

# In-silico prediction of anti-breast cancer activity of ginger (*Zingiber officinale*) using machine learning techniques

Marisca Evalina Gondokesumo<sup>a</sup> and Muhammad Rezki Rasyak<sup>b,c,\*</sup>

<sup>a</sup>*Faculty of Pharmacy, University of Surabaya, Surabaya, Indonesia*

ORCID: <https://orcid.org/0009-0004-9774-4467>

<sup>b</sup>*Eijkman Research Centre for Molecular Biology, National Research, and Innovation Agency, Jakarta, Indonesia*

ORCID: <https://orcid.org/0000-0002-4016-4072>

<sup>c</sup>*Graduate School, Hasanuddin University, Makassar, Indonesia*

## Abstract.

**INTRODUCTION:** Indonesian civilization extensively uses traditional medicine to cure illnesses and preserve health. The lack of knowledge on the security and efficacy of medicinal plants is still a significant concern. Although the precise chemicals responsible for this impact are unknown, ginger is a common medicinal plant in Southeast Asia that may have anticancer qualities.

**METHOD:** Using data from Dudedocking, a machine-learning model was created to predict possible breast anticancer chemicals from ginger. The model was used to forecast substances that block KIT and MAPK2 proteins, essential elements in breast cancer.

**RESULT:** Beta-carotene, 5-Hydroxy-74'-dimethoxyflavone, [12]-Shogaol, Isogingerenone B, curcumin, Trans-[10]-Shogaol, Gingerenone A, Dihydrocurcumin, and demethoxycurcumin were all superior to the reference ligand for MAPK2, according to molecular docking studies. Lycopene, [8]-Shogaol, [6]-Shogaol, and [1]-Paradol exhibited low toxicity and no Lipinski violations, but beta carotene had toxic predictions and Lipinski violations. It was anticipated that all three substances would have anticarcinogenic qualities.

**CONCLUSION:** Overall, this study shows the value of machine learning in drug development and offers insightful information on possible anticancer chemicals from ginger.

Keywords: Molecular docking, machine learning, KIT, MAPK2

## 1. Introduction

Human life has long been a concern for public health issues. Traditional medicine consumption is still common across several ASEAN nations and other countries, such as Japan, Korea, and China [1,2]. For generations, Indonesian society has relied on traditional

herbal medicines to treat illness and maintain wellness. The generic name for this herbal remedy is jamu [3]. However, herbal medicine treatment still needs to be improved due to inadequate efficacy monitoring and a need for more information about the effectiveness of diverse medicinal plants [4].

Southeast Asian-born ginger is a traditional medicine frequently found in meals and beverages. Ginger is a traditional herbal antioxidant and anti-inflammatory medicine [5]. Ginger has anticancer effects and antioxidant and anti-inflammatory properties, as reported in several publications. These publications include those on gastrointestinal cancer [6], pancreatic cancer [7],

---

\* Corresponding author: Muhammad Rezki Rasyak, Eijkman Research Centre for Molecular Biology, National Research and Innovation Agency, Jakarta, Indonesia and Cisehat Park Residence, Blok A, No.6, Sirnagalih, Tamansari, 16611, Kab. Bogor, Jawa barat, Indonesia. Tel.: +62 85882394737; E-mail: rezkirasyak@gmail.com.

and anti-cancer activity against human breast cancer cell lines when ginger extract is combined with turmeric and garlic [8]. Clinical research and animal models have shown that ginger and its contents effectively prevent and treat disease. However, the exact molecules that give ginger its anticancer properties remain unknown. One substance that may be anticancer from ginger is called valinoids [9]. Bioinformatic and pharmacoinformatic research is required to understand the ginger component that may serve as an anti-cancer.

The quantitative structure-activity relationship (QSAR) model of the chemicals dataset is currently being built using machine learning as a component of artificial intelligence to obtain crucial descriptors to predict a specific biological activity from unknown compounds [10]. To develop a model prediction, machine learning requires a dataset for training and testing [11]. Several protein inhibitor datasets have been gathered to produce drugs, such as Dudedocking (<http://dude.docking.org/>). This website offers information on chemicals that inhibit proteins and components that act as a decoy, which are used to create and test machine-learning models that can predict protein inhibitors [12].

