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Activities of Chalcone Derivatives from Boesenbergia rotunda Against Human Estrogen Receptor Alpha of Breast Cancer by In Silico

Maria Claudya[1], Dini Kesuma[2*], Aguslina Kirtishanti[3], I Gede Ari Sumartha[2], Marsha Anggita Amelia[1]

[1] Program Pendidikan Magister Farmasi Industri, Fakultas Farmasi, Universitas Surabaya, Surabaya Indonesia.
[2] Departemen Kimia Farmasi, Fakultas Farmasi, Universitas Surabaya, Surabaya Indonesia.
[3] Departemen Farmasi Klinis Komunitas, Fakultas Farmasi, Universitas Surabaya, Surabaya, Indonesia.

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Corresponding Author:
Dini Kesuma
dinikesuma1302@gmail.com

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Abstract: The high prevalence of cancer must be overcome with prompt and appropriate prevention and treatment. New drug design is an effort to develop existing drugs, and their molecular structure and biological activity have been known through structural modification. It encourages researchers to explore Indonesia's natural resources, especially plants with anticancer activity, namely by synthesizing chalcone-derived compounds derived from the isolation of Fingerroot rhizomes (*Boesenbergia rotunda*). The most common flavonoid compound found in rhizomes fingerroot plants is *pinostrobin*. *Pinostrobin* compounds and their derivatives are synthesized, resulting in chalcone compounds and their derivative modifications. The author conducted an in-silico test on *pinostrobin* compounds and 19 of their derivatives, chalcone compounds, and 18 derivatives using estrogenic-α receptors with PDB codes 3ERD and 1G50. The author hoped that from this silico test, compounds with more potential as anticancer for breast cancer would be obtained based on the results of docking with 3ERD and 1G50 receptors and can then be synthesized. In the results of this study, the compounds Bis-4-bromobenzyoxychalcone and Bis-4-chlorobenzyloxychalcone are the most appropriate compounds to be synthesized. It is hoped that in the future, they can be continued with activity tests of these compounds, both in vitro and in vivo, because these compounds are predicted to have the best activity and do not have hepatotoxic or other toxicity effects.

Keywords: Breast Anticancer; Chalcone; Cytotoxic Activity; Fingerroot rhizomes *(Boesenbergia rotunda)*; Structure Modification

Introduction

Cancer is a disease characterized by abnormal cells that can develop uncontrollably and attack and move between cells and tissues of the body (Sulung *et al*., 2018). One of the most common types of cancer in women is breast cancer (Kesuma *et al*., 2020). Breast cancer, also known as mammary carcinoma, is a malignant tumour that grows in breast tissue. The major factors causing breast cancer are obesity, alcohol consumption, genetics, and age. Genetic alterations lead to the dysregulation of several pathways related to cell proliferation and survival (Widyananda *et al*., 2022). Breast cancer overexpresses *estrogen* receptors (Er) about 70%. *Estrogen* receptors can be used to determine breast cancer sensitivity to *anti-estrogen* therapy and assess the sensitivity of preventive chemotherapy in patients at high risk of breast cancer. Er-α is a receptor that is generally reported to cause an increase in cell proliferation. Therefore, ER-α is a potential target for discovering and developing breast cancer drugs (Nurlelasari *et al*., 2023). One of the adherent cell lines that express the alpha estrogen receptor (ER-α) is MCF-7 breast cancer cells (Reynaldi & Setiawansyah, 2022).

Based on Global Burden Cancer (2020) data, there are 396,914 new cancer patients in Indonesia, with breast cancer ranked second at 65,858 (16.6%), and the death rate from breast cancer in Indonesia is 22,430 people (9.6%). The prevalence of breast cancer in 5 years (all

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ages) reached 201,143 cases (Effendi et al., 2023). The high prevalence of cancer must be overcome with prompt and appropriate prevention and treatment. Meanwhile, drugs used for a long time are gradually becoming less effective (Kar, 2007) and cancer cells tend to resist anticancer drugs (Goldman, 2003; Tartarone *et al*., 2013).

The main treatment for breast cancer is surgery with or without chemotherapy or radiotherapy, followed by hormone therapy. In patients with hormone receptor positives, *anti-estrogen* drugs such as Tamoxifen are usually used as hormone therapy. Tamoxifen is a triphenylethylene derivative pharmacologically classified as a selective ER modulator (SERM) that acts as an agonist in the uterus but as an antagonist in the breast (Chang, 2012). However, Tamoxifen has side effects, where the use of Tamoxifen for more than one year can cause the onset of endometrial cancer, hypertriglyceridemia, and liver and fatty liver disease (Aruminingsih et al., 2015).

Therefore, the development of new drugs that are selective and effective is carried out. The development or design of a new drug is an effort to develop an existing drug, and its molecular structure and biological activity are known through structural modification (Siswandono, 2016). Synthesizing several derivatives of the parent compound, identifying the structure, and testing its biological activity are all methods used in modifying the structure. Before a compound is synthesized, it is necessary to predict its molecular chemical properties, pharmacokinetic properties (ADMEs), toxicity, and drug interactions with receptors in a silico manner (Schlick, 2010). It happens because structural changes will alter the physicochemical properties of compounds, including lipophilic, electronic, and steric properties, as well as their biological activity (Hardjono, 2012; Hardjono *et al*., 2016). Molecular modeling is a technique that is currently being developed (Kesuma *et al*., 2018). The in-silico approach has filtered drug candidates from natural ingredient compounds. In addition, the in-silico approach can also be used to explain how a natural compound inhibits a target protein (Nurlelasari *et al*., 2023).

This encourages researchers to explore Indonesia's natural resources, especially plants with anticancer activity, namely by synthesizing chalcone-derived compounds derived from the isolation of rhizomes fingerroot rhizomes (*Boesenbergia rotunda*). *Boesenbergia rotunda* belongs to the Zingiberaceae family that grows in Southeast Asia, India, Sri Lanka, and southern China. There are bioactive compounds in Boesenbergia rotunda that are suspected to have anticancer properties (Widyananda et al., 2022). Fingerroot rhizomes (*Boesenbergia rotunda*) can increase the number of lymphocytes and specific antibodies and kill cancer cells. Based on phytochemical screening, rhizome fingerroot extract contains a lot of flavonoids, alkaloids, and phenolics (Atun & Handayani, 2017). The most common flavonoid compound found in the fingerroot rhizomes plant (Boesenbergia rotunda) is *pinostrobin* (Parwata *et al*., 2014). Most studies show that *pinostrobin* compounds function as antivirals, antioxidants, and anticancers (Charoensin *et al*., 2010). *Pinostrobin* compounds and their derivatives are synthesized to produce chalcone compounds and their derivative modifications. It occurs because the availability of chalcone compounds from natural materials is minimal. A study showed that chalcone and its derivatives can inhibit estrogen receptors in breast cancer. In addition, it has been found that chalcone has antiproliferative activity against MCF-7 breast cancer cells (Dona *et al*., 2015).

Based on the description above, in order to obtain compounds that are estimated to have anticancer activity in breast cancer, in this study, the author conducted an in-silico test on *pinostrobin* compounds and 19 of their derivative compounds, as well as chalcone compounds and 18 derivative compounds using *estrogen*-α receptors with PDB codes: 3ERD and 1G50. It is hoped that from this in silico test, compounds with more potential as breast anticancers will be obtained based on the results of docking against the 3ERD and 1G50 receptors and then can be synthesized.

Method

Materials

In this study, computer hardware with Intel(R) Core (TM) i7-9700F CPU specifications @ 3.00GHz, 16384MB RAM equipped with Windows 10 Education 64-bit operating system (University of Surabaya) was used. This study used *pinostrobin* compounds and 19 derivatives and 18 fibrous chalcone compounds in the 3D form downloaded from *MarvinSketch* software in (.mol2) format; Molecular Graphics Laboratory (MGL) Tools (including *AutoDock* Vina, *AutoDock* Tools 4.1, and Python 2.5.2) which are used for grid centre selection on protein structures and molecular docking; BIOVIA Discovery Studio Visualizer to visualize docking results; *estrogen*- α receptors are obtained from the Protein Data Bank (PDB) (https://www.rcsb.org/) in .pdb format with PDB codes 3ERD and 1G50; and Tamoxifen as a comparator.

Ligand Preparation

Pinostrobin compounds and their derivatives, chalcone, and its derivatives are referred to as ligands. *MarvinSketch* software is used to draw the ligand structure in the ligand preparation process. *AutoDockTools* 1.5.6 software prepares the ligand and arranges the grid box exactly where the ligand attaches to the receptor.

Receptor Preparation

Estrogen-α receptors with PDB codes 3ERD and 1G50 and Tamoxifen obtained from the Protein Data Bank (https://www.rcsb.org/). The resolution of these proteins is 2.03 Å and 2.90 Å, respectively. The receptor preparation process is carried out using *AutoDockools* 1.5.6 software. The method is valid if the RMSD value obtained is 3Å.

