT AREA AND CATEGORY

Pharmacology, Toxicology and Pharmaceutics
- Drug Discovery
- Pharmacology

PUBLISHER

EManuscript Technologies

H-INDEX

25

PUBLICATION TYPE

Journals

ISSN

09753575

COVERAGE

2009-2021

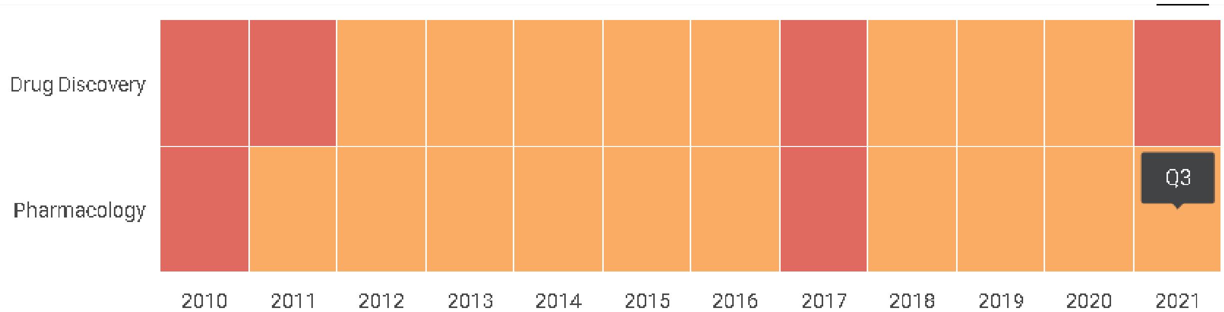
INFORMATION

Homepage

How to publish in this journal

editor@phcogj.com

Quartiles



SJR

2013	0.238
2014	0.255
2015	0.242
2016	0.265
2017	0.176
2018	0.254
2019	0.227
2020	0.268
2021	0.258

Total Documents