Cancer occurs when cells in a specific body area multiply and expand uncontrolled. Cancerous cells have the potential to penetrate and damage nearby healthy tissue, including organs. There are numerous pathways, and the cancer route includes several proteins. Over 30% of all human cancers include overactive MAPK1/2 (ERK1/2) proteins [13]. Mitogen-activated protein kinase (MAP kinase) cascades transmit and amplify signals relevant to cell growth and death. These signal transduction pathways allow us to assess the level of trafficking induced by various growth factors, steroid hormones, and G protein receptor-mediated ligands [13]. KIT protein is an additional crucial protein. KIT protein overexpression or mutations can accelerate the growth and spread of tumors in various human malignancies [14]. KIT signaling is linked to various physiological processes, including hematopoiesis, gastrointestinal motility, and pigmentation. It is an essential regulator of cell proliferation, survival, and migration [14]. This study's objective is to identify possible breast anti-cancer chemicals in ginger, where both protein MAPK2 and KIT are mentioned as essential nodes in breast cancer in the KEGG pathway map (Fig. 1) utilizing machine learning approaches, molecular docking research, ADME analysis, and molecular pharmacophore analysis.

## 2. Material and methods

### 2.1. Data mining and fingerprint extraction

algorithm. A machine learning algorithm predicted protein KIT and MAPK2 inhibitors in ginger. Ginger compound data is gathered from the Knapsack database core system using the keyword *Zingiber officinale* [15]. Using the open-source RDKit in Python software base (<https://www.rdkit.org/>), smile structures from all compounds are extracted to create Klekota-Roth fingerprints. There are 4860 substructures in the Klekota-Roth fingerprint, each with a binary score of one or zero [16], through Dudedocking, a dataset of chemicals that inhibit KIT and MAPK2 proteins was gathered [12]. The website also provides a decoy compound that can be utilized as a non-active compound. Machine learning models would be created using active and inactive substances. Before developing a model, each substructure is obtained using the fingerprint extractor from RDKit.

### 2.2. Machine learning model development

Scikit-learn, a Python-based program, is used to create machine learning models [17]. Jupyter notebooks are used to write and implement the code [18]. The AUC/ROC score was used to select the most effective model. In this analysis, we use three algorithms that have been often referenced in other works. Random forest (RF), Support vector machine (SVM), and Logistic regression are three algorithms (RF). The three methods are compared, and the model with the highest Score is utilized to forecast the active chemicals in ginger.

### 2.3. Molecular docking from predicted active compound and interaction analysis

A machine learning-predicted active substance is subjected to molecular docking investigation. To determine the probable binding affinities of each component from ginger, we used the PLANTS 1.1 software [19]. The ligand's minimal energy conformation in the protein's binding region is determined using an artificial ant colony [20]. Two empirical scoring functions, PLANTSCHEMPLP and PLANTSPLP, were created for the docking method PLANTS (Protein-Ligand ANT System), which is based on ant colony optimization (ACO). The optimal parameter settings for the search algorithm have been found, and they can be used to Balance pose prediction accuracy with search speed [19].