Molecular Docking

In docking, it is necessary to prepare a working folder containing autogrid4.exe and autodock4.exe, as well as receptors and ligands in the *pdbqt* format that have been prepared. In this study, molecular docking was carried out using Molecular Graphics Laboratory (MGL) Tools software, including *AutoDock* Vina, *AutoDock* Tools 4.1, and Python 2.5.2, after which it was run using Command prompt (CMD). Pyrx software was also used in this study and can be downloaded via https://pyrx.sourceforge.io/. BIOVIA Discovery Studio Visualizer (DSV) software is used to visualize the results of docking ligand bonds with amino acids on receptors in 2D and 3D.

Prediction of Physicochemical Properties and Toxicity of Compounds

Prediction of compound activity is carried out through the PASS Online (Prediction of Activity Spectra for Substance) website https://www.way2drug.com/PASSOnline/index.php; *pkCSM* (Predicting Small-Molecule Pharmacokinetic and Toxicity Properties Using Graph-Based Signature) website https://biosig.lab.uq.edu.au/pkcsm/ conducted to predict toxicity and bioavailability; http://www.scfbio-iitd.res.in/software/drugdesign/lipinski.jsp website is used for the analysis of lipophilic properties of compounds based on Lipinski's Rule of Five, and website https://tox.charite.de/protox3/# is used to view toxicity doses and toxicity classes using *Protox* online tools.

Result and Discussion

According to Praditapuspa et al., (2021), the potency and selectivity of compounds can be enhanced through structural modification. Several methods can be used to design potent and selective compounds, one of which is in silico methods. Optimizing activity, geometry, and reactivity before experimental synthesis is a key advantage of this approach. This can help shorten the synthesis process, which requires significant time and cost. To enhance its anticancer activity, the structure of pinostrobin was modified by adding acyl groups. The choice of substituents depends on how lipophilic, electronic, and steric properties change. In this study, several initial stages in the development of new drugs have been conducted. These stages are based on the principles of rational drug discovery and development (Praditapuspa *et al*., 2021).

In a previous study conducted by Mass *et al*. (2022), chalcone was used as a pharmacophore, which was synthesized into Dihydropyrimidone Chalcone compounds and subsequently confirmed using H-NMR Spectroscopy, resulting in 10 compounds derived from Dihydropyrimidone Chalcone. After that, 3 of the obtained compounds were tested in silico through molecular docking with the ER α receptor using Protein Data Bank (PDB) code 6CHZ and ER-β1 using PDB code 3OLS. The results showed that the best binding energy value was observed for ER α with PDB code 6CHZ. The in silico study indicated that the 3 compounds located at the active site of ER-α have the potential to act as antagonistic molecules that can disrupt cell proliferation processes . Therefore, this study will focus on the development of new breast cancer drugs, starting with molecular docking against ER-α using PDB code 6CHZ (Mass *et al*., 2022).

Figure 1 and Table 1 show the chemical structure of *pinostrobin* compounds and their derivatives, chalcone compounds and their derivatives, and tamoxifen comparator compounds.

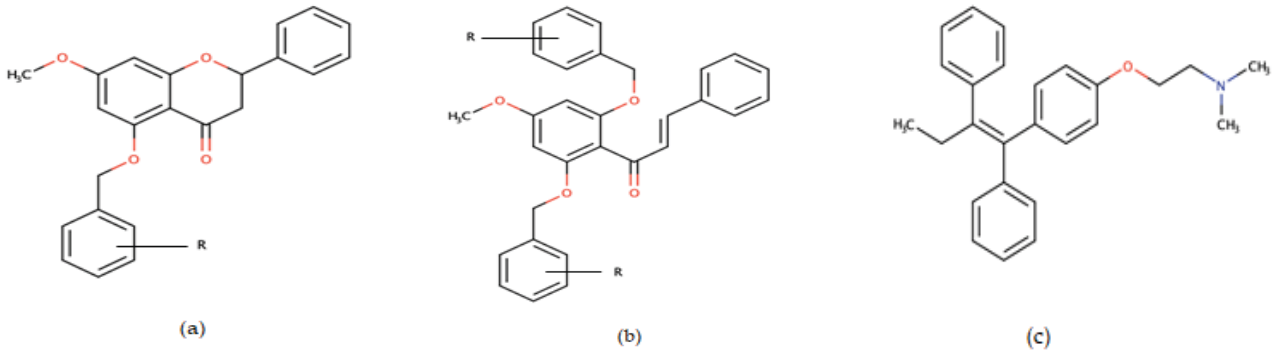

Figure 1. *Pinostrobin* compound (a), Chalcone Compound (b) and Tamoxifen Comparator Compound

Table 1. Chemical structure of *pinostrobin* and chalcone derivatives

No. Senyawa	Posisi	R	Nama Senyawa
1.	–	–	5-O-benzylpinostrobin
2.	4	Cl	5-O-(4-chloro-benzyl)pinostrobin
3.	3,4	2 Cl	5-O-(3,4-dichloro-benzyl)pinostrobin
4.	3 4	CF_3 Cl	5-O-(3-trifluoromethyl-4-chloro-benzyl)pinostrobin
5.	3 4	CF_3 NO_2	5-O-(3-trifluoromethyl-4-nitro-benzyl)pinostrobin
6.	4	CF_3	5-O-(4-trifluoromethyl-benzyl)pinostrobin
7.	4	Br	5-O-(4-bromo-benzyl)pinostrobin
8.	4	I	5-O-(4-iodo-benzyl)pinostrobin
9.	2,4	2 Cl	5-O-(2,4-dichloro-benzyl)pinostrobin
10.	4	NO_2	5-O-(4-nitro-benzyl)pinostrobin
11.	3	Cl	5-O-(3-chloro-benzyl)pinostrobin
12.	2	Cl	5-O-(2-chloro-benzyl)pinostrobin
13.	2	OCH_3	5-O-(2-methoxy-benzyl)pinostrobin
14.	4	F	5-O-(4-fluoro-benzyl)pinostrobin
15.	4	$C(CH_3)$	5-O-(4-tert-butyl-benzyl)pinostrobin
16.	3	CF_3	5-O-(3-trifluorometil-benzyl)pinostrobin
17.	3,5	2 Cl	5-O-(3,5-dichloro-benzyl)pinostrobin
18.	4	CH_3	5-O-(4-methoxy-benzyl)pinostrobin
19.	4	NH_2	5-O-(4-amino-benzyl)pinostrobin
20.	4	OH	5-O-(4-hydroxy-benzyl)pinostrobin
21.	–	–	2-6-dibenzyloxykalkon
22.	4	Cl	Bis-4-chlorobenzyloxychalcone
23.	3,4	Cl	Bis-3,4-dichloro-benzyloxychalcone
24.	3 4	CF_3 Cl	Bis-3-trifluoromethyl-4-chloro-benzyloxychalcone
25.	3 4	CF_3 NO_2	Bis-3-trifluoromethyl-4-nitro-benzyloxychalcone
26.	4	CF_3	Bis-4-trifluoromethylbenzyloxychalcone
27.	4	Br	Bis-4-bromobenzyloxychalcone
28.	4	I	Bis-4-iodobenzyloxychalcone
29.	2,4	2 Cl	Bis-2,4-dichlorobenzyloxychalcone
30.	4	NO_2	Bis-4-nitrobenzyloxychalcone
31.	3	Cl	Bis-3-chlorobenzyloxychalcone
32.	2	Cl	Bis-2-chlorobenzyloxychalcone
33.	2	CH_3	Bis-2-methoxybenzyloxychalcone
34.	4	F	Bis-4-fluorobenzyloxychalcone
35.	4	$C(CH_3)$	Bis-4-tertbutyl-benzyloxychalcone
36.	3	CF_3	Bis-3-trifluoromethyl-benzyloxychalcone
37.	4	CH_3	Bis-4-methoxy-benzyloxychalcone
38.	4	NH_2	Bis-4-amino-benzyloxychalcone
39.	4	OH	Bis-4-hydroxy-benzyloxychalcone
40.		Comparative Compund	Tamoxifen

Prediction of Physicochemical Properties and Toxicity of Compounds

Pinostrobin compounds and 19 derivatives, chalcone compounds and 18 derivatives, and tamoxifen comparative compounds were predicted for physicochemical properties based on the Lipinski Rule of Five (RO5). It prevents the compound's failure when it is developed into a drug due to low permeation or absorption. The Lipinski Rule of Five has requirements consisting of its molecular weight not exceeding 500 Da, the log value of the octanol/water partition coefficient (log P) is not more than 5, the donor's H-bond (HBD), expressed by the number of O-H and N-H groups, must be less than 5; and the H-bond of the acceptor (HBA), expressed by the number of O and N atoms, must be less than 10. The results of the Lipinski Rule of Five predictions are presented in Table 2. Based on the data obtained, it was concluded that several compounds derived from pinostrobin and chalcone did not meet the requirements of the Lipinski Rule of Five.