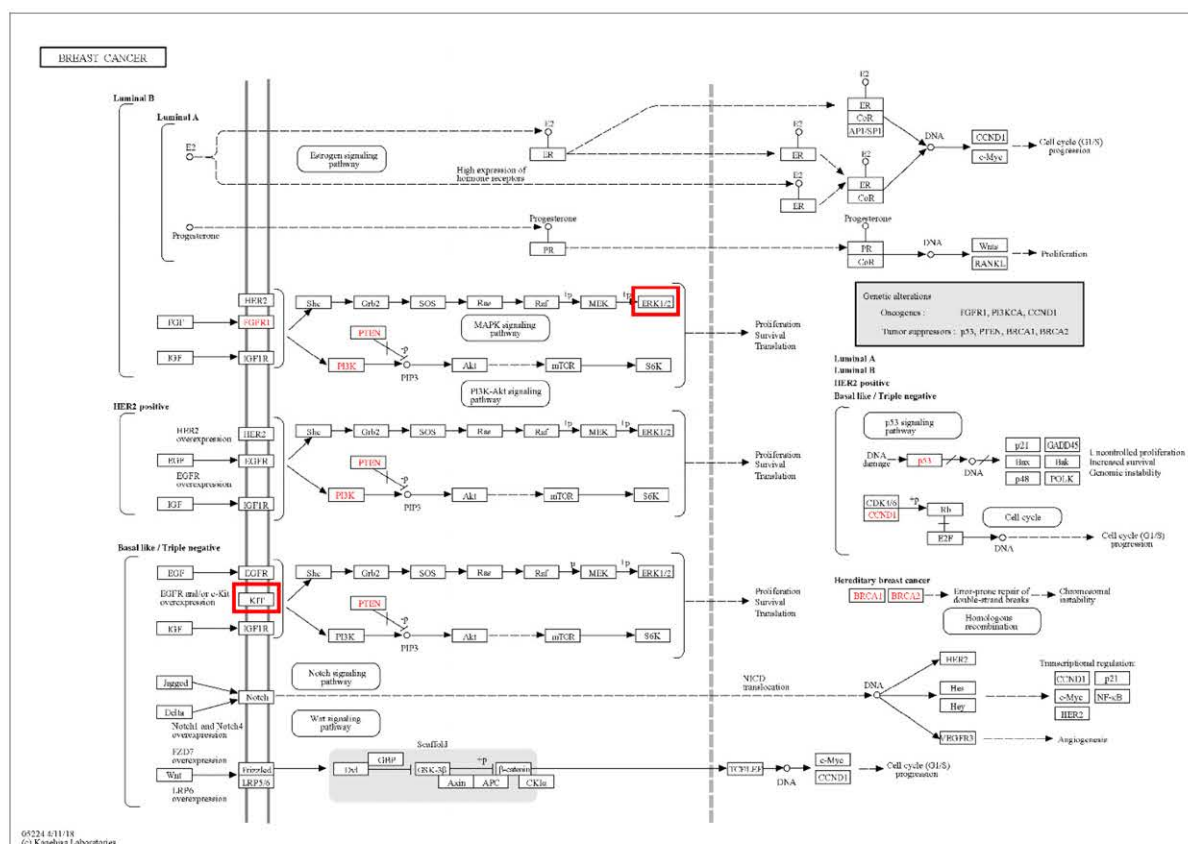


Fig. 1. KIT and MAPK2 protein in breast cancer map pathway.

PRODIGY was used to calculate binding affinity ( $\Delta G$ ) after molecular docking [21]. PRODIGY protein-ligand principles (<https://wenmr.science.uu.nl/prodigy/lig>) by appropriately modifying the small ligand prediction technique to use atomic interactions rather than residue contacts. PRODIGY advantages LIGs include their simplicity, generality, and applicability to all protein-ligand complexes [22].

#### 2.4. ADME (Absorption, Distribution, Metabolism, and Excretion) and toxicity analysis

The purpose of ADME analysis is to evaluate how much each chemical resembles a medicine expected to be active by machine learning. To ensure a drug's pharmacokinetics, an examination called an ADME analysis (Absorption, Distribution, Metabolism, and Excretion) is performed. SwissADME is used for the ADME analysis (<http://www.swissadme.ch/>) [23]. Using Tox-tree, each compound's toxicity is examined [24]. The toxicological concern threshold is frequently called the

toxicity level (TTC). TTC refers to determining an exposure threshold for all substances below which there is no appreciable danger to human health [24]. The Lipinski rule of five is a frequently used metric to measure drug-likeness, which includes (1). a maximum of five hydrogen bond donors (the sum of the bonds between hydrogen and oxygen and nitrogen), (2). ten or fewer (all nitrogen or oxygen atoms) hydrogen bond acceptors; (3). fewer than 500 daltons for the molecular weight (4). No more than 4.15 LogP [25].

Blood-brain barrier (BBB) and human intestinal absorption (HIA) analyses are frequently combined with toxicity analysis to predict the number of compounds that can be absorbed by the gastrointestinal tract (GI) [26]. Toxicity analysis indicates whether these compounds can pass through the blood-brain barrier.