Table 2. In silico prediction of the physicochemical property parameters of Pinostrobin derivatives, Chalcone, and comparator compounds using the pkCSM online tool. MW = Molecular Weight; LogP = Logarithm of the Octanol/Water Partition Coefficient; RB = Rotation Bonds; HBA = Hydrogen Bond Acceptors; HBD = Hydrogen Bond Donors; PSA = Polar Surface Area.

No. Senyawa	MW	Log P	RB	HBA	HBD	PSA (A^2)
1.	270,284	3,1073	2	4	1	116,125
2.	394,854	5,6341	5	4	0	168,170
3.	429,299	6,2875	5	4	0	178,473
4.	462,851	6,6529	5	4	0	187,031
5.	473,403	5,9077	6	6	0	191,381
6.	428,406	5,9995	5	4	0	176,728
7.	439,305	5,7432	5	4	0	171,734
8.	486,305	5,5853	5	4	0	177,128
9.	429,299	6,2875	5	4	0	178,473
10.	405,406	4,8889	6	6	0	172,520
11.	172,520	5,6341	5	4	0	168,17
12.	394,854	5,6341	5	4	0	168,17
13.	390,435	4,9893	6	5	0	169,345
14.	378,399	5,1198	5	4	0	162,032
15.	416,517	6,2782	5	4	0	183,326
16.	428,406	5,9995	5	4	0	176,728
17.	429,299	6,2875	5	4	0	178,473
18.	374,436	5,28912	5	4	0	164,232
19.	375,424	4,5629	5	5	1	163,207
20.	376,408	4,6863	5	5	1	162,661
21.	450,534	6,7493	10	4	0	199,605
22.	519,424	8,0561	10	4	0	220,211
23.	588,314	9,3629	10	4	0	240,818
24.	655,418	10,0937	10	4	0	257,935
25.	676,522	8,6033	12	8	0	266,634
26.	586,528	8,7869	10	4	0	237,328
27.	608326	8,2743	10	4	0	227,34
28.	702,326	7,9585	10	4	0	238,129
29.	588,314	9,3629	10	4	0	240,818
30.	540,528	6,5657	12	8	0	228,911
31.	519,424	8,0561	10	4	0	220,211
32.	519,424	8,0561	10	4	0	220,211
33.	510,586	6,7665	12	6	0	222,562
34.	486,514	7,0275	10	4	0	207,936
35.	562,75	9,3443	10	4	0	250,524
36.	586,528	8,7869	10	4	0	237,328
37.	450,534	6,7493	10	4	0	199,605
38.	519,424	8,0561	10	4	0	220,211
39.	588,314	9,3629	10	4	0	240,818
40.	655,418	10,0937	10	4	0	257,935

In Silico Predictions, Activity and Toxicity

The results of the in-silico test prediction of *pinostrobin* compounds and their derivatives, as well as chalcone with their derivatives on *estrogen*-α receptor targets (PDB codes: 3ERD and 1G50), are presented in Table 3. Based on the data obtained in the table, it is concluded that the binding energy values of *pinostrobin* compounds and their derivatives and chalcone and its derivatives can be predicted in their compound activity.

Several compounds have more binding energy values when compared to *pinostrobin* and chalcone compounds in the 3ERD PDB code, namely in compounds number 2, 3, 4, 5, 7, 8, 9, 11, 12, 15, 16, 22, and 27. Compound number 27 (Bis-4-bromobenzyloxykalkon) is the compound that has the best binding energy value of -10.77 kcal/mol. Compound number 27 has a smaller binding energy value when compared to *pinostrobin* compounds (-8.73 kcal/mol), chalcone compounds (-9.96 kcal/mol), and tamoxifen comparator compounds (-8.61 kcal/mol).

There are several compounds with more binding energy values when compared to *pinostrobin* and

chalcone compounds in the PDB code 1G50, namely in compounds number 2, 3, 7,9, 11, 12, 13, 15, 16, 17, 18, 22, and 27. Compound number 22 (Bis-4-chlorobenzyloxykalkon) is the compound that has the best binding energy value of -11.01 kcal/mol. Compound number 22 has a smaller binding energy value when compared to *pinostrobin* compounds (-8.75 kcal/mol), chalcone compounds (-10.04 kcal/mol), and tamoxifen comparator compounds (-5.65 kcal/mol). The smaller the binding energy value of a compound, the greater its activity potential and stable ligand-receptor binding. The selected compounds are compounds number 22 and 27, namely Bis-4-chlorobenzyloxykalcone and Bis-4-bromobenzyloxykalcone. The compound was chosen because it does not cause hepatotoxic effects.

Table 3. In silico prediction of anticancer activity and toxicity against the ER-α receptor of Pinostrobin derivatives, Chalcone, and comparator compounds using AutoDock Vina and *PyRx* (*), *pkCSM* (**), *and Protox online tool* (***)

No. Senyawa	Activity					Toxicity	
	Binding Energy* (Kode PDB: 3ERD)	Binding Energy* (Kode PDB: 1G50)	Ames Toxicity**	Hepa-totoxicity**	Skin Sensitization**	LD_{50} Acute**	Class***
1	-8.73	-8.75	No	No	No	2147	5
2	-8.82	-8.79	No	No	No	2507	5
3	-9.3	-9.13	No	Yes	No	2635	5
4	-9.21	-8.59	No	Yes	No	2816	5
5	-8.86	-8.15	No	Yes	No	2553	5
6	-8.43	-8.75	No	Yes	No	2721	5
7	-8.99	-8.76	No	Yes	No	2516	5
8	-8.92	-8.44	No	No	No	2530	5
9	-9.45	-9.18	No	No	No	2636	5
10	-8.63	-8.42	Yes	Yes	No	2480	5
11	-9.16	-9.38	No	No	No	2510	5
12	-9.23	-9	No	No	No	2542	5
13	-8.7	-8.82	Yes	No	No	2675	5
14	-8.33	-8.64	No	No	No	2676	5
15	-9.09	-9.08	No	Yes	No	2492	5
16	-8.9	-9.12	No	Yes	No	2725	5
17	-8.56	-9.08	No	Yes	No	2606	5
18	-8.68	-8.8	No	No	No	2446	5
19	-8.02	-8.45	No	Yes	No	2725	5
20	-8.26	-8.24	No	Yes	No	2606	5
21	-9.96	-10.04	No	Yes	No	2048	5
22	-10.46	-11.01	No	No	No	2198	5
23	-5.96	-8.04	No	No	No	2312	5
24	-3.16	-5.48	No	Yes	No	2500	5
25	0.8	-5.48	Yes	No	No	2543	5
26	-5.26	-5.9	No	Yes	No	2400	5
27	-10.77	-10.55	No	No	No	2198	5
28	-5.78	-6.43	No	No	No	2224	5
29	-7.74	-7.94	No	No	No	2373	5
30	-4.87	-6.94	Yes	Yes	No	2518	5
31	-8.86	-9.34	No	No	No	2211	5
32	-7.62	-8.56	No	No	No	2235	5
33	-7.73	-7.65	No	No	No	2363	5
34	-9.13	-9.7	No	No	No	2395	5
35	-3.21	-5.34	No	Yes	No	1952	4
36	-6.51	-8.12	No	Yes	No	2382	5
37	-6.67	-8.17	No	No	No	2754	5
38	-8.07	-7.92	No	No	No	2346	5
39	-7.82	-8.26	No	Yes	No	3210	5
40	-8.61	-5.65	No	Yes	No	2671	5

The compound's toxicity can be determined by conducting an Ames Toxicity test. This test was carried out using bacteria to assess the compound's mutagenic potential. Compounds can be mutagenic and act carcinogenic when the test results are positive. The data obtained in Table 3 concluded that several pinoistrobin-

derived compounds, chalcone-derived compounds, and tamoxifen comparator compounds are predicted to be non-mutagenic—chalcone-derived compounds. However, compound numbers 10, 13, 25, and 30 showed positive test results, so it was said that the compound was mutagenic. In addition, Table 3 shows that all compounds derived from *pinostrobin* and chalcone and comparator compounds do not cause skin sensitisation. In silico tests and toxicity classification of compounds based on the Globally Harmonized System (GHS) using the *Protox* online tool were conducted on toxicity per liquid in rodents (LD_{50}) of *pinostrobin* and chalcone derivative compounds. The data in Table 3 shows that several compounds derived from pinostrobin and chalcone have LD_{50} values in rodents between 1952 and 3210 mg/kg. This value is included in the toxicity class group of 5 GHS, meaning the compound has a low acute toxicity effect. However, in Table 3, compound number 35 has an LD_{50} value of 1952 mg/kg and is included in the toxicity class of 4 GHS, meaning the compound's toxicity is relatively low.