#### 2.5. Analysis of bioactivity prediction

The final technique we employed in this investigation was bioactivity prediction. The web-based

Table 1  
The score of each of the three models for MAPK2 protein

Model	Accuracy	Sensitivity	Specificity	AUC/ROC score
LR	0.981	1.000	0.962	0.997
SVM	0.943	0.923	0.962	0.991
RF	0.905	0.961	0.962	0.981

Table 2  
The score of each of the three models for KIT protein

Model	Accuracy	Sensitivity	Specificity	AUC/ROC score
LR	0.954	0.909	1.000	0.984
SVM	0.954	0.909	1.000	0.983
RF	0.954	0.909	1.000	0.980

PASS-SERVER allows for the prediction of bioactivity. This bioactivity prediction considers pharmacological effects, action mechanisms, toxic and adverse effects, interactions with metabolic transporters and enzymes, impact on gene expression, etc [27].

## 2.6. Tanimoto similarity for chemical structure and pharmacophore

Potential compounds already mentioned above are then converted to fingerprints. The fingerprint of each compound is used to calculate structure similarity with reference ligand control using RDKit in jupyter notebook [18]. The molecular docking result of each compound has to interact with several amino acids of the protein; the active residue that interacts with the ligand compound is also used to calculate the similarity interaction with the reference ligand as a control. This method tries to see if the ligand interacts similarly with the reference ligand using Pyplif-Hippus [28].

## 3. Results

### 3.1. Machine learning model development

Table 1 displays the Score for the MAPK2 protein prediction model. Regarding the final result, the AUC/ROC score (0.997).

It is also displayed by KIT protein, where logistic regression (LR) has the best Score regarding the AUC/ROC score (0.984) (Table 2). The logistic regression (LR) model is then used to predict potential active compounds from ginger that possibly inhibit MAPK2 and KIT protein.

We discovered ten compounds that a machine learning model suggested could potentially be a KIT protein inhibitor (Table 3), and a total of 64 compounds are predicted as active chemicals because of the MAPK2 protein model (Table 4). Compounds predicted as inhibitors for KIT and MAPK2 protein are subjected

to molecular docking to explore possible attachment in the binding pocket of KIT and MAPK2 protein.

### 3.2. Molecular docking from predicted active compound and interaction analysis

Software validation has been performed before using PLANTS 1.1 software for protein-ligand-docking. The PLANTS 1.1 software is used in a benchmarking analysis with data from Dudedocking [12]. Docking and binding affinity scores ( $\Delta G$ ) are calculated using active KIT and MAPK2 protein inhibitors and non-active (decoy) compounds. The docking and binding affinity scores ( $\Delta G$ ) are then projected to generate the AUC/ROC score for the PLANTS 1.1 software results using the predicted docking score and binding affinity of active and decoy compounds. This method was used to test whether the PLANTS 1.1 software could distinguish between active and decoy compounds based on the binding and affinity scores. The AUC/ROC score of retrospective analysis from PLANTS 1.1 software yields excellent results, with AUC ROC scores of 0.992 for KIT protein and 0.986 for MAPK2 protein (scale 0–1, the getting closer to 1 the better result) (Fig. 3).

KIT (PDB: 1T46) and MAPK2 (PDB: 3M2W) were the proteins used in this study. Both proteins have a reference ligand that acts as an inhibitor. Imatinib (Drug-Bank code: DB00619) is an inhibitor of the KIT protein (PubChem code: 5291). The drug has already docked with the KIT protein (PDB: 1T46). While the reference ligand for the MAPK2 protein is 2'-(2-fluorophenyl)-1-methyl-6',8',9',11'-tetrahydrospiro [azetidine-3,10'-pyrido [3',4':4,5] pyrrolo [2,3-f] isoquinolin], -7'(5'H)-one (PubChem code: 42646698). PLANTS 1.1 was used to perform 100 repetitions of re-docking reference ligand to validate the accuracy of the PLANTS 1.1 software (Fig. 3). The average docking score of a reference ligand to KIT protein is  $-142.904$ , while that of a MAPK2 reference ligand is  $-101.628$ .