In this study, compounds number 22 and 27 (Bis-4-chlorobenzyloxykalcone and Bis-4-bromobenzyloxychalcone) were selected by considering the compounds that are predicted to have the highest cytotoxic activity and are not toxic. The energy binding value of each of these compounds is -11.01 kcal/mol and -10.77 kcal/mol. These compounds were chosen because they do not have hepatotoxic or other toxicity effects. The two selected compounds can later be synthesized further. 3-D images of *estrogen* receptor targets- α PDB codes 3ERD and 1G50 with *pinostrobin* and chalcone derivative compounds and tamoxifen compounds as comparisons can be seen in Figure 2 and 3.

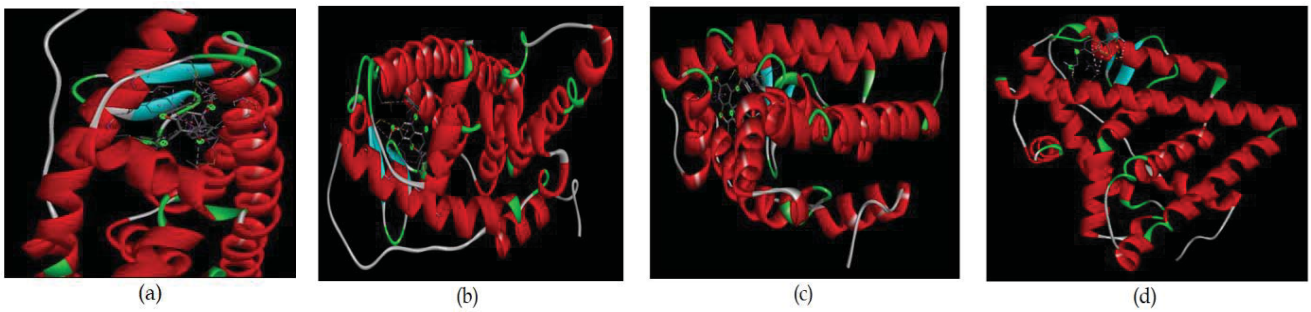

Figure 2. 3-D description of alpha *estrogen* receptor (ER– α) target 3ERD code with the compound ligands Bis-4-bromobenzyloxychalcone (a), *pinostrobin* (b), chalcone (c), and Tamoxifen (d)

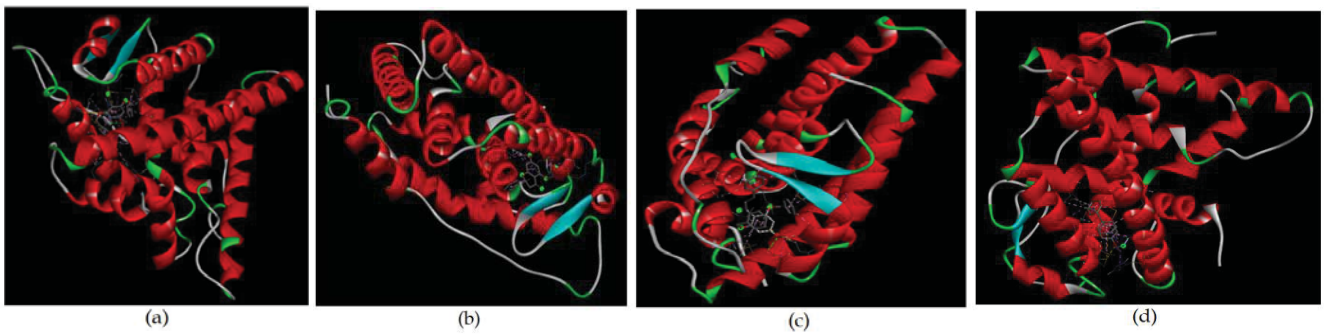

Figure 3. 3-D description of alpha *estrogen* receptor (ER-α) target 1G50 protein code with the compound ligands Bis-4-chlorobenzyloxychalcone (a), *pinostrobin* (b), chalcone (c), and Tamoxifen (d)

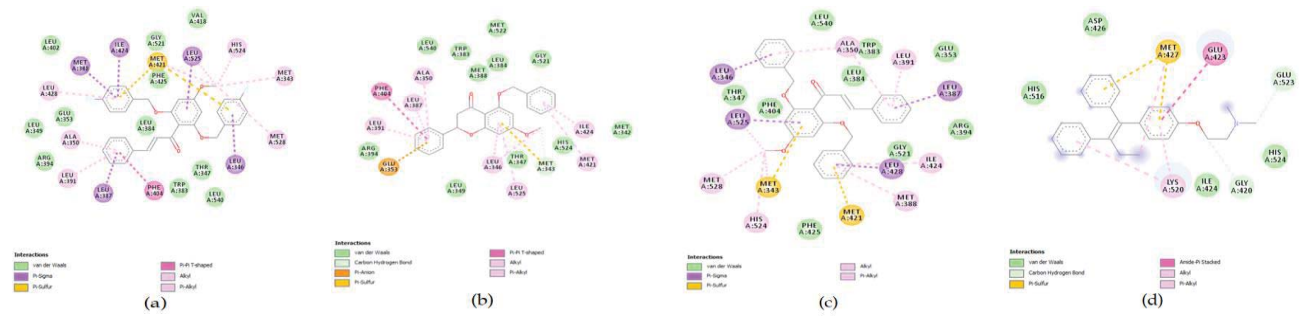

Figure 4. Visualization of the 2-D binding site on target *estrogen* receptor alpha (ER-α) code 3ERD with the compound ligands Bis-4-bromobenzyloxychalcone (a), *pinostrobin* (b), chalcone (c), and Tamoxifen (d)

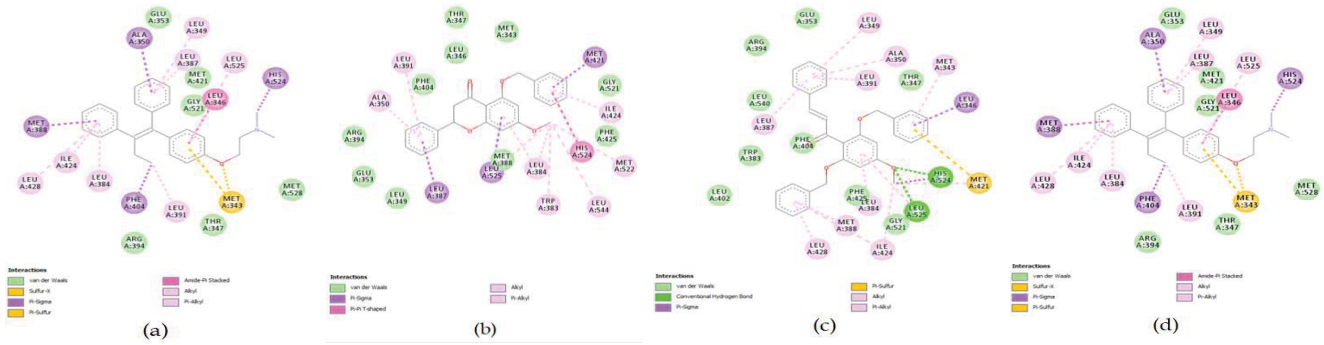

Figure 5. Visualization of the 2-D binding site on target *estrogen* receptor alpha (ER-α) code 1G50 with the compound ligands Bis-4-chlorobenzyloxychalcone (a), *pinostrobin* (b), chalcone (c), and Tamoxifen (d)

Ligand-receptor interactions involve various interactions between molecules, including Van der Waals, hydrogen bonds, sigma bonds, and others. Ligand-receptor interactions can be seen in Table 4.