Figure 3 shows the binding affinity calculation result after 100 repetitions. The average Root mean square

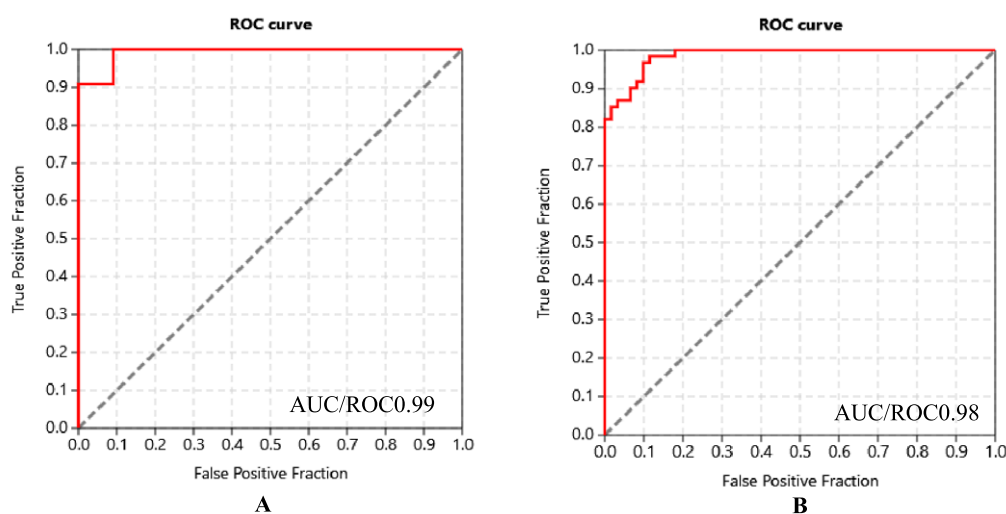


Fig. 2. AUC/ROC score for KIT protein (A) and AUC/ROC score for MAPK2 protein.

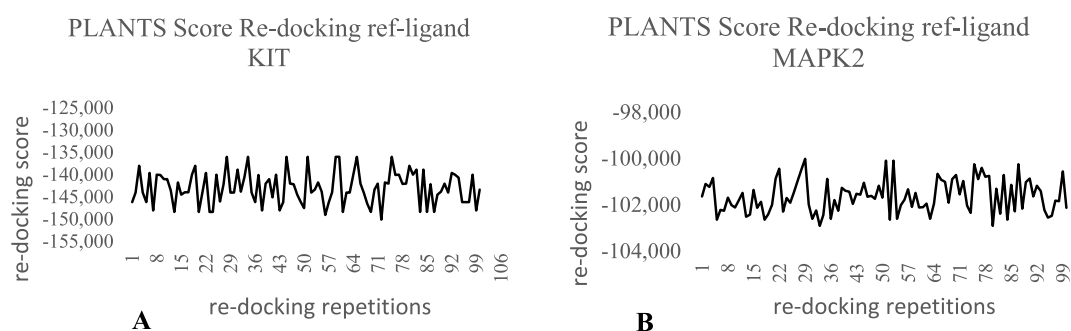


Fig. 3. PLANTS 1.1 docking Score between ref\_ligand to KIT protein (A) and MAPK2 protein (B) for 100 repetitions using PLANTS 1.1.

deviation (RMSD) of the reference ligand to KIT protein is 0.7365, while the RMSD of the reference ligand to MAPK2 protein is 1.3256. The RMSD after 100 repetitions of re-docking was stable. The figure shows that the RMSD of docking ligand to reference ligand after 100 repetitions to protein was stable below 2.0 Å [29].

Beta\_caroten is the only compound predicted as active from a machine learning model for KIT protein with a lower binding affinity score ( $\Delta G$ ) than the reference ligand (ref\_ligand). The binding energies score ( $\Delta G$ ) for the reference ligand is  $-10.4$  Kcal/mol, while the Score for beta-carotene is  $-14.3$  Kcal/mol. This finding indicates that beta-carotene may bind better to the KIT protein (Table 3). On the other side, 14 of the 64 compounds predicted as active by the machine learning model for the MAPK2 protein have lower binding energies than the reference ligand. Lycopene, 5-Hydroxy-7,4'-dimethoxyflavone, [12]-Shogaol, Isogingerenone

B, Curcumin, trans-[10]-Shogaol, Gingerenone A, Dihydrocurcumin, Demethoxycurcumin, [8]-Shogaol, [6]-Shogaol, [1]-Paradol, Bisdemethoxycurcumin, and alpha-Zingiberene are among the 14 compounds (Table 4).

After calculating compounds classified as active and inactive KIT and MAPK2 protein inhibitors, we found that a machine-learning model revealed promising results. Compounds grouped as an active protein to inhibit KIT have a binding affinity ( $\Delta G$ ) ranging from  $-7.1$  (Isovanilin) to  $-14.3$  (beta-carotene). No compounds with a lower binding affinity score than  $-7.0$  Kcal/mol are classified as active inhibitors of the KIT protein. A similar accurate prediction result was also shown in the MAPK2 protein. Binding affinity ( $\Delta G$ ) ranges from  $-7.4$  Kcal/mol (3-Octen-2-one) to  $-10.6$  Kcal/mol (Lycopene and 5-Hydroxy-7,4'-dimethoxyflavone) (Table 4). The compounds 5-Hydroxy-74'-dimethoxyflavone, lycopene [12]

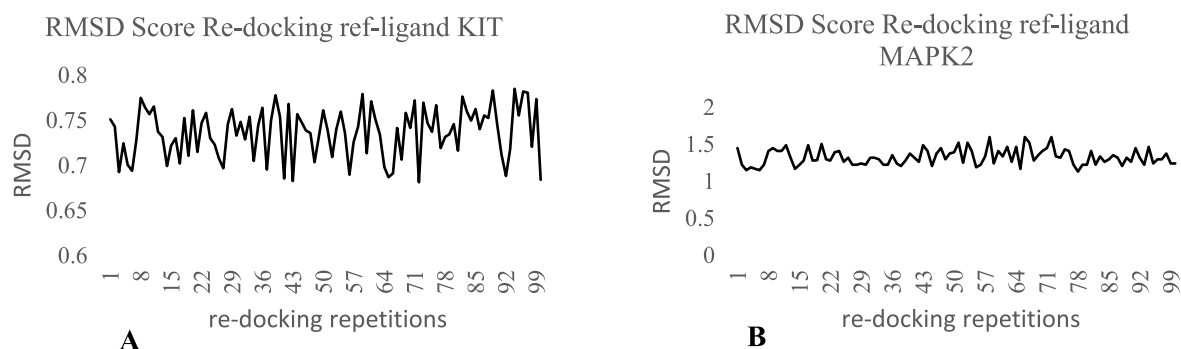


Fig. 4. Root means square deviation (RMSD) of re-docking between ref\_ligand to KIT protein (A) and MAPK2 (B) protein for 100 repetitions using PLANTS 1.1.

Table 3  
Docking and binding affinity score ( $\Delta G$ ) for the predicted compound as an inhibitor for KIT protein

Compound	Docking score	Binding affinity ( $\Delta G$ ) Kcal/mol
ref_ligand	-148	-10.4
Zingiberoside A	-75.4	-9.1
Vanillin	-65	-7.2
Vanilic acid	-65.4	-7.2
Trans 2 Octenal	-66.6	-7.5
Isovanilin	-66	-7.1
beta caroten	-121	-14.3
alpha,4-Dimethylstyrene	-68	-8.2
4-Hydroxybenzaldehyde	-62	-7.3
3-Octen-2-one	-66.6	-7.4

-Shogaol, Isogingerenone B, curcumin, Trans-[10]-Shogaol, Gingerenone A, Dihydrocurcumin, and Demethoxycurcumin were found to be more effective than the reference ligand, despite having a lower binding affinity. While [8]-Shogaol, [6]-Shogaol, [1]-Paradol, Bisdemethoxycurcumin, and alpha-Zingiberene appear to be similar but better than the reference ligand.