Table 4. Ligan-Receptor Interactions

Kode PDB	Senyawa	Asam Amino	Jenis Interaksi
3ERD	Bis-4-bromobenzyloxykalkon	Arg 394; Glu 353; Gly 521; Leu 349; Leu 384; Leu 402; Leu 540; Phe 425; Thr 347; Trp 383; Val 418; Ile 424; Leu 346; Leu 387; Leu 525; Met 388; Met 421; Phe 404; Ala 350; His 524; Leu 391; Leu 428; Met 343; Met 528	Van der Waals, Pi-Sigma, Pi-Sulfur, Pi-Pi T-shaped, Alkyl, Pi-Alkyl
	Pinostrobin	Arg 394; Gly 521; His 524; Leu 349; Leu 388; Leu 540; Met 342; Met 388; Met 522; Thr 347; Trp 383; Met 343; Glu 353; Phe 404; Ala 350; Ile 424; Leu 346; Leu 387; Leu 391; Leu 525; Met 421	Van der Waals, Carbon Hydrogen Bond, Pi-Anion, Pi-Sulfur, Pi-Pi T-shaped, Alkyl, Pi-Alkyl
	Kalkon	Arg 394; Glu 353; Gly 521; Leu 384; Leu 540; Phe 404; Phe 425; Thr 347; Trp 383; Leu 346; Leu 387; Leu 428; Leu 525; Met 343; Met 421; Ala 350; His 524; Ile 424; Leu 391; Met 388; Met 528	Van der Waals, Pi-Sigma, Pi-Sulfur, Alkyl, Pi-Alkyl
	Tamoxifen	Asp 426; His 516; His 524; Ile 424; Glu 523; Gly 420; Met 427; Glu 423; Lys 520	Van der Waals, Carbon Hydrogen Bond, Pi-Sulfur, Amide-Pi Stacked, Alkyl, Pi-Alkyl
1G50	Bis-4-chlorobenzyloxykalkon	Arg 394; Glu 353; Gly 521; Met 421; Met 528; Thr 347; Met 343; Ala 350; His 524; Met 388; Phe 404; Leu 346; Ile 424; Leu 349; Leu 384; Leu 387; Leu 391; Leu 428; Leu 525	Van der Waals, Sulfur-X, Pi-Sigma, Pi-Sulfur, Amide-Pi Stacked, Alkyl, Pi-Alkyl
	Pinostrobin	Arg 394; Glu 353; Gly 521; Leu 346; Leu 349; Met 343; Met 388; Phe 404; Phe 425; Thr 347; Leu 387; Leu 525; Met 421; His 524; Ala 350; Ile 424; Leu 384; Leu 391; Leu 544; Met 522; Trp 383	Van der Waals, Pi-Sigma, Pi-Pi T-shaped, Alkyl, Pi-Alkyl
	Kalkon	Arg 394; Glu 353; Gly 521; Leu 402; Leu 540; Phe 404; Phe 425; Thr 347; Trp 383; His 524; Leu 525; Leu 346; Met 421; Ala 350; Ile 424; Leu 349; Leu 384; Leu 387; Leu 391; Leu 428; Met 343; Met 388	Van der Waals, Carbon Hydrogen Bond, Pi-Sigma, Pi-Sulfur, Alkyl, Pi-Alkyl
	Tamoxifen	Arg 394; Glu 353; Gly 521; Met 421; Met 528; Thr 347; Met 343; Ala 350; His 524; Met 388; Phe 404; Leu 346; Ile 424; Leu 349; Leu 384; Leu 387; Leu 391; Leu 428; Leu 525	Van der Waals, Sulfur-X, Pi-Sigma, Pi-Sulfur, Amide-Pi Stacked, Alkyl, Pi-Alkyl

Based on Table 4, the *pinostrobin* compound in the 3ERD protein code binds as many as 21 amino acids and has 1 hydrogen bond in MET 343. The bond occurs between the C atom in *pinostrobin* and the H atom in the MET 343 amino acid. The tamoxifen compound in the PDB code 3ERD binds as many as 9 amino acids and has 2 hydrogen bonds. The bond occurs between the C atom in Tamoxifen and the H atom in the amino acids GLY 420 and GLU 523. The chalcone compound in the PDB code 1G50 binds as many as 22 amino acids and has 2 hydrogen bonds. The bond occurs between the O atom in the chalcone and the H atom in the amino acids HIS 524 and LEU 525. Afliana & Ariyanti (2024) In the interaction between the ligand and the receptor, there are many important residues, such as those involved in hydrogen bonding and hydrophobic interactions, which are always present in every ligand-receptor interaction. These interactions play a crucial role in the binding site area (Afliana & Ariyanti, 2024). Faqiha *et al*. (2022) stated that the greater the hydrophobic interaction between non-polar molecules, the higher the stability of the ligand binding to the receptor (Ami Fini Faqiha *et al*., 2022). Putri *et al*., (2024) hydrophobic interactions occur when two nonpolar groups, such as the nonpolar groups of the ligand and the nonpolar groups of the receptor, come close together and merge, causing disruption in the molecular structure of water, which can no longer form hydrogen bonds with other water molecules. This disruption can increase entropy and reduce binding energy, which in turn helps stabilize the ligand-receptor complex. Hydrophobic interactions play a crucial role in determining the strength of this interaction. Types of hydrophobic interactions include pi-pi, pi-alkyl, pi-sigma, pi-sulfur, pi-anion, and pi-cation interactions (Putri *et al*., 2024). Other bonds, such as Van der Waals involving a hydrophobic group on the test compound with a hydrophobic group on the receptor, pi-sigma bonds involving a group that has a pi bond on the test compound with a group that has a sigma bond on an amino acid, a stacked amide-pi bond involving an N atom on a test compound with a group that has a pi bond on an amino acid, alkyl and pi-alkyl interactions involving alkyl groups on an amino acid test compound.

Conclusion

The results of this study concluded that the compounds Bis-4-bromobenzyoxychalcone and Bis-4-chlorobenzyloxychalcone are the most appropriate compounds to be synthesized, and it is hoped that in the future, they can be continued with activity tests of these compounds, both in vitro and in vivo. This is because these compounds are predicted to have the best activity and do not have hepatotoxic or other toxicity effects.

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Author Contributions

All authors contribute to designing the research, collecting and analyzing data, and writing the initial draft of the manuscript to completion.

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Conflicts of Interest

The authors declare no conflict of interest.

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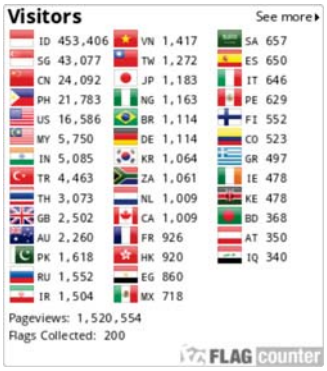

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Analysis of Clean and Healthy Living Behavior in Improving the Ecological Intelligence of Elementary School Students

Sinta Maria , Harmawati , Yulistina Nur DS , Sri Wulan Anggraeni , Fahmi Rizal 7390-7396

DOI: 10.29303/jppipa.v10i10.8742
Statistics: 54 | 22

PDV

Beach Quality Evaluation as a Strategy for Sustainable Coastal Tourism Management

Kenedi Kenedi , April Laksana , Miftahul Huda 7397-7408

DOI: 10.29303/jppipa.v10i10.8792
Statistics: 148 | 66

PDV

Curriculum Adaptation in Science Subjects at Banda Aceh Inclusive Elementary School

Aishah , Udin Syaefudin Sa'ud , Danny Meirawan , Diding Nurdin 7409-7414

DOI: 10.29303/jppipa.v10i10.8773
Statistics: 62 | 28

PDV

The Effect of Kupin Media to Increase Motivation in IPAS Learning Based on the Merdeka Curriculum at the Elementary School Level

Tia Latifatu Sadiah , Maman Faturrohman , Suroso Mukti Leksono , Yulistina Nur DS , Depi Prihamdani 7415-7419

DOI: 10.29303/jppipa.v10i10.8713
Statistics: 44 | 22

PDV

Development of Interactive Learning Media on Endocrine System Material to Increase Learning Motivation for Class XI SMA Students

Tutik Utika Sari , Tien Aminatun 7420-7430

DOI: 10.29303/jppipa.v10i10.8465
Statistics: 47 | 36

PDV

Ethno-STEAM Based E-Comic "Lilis Lamiang", is it Necessary to Use it on Science Learning in Elementary Schools?

Wndari Sabella , Fathul Zannah 7431-7436

DOI: 10.29303/jppipa.v10i10.8337
Statistics: 94 | 51

PDV

Authentic Assessment Instrument on Redox Reactions to Assess Students' Cognitive Skills

Qurratu 'Ainillana , Isana Supiah Yosephine Louise 7437-7446

DOI: 10.29303/jppipa.v10i10.8791
Statistics: 56 | 26

PDV

Characterization of Bioactive Compounds and Stability of Mangrove Extract Rhizopora Sp.