### 3.3. ADME (Absorption, Distribution, Metabolism, and Excretion) and toxicity analysis

However, after ADME analysis, beta carotene is the only ligand with a lower binding affinity than the reference ligand of the KIT protein. Beta caroten has two Lipinski violations and is classified as intermediate or high due to toxic prediction using toxtree (Table 5). Lycopene, [8]-Shogaol, [6]-Shogaol, [1]-Paradol, and alpha-Zingiberene were identified as toxtree low toxicants. Due to Lipinski rules in ADME analysis,

each compound also shows no Lipinski violation. The compounds [8]-Shogaol, [6]-Shogaol, and [1]-Paradol have docking scores identical to those of the reference ligand. The binding affinity score for reference ligands is  $-9.2$  Kcal/mol, while the scores for [8]-Shogaol, [6]-Shogaol, and [1]-Paradol are all  $-9.3$  Kcal/mol. Compounds classified as at least intermediate (Class 2) in toxic prediction using toxtree software [24] with no violations of the Lipinski rule [25] are subjected to bioactivity prediction analysis using pass-server (<http://www.way2drug.com/passonline>) [27]. Lycopene, [12]-Shogaol, [8]-Shogaol, [6]-Shogaol, [1]-Paradol, and alpha-Zingiberene are among the compounds filtered from Lipinski and toxtree (Table 6).

### 3.4. Analysis of bioactivity prediction

The outcome of bioactivity is then visualized using orange [30]. The heatmap analysis (Fig. 4) reveals a variety of potential activities for each compound. We discovered that each compound chosen has the potential to be an apoptosis agonist [31], which increases apoptosis in cancer cells. Except for [1]-Paradol, all compounds discovered have bioactivity as a proliferative disease treatment, which means that each of the compounds mentioned can both inhibit and aid in the proliferation of cancer cells. All chosen compounds have the potential to be anticarcinogenic. Only [1]-Paradol and alpha-Zingiberene lacked potential antineoplastic activity. Alpha-Zingiberene is also the only compound that did not exhibit TP53 expression enhancer activity, which is responsible for suppressing the cancer development process. The TP53 gene causes cell-cycle arrest, senescence, or apoptosis in response to cellular stressors such as DNA damage, hypoxia,

Table 4  
Docking and binding affinity score ( $\Delta G$ ) for the predicted compound as an inhibitor for MAPK2 protein

Compounds	Docking score	Binding affinity ( $\Delta G$ ) Kcal/mol
ref_ligand	-101	-9.2
Lycopene	182	-10.6
5-Hydroxy-7,4'-dimethoxyflavone	-83	-10.6
[12]-Shogaol	-102	-10.2
Isogingerenone B	-88	-10.2
Curcumin	-90.6	-10
trans-[10]-Shogaol	-96	-9.8
Gingerenone A	-93.4	-9.8
Dihydrocurcumin	-91.2	-9.7
Demethoxycurcumin	-93.6	-9.5
[8]-Shogaol	-93	-9.3
[6]-Shogaol	-92	-9.3
[1]-Paradol	-90.4	-9.3
Bisdemethoxycurcumin	-93	-9.3
alpha-Zingiberene	-76	-9.3
5,7-Dimethoxyflavone	-76	-9.1
Demethoxy[6]-shogaol	-93	-9.1
Zerumbone	-72	-9
alpha-calacorene	-76.4	-9
alpha-Caryophyllene	-72	-9
Dibutyl phthalate	-87	-9
Xanthorrhizol	-84.5	-8.9
[4]-Shogaol	-83.7	-8.9
Delphinidin	-92	-8.9
cis-Nuciferol	-83	-8.9
Diisobutyl phthalate	-84	-8.9
Farnesal	-85	-8.9
(E,E)-Farnesal	-86	-8.8
(R)-(-)-alpha-Curcumene	-81.4	-8.8
3,7-Dimethyl-2,6-octadiene	-79	-8.8
alpha-Curcumene	-81	-8.8
alpha-Farnesene	-82	-8.8
cis-beta-Farnesene	-82	-8.8
Quercetin	-81	-8.8
Farnesol	-87	-8.8
Genistein	-82	-8.8
Homofarnesyl cyanide	-85	-8.7
Galangin	-78	-8.7
(E)-Nuciferol	-86	-8.6
(S)-(+)-Curcumene	-74	-8.4
Methyl [6]-Shogaol	-80	-8.4
Zingerone methyl ether	-72	-8.1
Zingerol	-73	-8.1
4-(4-Hydroxy-3-methoxyphenyl)-2-butanone	-73	-8.1
alpha-Phellandrene	-63	-7.9
Myristicin	-69	-7.9
Dihydroferulic acid	-74	-7.9
Nerol	-71	-7.8

Table 4 (Continued).