Dirk Y. P. Runtuboi , Ervina Indrayani , Imam Mishbach , Gabriela Olivia Karisoh 7447-7455

DOI: 10.29303/jppipa.v10i10.8674
Statistics: 76 | 56

PDV

Farmers Response to the Partnership System in Broiler Chicken Livestock Business in East Lombok District

Muhamad Yasin 7456-7463

DOI: 10.29303/jppipa.v10i10.9093
Statistics: 45 | 21

PDV

The Effectiveness of Using Telenursing in Supporting Patient Adherence to Antimalarial Medication

Diana Tati Haryati , Syamsul Anwar , Siti Badriah 7464-7473

DOI: 10.29303/jppipa.v10i10.9087
Statistics: 76 | 44

PDV

The Effect of Using Open the Box Type Wordwall Educational Game on Students' IPAS Cognitive Learning Outcomes

Yulistina Nur DS- , Tia Latifatusadiah , Hesti Widiastuti , Anggy Giri Prawiyogi , Meilani Amelia 7474-7479

DOI: 10.29303/jppipa.v10i10.8711
Statistics: 62 | 38

PDV

The Effect of a Jigsaw Type Cooperative Learning Approach Towards Primary Students' Understanding Concepts of Science Learning in Primary Schools

Anggy Giri Prawiyogi , Yulistina Nur DS , Tia Latifatusadiah , Tarpan Suparman , Hesti Widiastuti 7480-7485

DOI: 10.29303/jppipa.v10i10.8717
Statistics: 41 | 22

PDV

Development of Diagnostic, Formative and Summative Assessment Instruments in the PjBL Model to Stimulate Students' Critical and Creative Thinking Skills

Sintya Asiah , Festiyed 7486-7492

DOI: 10.29303/jppipa.v10i10.8757
Statistics: 68 | 43

PDV

Analysis of Biological Factors Associated with Preeclampsia in Pregnant Women

Nanik Yuliwati , Siti Juhariyah , Irmala Dewi , Irma Yuliawati , Ika Sartika Dewi 7493-7503

DOI: 10.29303/jppipa.v10i10.8692
Statistics: 53 | 24

PDV

The Effect of Counseling with Decision Making Tools (ABPK) on the Fertilization Inhibition Process in the Postpartum Period in 2024

Ita Herawati , Nyai Sulastri , Rusnah , Yeti Urianty , Eva Nova Lestarida Silaen 7504-7511

DOI: 10.29303/jppipa.v10i10.8856
Statistics: 38 | 16

PDV

Measuring Students' Understanding of Concepts, Law, and the Impact of Bullying

Sigit Haryanto , Ririn Purwani Mardi Lestari , Sofyan Anif 7512-7519

DOI: 10.29303/jppipa.v10i10.8604
Statistics: 40 | 34

PDV

Development of Diagnostic, Formative and Summative Assessment Instruments in the PjBL Model to Strengthen the Profile of Pancasila Physics Students

Marjuni , Festiyed 7520-7526

DOI: 10.29303/jppipa.v10i10.8758
Statistics: 65 | 24

PDV

The Influence of Project Based Learning Model in Training Students' Argumentation Skills

Dewi Nurdiyanti , Dewiantika Azizah , Anita Fatimatuzzahra 7527-7533

DOI: 10.29303/jppipa.v10i10.5062
Statistics: 42 | 24

PDV

Development of Powtoon Media in IPAS Learning Assisted by The PBL Model in Fourth Grade Elementary School

Chindy Yuginta Wanti , Hadiyanto , Desyandri , Yeni Erita 7534-7540

DOI: 10.29303/jppipa.v10i10.8976
Statistics: 42 | 18

PDV

Development of Ebook Teaching Materials Based on the PBL Model Assisted by the Kvisoft Flibbook Maker Application in Class IV Elementary Schools

Aprien Rahma Putri , Desyandri , Syafri Ahmad , Fetri Yeni J , Riduan AD , Ernawati 7541-7547

DOI: 10.29303/jppipa.v10i10.8868
Statistics: 48 | 27

PDV

Efforts to Improve Science Learning Outcomes Through Experimental Methods in Grade IV Students

Hesti Widiastuti , Yulistina Nur DS , Eri Subekti , Sri Rohartati , 7548-7553

Tia Latifatu Sadiah

DOI: 10.29303/jppipa.v10i10.8804
Statistics: 34 | 14

Citations 0

PDV

Survey of Students' Gadget Utilization to Know the Readiness of Personal Digital Inquiry Learning Implementation

Mahmudah Nur Cahyaningrum , Topik Hidayat , Kusnadi 7554-7561

DOI: 10.29303/jppipa.v10i10.7950
Statistics: 62 | 27

Citations 0

PDV

Development of Augmented Reality Learning Media on IPAS Subject Matter of the Respiratory System

Hanik Puji Rahayu , Desi Wulandari 7562-7571

DOI: 10.29303/jppipa.v10i10.7740
Statistics: 64 | 35

Citations 0

PDV

Development of Small-Scale Kits and Flipbooks for Practical Acid-Base Instruction

Ely Puspita Sari , Fera Kurniadewi , Muktiningsih Nurjayadi 7572-7580

DOI: 10.29303/jppipa.v10i10.7586
Statistics: 39 | 16

Citations 0

PDV

Cultivation of Microalgae Mixed Culture from Mahoni Small Lake UI Campus Depok using Zeolite Substrate with Varying Pb Concentration

Sri Mutmainah , Nining Betawati Prihantini 7581-7587

DOI: 10.29303/jppipa.v10i10.8989
Statistics: 52 | 29

Citations 0

PDV

Development of Video Learning Media Based on Robert Gagne's Theory (Nine Events of Instruction) in Informatics Subjects at Junior High School

Sri Mulyani , Darmansyah Darmansyah , Zelhendri Zen , Fetri Yeni J 7588-7596

DOI: 10.29303/jppipa.v10i10.8776
Statistics: 49 | 61

Citations 0

PDV

Development of Android-Based E-Learning Platform with RBL - STEM Approach to Improve Digital Literacy

Rina Sugiarti Dwi Gita , Fauzan Adhim , H.B.A Jayawardana , Febri Hariyanto 7597-7605

DOI: 10.29303/jppipa.v10i10.8901
Statistics: 63 | 35

Citations 0

PDV

The Impact of the Externality of Tofu Manufacturing Business on the

Social, Economic, and Environmental Aspects of the Community

Nurliani , Ida Rosada , Sitti Nurani Sirajuddin , Mukhlis

7606-7612

DOI: 10.29303/jppipa.v10i10.8890

Implementation of STEM-Integrated Modules and Wasaka Character Values to Improve Learning Outcomes

Muhsinah Annisa , Dasim Budimansyah , Mupid Hidayat , Atiek Winarti , Teguh Prasetio

7613-7618

DOI: 10.29303/jppipa.v10i10.9063

Implementation of a STEM and Wasaka Character-Integrated Module to Internalize Wasaka Character

Muhsinah Annisa , Dasim Budimansyah , Mupid Hidayat , Atiek Winarti , Teguh Prasetio

7619-7623

DOI: 10.29303/jppipa.v10i10.8941

Improving Critical Thinking Skills of Elementary Students Through Science Learning with Interactive Teaching Materials and Problem Based Learning

Fifi Nofitri , Desyandri , Fitri Eriyanti , Yerizon

7624-7633

DOI: 10.29303/jppipa.v10i10.7503

Hylopoly-Bag: Environmentally Friendly Bioplastic Innovation Made from Dragon Fruit (Hylocereus polarizes) Peel Waste to Support Golden Indonesia 2045

Tri Sunan Agung , Belinda Safa Salsabila Zuhri , Shinfi Wazna Auvaria

7634-7644

DOI: 10.29303/jppipa.v10i10.7703

Validation of Physics Kit Based on Sensor and PjBL Model to Improve Students' Digital Literacy, Science Process Skills, and Learning Outcomes

Fahmi Firdaus , Susilawati , Ahmad Harjono

7645-7651

DOI: 10.29303/jppipa.v10i10.9222

Analysis of Naïve Bayes and K-Nearest Neighbors Algorithms for Classifying Fishermen Aid Eligibility

Muhammad Nasrullah , Bayu Surarso , Oky Dwi Nurhayati

7652-7664

DOI: 10.29303/jppipa.v10i10.8818

PDV

Agribusiness System and Maize Agriculture Development Strategy in Palolo District Sigi Regency

Sofya A. Rasyid , Made Antara , Alam Anshary , Effendy , Hadayani
7665-7676

DOI: 10.29303/jppipa.v10i10.9376

Optimizing Tuna Fish Quality through a Science-Based Sustainable Partnership Approach and Ecological Management in Boneoge Village, Central Sulawesi

Nurfadilah , Asriani Hasanuddin , Nasmia
7677-7687

DOI: 10.29303/jppipa.v10i10.9364

Accessibility of Sustainable Beef Cattle Business Development in Mattiro Bulu District, Pinrang Regency

Ilham Rasyid , Indra Wirawan , Sitti Nurani Sirajuddin , Mukhlis
7688-7695

DOI: 10.29303/jppipa.v10i10.9083

Fabrication of Aluminium Matrix Composite Powder Reinforced with Silicon Dioxide Tailings for Non-Asbestos Brake Pads (NOB)

Sukanto , Ilham Ary Wahyudie , Erwanto , Yudi Oktriadi , Rodika , Ricky Irwansyah , Husman , Devrin Dwiki Saputra , Haradat Tahrir Algaza
7696-7704

DOI: 10.29303/jppipa.v10i10.9208

Durian Agribusiness Development Strategy in Boven Digoel Regency

Dadan Moh Ramdan , Ma'mun Sarma , Adi Hadianto
7705-7711

DOI: 10.29303/jppipa.v10i10.9413

Analysis of Mangrove Forest Management in Teluk Lembar, West Lombok, Indonesia

Muhammad Al'Awali Salahuddin , Nyoto Santoso , Rachmad Hermawan
7712-7725

DOI: 10.29303/jppipa.v10i10.9485

Development of An Integrated Assessment Instrument to Measure Students' Critical Thinking and Chemical Literacy Skills for Rate of Reaction Topic

Nurlaila Widyanarti Ariefiani , Endang Widjajanti Laksono
7726-2234

DOI: 10.29303/jppipa.v10i10.9069
Statistics: 66 | 48

Citations 0

PDV

Growth Increase of Gelam (Melaleuca Leucadendron) Burnt Peatland Through the Provision of Soil Conditioner (Study in Londerang Peat Protection Forest)

Rike Puspitasari Tamin , Richard Robintang Parulian Napitupulu , Jenny Rumondang , Rizky Ayu Hardiyanti

7735-7740

DOI: 10.29303/jppipa.v10i10.8786
Statistics: 39 | 22

Citations 0

PDV

Digital Student Worksheet on Ecology and Biodiversity to Enhance Critical Thinking and Digital Literacy for Middle School Students

Novita Anggraini , Hanum Isfaeni , Ratna Komala

7741-7747

DOI: 10.29303/jppipa.v10i10.8947
Statistics: 48 | 37

Citations 0

PDV

Spatially Varying Regression Coefficient Model For Predicting Stunting Hotspots In Indonesia

Ukhti Nurfajriah Sasmita Ijonu , I Gede Nyoman Mindra Jaya , Restu Arisanti

7748-7755

DOI: 10.29303/jppipa.v10i10.8270
Statistics: 41 | 19

Citations 0

PDV

Feasibility of Biopreneurship Project-Based Science Module for Students in the Bagek Kembar Ecotourism Area

X Zardht Alex Hidayat , I Putu Artayasa , A Wahab Jufri

7756-7764

DOI: 10.29303/jppipa.v10i10.9278
Statistics: 48 | 24

Citations 0

PDV

Black Cumin Seed Extract as Copper Corrosion Inhibitor in H2SO4 1M: An Experimental and Theoretical Study

Putri Elsa , Saprini Hamdiani , Emmy Yuanita , Saprizal Hadisaputra

7765-7774

DOI: 10.29303/jppipa.v10i10.8739
Statistics: 92 | 44

Citations 0

PDV

Reproductive Aspects of Blue Swimming Crab (Portunus pelagicus) Landed on the South End Coast of East Lombok

Lisnawati , Karnan , Abdul Syukur

7775-7783

DOI: 10.29303/jppipa.v10i10.9097
Statistics: 61 | 32

Citations 0

PDV

Development of Web-Based Interactive Learning Media on Excretory

System Materials to Increase Learning Interest

Nurul Kholiza Priani , Kartika Ratna Pertiwi
7784-7789

DOI: 10.29303/jppipa.v10i10.7962
Statistics: 39 | 23

PDV

Application of the Inquiry-Based Learning Model with Education for Sustainable Development to Enhance Critical Thinking Skills and Sustainable Awareness

Lidya Betty Setiyaningsih , Riandi , Amprasto , Mardiyah
7790-7802

DOI: 10.29303/jppipa.v10i10.8943
Statistics: 70 | 18

PDV

Arithmetic Proficiency of Pre-Service Science Teachers: An Empirical Study

Heni Yunilda Hasibuan , Yayat Ruhiat , Cecep Anwar Hadi Firdos Santosa
7803-7812

DOI: 10.29303/jppipa.v10i10.9195
Statistics: 71 | 15

PDV

Modification of Additional Check Valves and Tube Pressure to Enhance Hydram Pump Capacity and Performance for Agricultural Applications

Umar Husein Abdullah , Yusran Akbar , Lukman Martunis , Irhami Irhami , Sri Agustina , Muhammad Afdhal , Andriy Anta Kacaribu , Khairun Nisa
7813-7822

DOI: 10.29303/jppipa.v10i10.8478
Statistics: 57 | 19

PDV

Utilization Ecdysterone Hormone of Krokot (Portulaca oleracea) Extract on Molting Activity in Mud Crabs (Scylla serrate)

Gusti Abdillah Ihsan , Maheno Sri Widodo , Abd. Raheem Faqih , Akhsan Fikrillah Paricahya
7823-7831

DOI: 10.29303/jppipa.v10i10.8074
Statistics: 39 | 29

PDV

The Ability of Endophytic Bacteria in Phosphate Solubilization and IAA Production on Chili Plant Growth

Zulfatma Amanda , Erman Munir , Isnaini Nurwahyuni
7832-7838

DOI: 10.29303/jppipa.v10i10.8297
Statistics: 48 | 36

PDV

Effectiveness of Thermodynamics Textbooks Assisted by Heyzine Flipbook to Improve Students' Generic Science, Critical Thinking and Conceptual Understanding

Aris Doyan , Wahyudi , Syahrial Ayub , Ahmad Harjono , Susilawati
7839-7844

DOI: 10.29303/jppipa.v10i10.9091
Statistics: 37 | 25

PDV

Development of an E-Module Based on 3D Pageflip Professional on the Concept of Vibration and Wave

Melisa Damayanti R. Saleh , Tirtawaty Abdjul , Mohamad Jahja , Mursalin , Ritin Uloli , Asri Arbie
7845-7851

DOI: 10.29303/jppipa.v10i10.9138
Statistics: 50 | 25

PDV

Canva-Based Animation Comic Video Media in Informatics Learning

Liza Mustika Sari , Asrul Huda , Hansi Effendi , Muhammad Giatman
7852-7860

DOI: 10.29303/jppipa.v10i10.8514
Statistics: 43 | 28

PDV

Development of Salt Hydrolysis Module Based on Problem Based Learning Integrated with TPACK to Improve Numeracy Literacy Skills of Phase F SMA Students

Putty Zinda Febrila , Yerimadesi , Andromeda , Alizar
7861-7872

DOI: 10.29303/jppipa.v10i10.8615
Statistics: 53 | 119

PDV

Isolation and Inhibitory Activity Testing of Alpha-Glucosidase Enzyme from Endophytic Bacteria in Kumis Kucing (Orthosiphon aristatus (Blume) Miq.) Leaves

Indah Tamara Herman Putri , Rustini , Friardi Ismed , Valdy F Sardi , Nurwahidatul Arifah
7873-7884

DOI: 10.29303/jppipa.v10i10.9264
Statistics: 44 | 30

PDV

Development of Digital Learning Materials Using a QR Code Based Book Creator Application to Improve Student Learning Outcomes in Science Subjects

Adima Putri Widanti , Moh. Fathurrahman
7885-7893

DOI: 10.29303/jppipa.v10i10.7933
Statistics: 59 | 23

PDV

Ethnobotany Study Tradition Buang Abu Melayu Sambas as a Biology Learning Resource

Nurdiana , Hanum Mukti Rahayu , Mahwar Ourbaniah
7894-7903

DOI: 10.29303/jppipa.v10i10.8096
Statistics: 45 | 24

PDV

Website-Based Learning Media Using Google Sites to Improve Student Learning Outcomes in Natural and Social Sciences Subjects on Biodiversity Material

Fadilah Nur Jannah Nasution , Tri Astuti
7904-7913

DOI: 10.29303/jppipa.v10i10.7967
Statistics: 90 | 47

Citations 0

PDV

Development of Learning Media for the Katapel Quiz Application on the Concept of Energy in Living Systems

Sridiyanti S. Dunggio , Tirtawaty Abdjul , Citron S. Payu , Masrid Pikoli , Ritin Uloli , Abdul Haris Odja
7914-7923

DOI: 10.29303/jppipa.v10i10.9031
Statistics: 41 | 11

Citations 0

PDV

The Effect of Implementation Socio-Scientific Issue Approach in the Context of Controversial Environmental Issues on Students' HOTS (Higher Order Thinking Skills)

Army Auliah , Jasri Djangi , Dewiyanti Fadly
7924-7930

DOI: 10.29303/jppipa.v10i10.8463
Statistics: 53 | 33

Citations 0

PDV

Evaluation of Environmental Risk from Heavy Metals in Sediments in Port Areas

Yusrizal , Nuryasin Abdillah , Andri Hendrizal
7931-7935

DOI: 10.29303/jppipa.v10i10.8760
Statistics: 69 | 37

Citations 0

PDV

The Affect of Physical Parameters on Flood Potential in the Upstream River and the Musi Watershed of Kepahiang, Indonesia

Supiyati , Imania Elisa , Halauddin
7936-7945

DOI: 10.29303/jppipa.v10i10.7442
Statistics: 43 | 19

Citations 0

PDV

α-Glucosidase Enzyme Inhibitory Activity of Extracts from the Fermentation of Endophytic Bacteria from Periwinkle (Catharanthus roseus (L.) G. Don) Leaves

Ulfa Rosiatul Huda , Friardi Ismed , Nurwahidatul Arifah , Valdy Filando Sardy , Rustini
7946-7953

DOI: 10.29303/jppipa.v10i10.9178
Statistics: 55 | 26

Citations 0

PDV

Profile of Green Chemistry on Chemistry Education Students: Study on

Developing Green Chemistry Practical Module to Support Sustainable Development Goals (SDGs)

Mutiara Dwi Cahyani , Tania Avianda Gusman , Ari Yustisia Akbar 7954-7959

DOI: 10.29303/jppipa.v10i10.7796
Statistics: 66 | 41

PDV

What Do Chemistry Teachers Say About Scientific Creativity and the Development of Rosella Flower Extract Indicators as a Learning Medium for Acid-Base Titration?

Meli Safitri , Noor Fadiawati , Chansyanah Diawati 7960-7967

DOI: 10.29303/jppipa.v10i10.7067
Statistics: 41 | 18

PDV

Phylogenetic and Genetic Diversity of the Spiny Eel Mastacembelus unicolor (Mastacembelidae) from Kediri, East Java, Indonesia

Ifa Sufaichusan , Maheno Sri Widodo , Ating Yuniarti , Bela Fatma Hani Ayu Lestari , Wahyu Endra Kusuma 7968-7975

DOI: 10.29303/jppipa.v10i10.6138
Statistics: 47 | 29

PDV

Characterization Bio-Based Edible Film from Mango Seed Starch and Semi-Refined Carrageenan (Euchema cottonii) Using Sorbitol Plasticizer for Potential Food Contact Materials

Sintha Soraya Santi , Ika Nawang Puspitawati , Tim Pasang 7976-7983

DOI: 10.29303/jppipa.v10i10.8601
Statistics: 91 | 35

PDV

Development of Canva-Based Science Infographic Learning Media to Improve Students' Learning Outcomes

Sevi Ristanti , Barokah Isdaryanti 7984-7992

DOI: 10.29303/jppipa.v10i10.9506
Statistics: 60 | 40

PDV

Development of Encyclopedia Based on Ethnogastronomy of Sambas Malay Porridge

Dita Aulianti , Sunandar Ari , Hanum Mukti Rahayu 7993-8001

DOI: 10.29303/jppipa.v10i10.8375
Statistics: 40 | 13

PDV

Development of Electronics Student Worksheets Based on the Nature of Science in the Organic Chemistry on Polymer Materials Course

Nanda Salwa Aulia , Susilawati , Jimmi Copriady 8002-8014

DOI: 10.29303/jppipa.v10i10.8687
Statistics: 42 | 31

Citations 0

PDV

The Effect of Using Virtual Laboratories Using the Guided Discovery Learning Model on Students' Conceptual Understanding of Static Electricity Material

Haeratunisah , Aris Doyan , Muhammad Taufik 8015-8022

DOI: 10.29303/jppipa.v10i10.8682
Statistics: 42 | 26

Citations 0

PDV

Development of Science Mobile Learning as an Innovation in Learning Media in Elementary Schools

Nuraini , Zul Hidayatullah , Laxmi Zahara , Nunung Ariandani 8023-8029

DOI: 10.29303/jppipa.v10i10.8855
Statistics: 42 | 18

Citations 0

PDV

Development of E-Module Based Teaching Materials in the Subject of Ship Main Procovery Machinery

Mahzuardi , Refdinal , Ambiyar , Hasan Maksum 8030-8041

DOI: 10.29303/jppipa.v10i10.8644
Statistics: 42 | 21

Citations 0

PDV

The Relationship of Hand Washing Behavior and Type of Latrine with Stunting Incident

Theodorus Teddy Bambang Soedjadi , Deli Syaputri , Samuel Marganda Halomoan Manalu , Leo Eykel Timanthar 8042-8049

DOI: 10.29303/jppipa.v10i10.5114
Statistics: 50 | 23

Citations 0

PDV

Exploring Integrated Learning with Local Wisdom: Sendang Made Ecosystem E-book to Train Critical Thinking Skills for Class X High School Students

Lazulfah Nadhifatul Maulani , Dyah Hariani , Rinie Pratiwi Puspitawati 8050-8061

DOI: 10.29303/jppipa.v10i10.8511
Statistics: 35 | 23

Citations 0

PDV

Empirical Foundations for Developing New Learning Models to Improve Chemical Literacy, Scientific Habits of Mind, and Science Process Skills of Chemistry Education Students

Faiz Ilham Pratama , Eli Rohaeti , Endang Widjajanti Laksono 8062-8069

DOI: 10.29303/jppipa.v10i10.8661
Statistics: 54 | 41

Citations 0

PDV

Development of Flipped Classroom Based Learning Devices Assisted by the Nearpod Application in Integrated Thematic Learning in Third Class of Elementary Schools

Santia Indah Purnama , Yeni Erita , Ahmad Fauzan , Darmansyah , Darnelis 8070-8080

DOI: 10.29303/jppipa.v10i10.8826

Evaluation of Ratoon Potential and Yield of Some Sorghum Varieties (Sorghum bicolor L)

Akhmad Zubaidi , Dwi Ratna Anugrahwati , Baiq Erna Listiana , Novita Hidayatun Nufus , Anjar Azhari Pranggawan 8081-8087

DOI: 10.29303/jppipa.v10i10.8374

The Influence of the Problem Based Learning Model on the Scientific Attitudes and Science Learning Outcomes of Fifth Grade Elementary School Students

Vania Desiyanti , Ikhlasul Ardi Nugroho 8088-8097

DOI: 10.29303/jppipa.v10i10.8623

Exploration and Identification of Arbuscular Mycorrhizal Fungi (FMA) in Sungkai Plants (Peronema canescens Jack) at Various Soil Depths

Rike Puspitasari Tamin , Suci Ratna Puri 8099-8104

DOI: 10.29303/jppipa.v10i10.9011

Profile of Students' Critical and Creative Thinking Skills on Virus Material: The Need for Learning Innovation

Oktaviariesta Habibatus Sholikhah , Suranto , Slamet Santosa 8105-8116

DOI: 10.29303/jppipa.v10i10.7222

Activities of Chalcone Derivatives from Boesenbergia rotunda Against Human Estrogen Receptor Alpha of Breast Cancer by In Silico

Maria Claudya , Dini Kesuma , Aguslina Kirtishanti , I Gede Ari Sumartha , Marsha Anggita Amelia 8117-8126

DOI: 10.29303/jppipa.v10i10.8865

Development of Interactive Learning Media Based on Smart Apps Creator to Enhance Elementary School Students' Science Learning

Outcomes

Siti Rukoyah , Kurniana Bektiningsih 8127-8135

DOI: 10.29303/jppipa.v10i10.8046
Statistics: 58 | 34

Citations 0

PDV

Comparison of Discovery Learning Models Assisted by Student Books and Videos on Student Motivation, Activity, and Learning Outcomes

Budi Setiawan , Adnan , Firdaus Daud 8136-8148

DOI: 10.29303/jppipa.v10i10.9003
Statistics: 44 | 24

Citations 0

PDV

Study of Wordwall Web Based Learning Media to Increase Student Learning Interest in Science Learning

Bernika Irnadialis Pramudita , Ali Sunarso 8149-8157

DOI: 10.29303/jppipa.v10i10.9502
Statistics: 62 | 29

Citations 0

PDV

Development of Socioscientific-Issue-Based Electronic Modules on Virus Material to Increase Interest and Argumentation Skills

Sarah Rapma Kristina Sitanggang , Bernadetta Octavia , Anggi Tias Pratama 8158-8165

DOI: 10.29303/jppipa.v10i10.8597
Statistics: 36 | 18

Citations 0

PDV

Determining Tourism Area Using TOPSIS Analysis in the Dampier Strait Conservation Area

Anisa Kusumadewi Zulfikar Zulfikar , Yonvitner , Fery Kurniawan , Adrian Hidayat 8166-8172

DOI: 10.29303/jppipa.v10i10.8695
Statistics: 31 | 15

Citations 0

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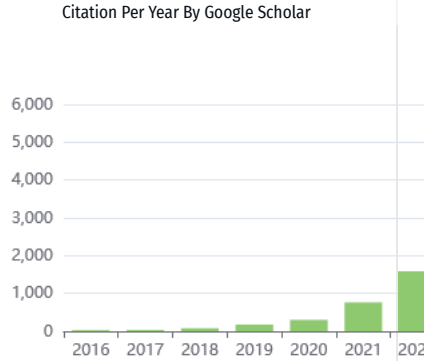

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