Compounds	Docking score	Binding affinity ( $\Delta G$ ) Kcal/mol
8-Hydroxygeraniol	-74	-7.8
cis-Citral	-70	-7.8
Geraniol	-71	-7.8
trans-Citral	-70	-7.8
Perillene	-66	-7.8
Safrole	-68	-7.7
cis-ocimene	-63	-7.6
cis-beta-Ocimene	-63	-7.6
(E)-beta-Ocimene	-65	-7.6
(E)-Ocimene	-65	-7.6
Isogeraniol	-67	-7.5
beta-Myrcene	-64	-7.5
6-Methyl-5-hepten-2-one	-60	-7.5
3-Octen-2-one	-62	-7.4

nutritional deficiency, and oncogenic signaling [32]. Approximately half of all human cancers have lost or altered the tumor suppressor p53 [33].

Lycopene was discovered to be antineoplastic in certain cancers, including breast cancer. The anticancer activity is also shown in beta-carotene. Although beta-carotene has two Lipinski violations after ADME analysis, the antineoplastic properties of beta-carotene have been found in the brain, lung, lymphoma, pancreatic, and solid tumors. Beta-carotenes can increase apoptosis, stop the cell cycle at various stages, and prevent cell proliferation [34]. Lycopene is also one potential active compound that has antineoplastic potential in liver cancer, lung cancer, ovarian cancer, and renal cancer. Lycopene has also been identified as an antineoplastic enhancer. Lycopene has also been shown to have anti-cancer properties in the development of gastric cancer [35]. Some of the signal transduction pathways regulated by lycopene include the manipulation of the insulin-like growth factor system, the inhibition of the activity of sex steroid hormones, the modification of significant gene expression, and the alteration of mitochondrial function [36]. It is also found that alpha-zingiberene is the only compound with antineoplastic activity in pancreatic cancer cells (Fig. 5).

### 3.5. Tanimoto similarity for chemical structure and pharmacophore

Beta-carotene is shared about 6.55% similarity structure with the reference ligand for KIT protein inhibitor Imatinib (PubChem code: 5291), while

Table 5  
ADME and toxicity prediction of predicted ligand inhibitor for KIT protein

Molecule	Canonical SMILES	PubChem ID	Lipinski rule		Log P	GI absorption	BBB permeant	Lipinski violations	Toxic prediction	
			Molecular weight	H-bond donor	H-bond acceptors				Cramer rules	Cramer rules with extensions
Beta-Carotene	<chem>CC(=CC=CC=C(C=CC=C(C=CC1=C(C)CCCC1(C)C)C=CC=C(C=CC1=C(C)CCCC1(C)C)C</chem>	10556789	536.87	0	0	11.11	Low	No	2	Intermediate (Class II)



Table 6  
ADME and toxicity prediction of predicted ligand inhibitor for MAPK2 protein

Molecule	Canonical SMILES	PubChem ID	Lipinski rule			GI absorption	BBB permeant	Lipinski violations	Toxic prediction		
			Molecular weight	H-bond donor	H-bond acceptors				Log P	Cramer rules	Cramer rules with extensions
Lycopene	CC1=CC=CC=C(C=CC=C(C=CC=C(CCC=C(C(C)C)O)C=CC=C(C=C(C=CC=CC(C)C)C)O)C	446925	536.87	0	0	9.21	Low	No	2	Low (Class I)	Low (Class I)
5-Hydroxy-7,4'-dimethoxyflavone	COC1=CC=C(C(C=C1)C2=CC(=O)C3=C(C(=C(C=C3)O2)C4C(C(C(CO4)O)O)O)OC)C5C(C(C(CO5)O)O)O)CCCCCCCCC=C(C=C1)O)C	44258362	562.52	7	13	-3.02	Low	No	3	High (Class III)	High (Class III)
[112]-Shogaol	CCCCCCCCC=C(C=C1)O)C	9975813	360.53	1	3	4.25	High	No	1	Low (Class I)	Low (Class I)
Isogergerenone B	COC1=CC(=CC(=C1O)OC)CCC(=O)C=CCCC2=CC(=C(C=C2)O)OC	5318568	386.44	2	6	2.11	High	No	0	High (Class III)	High (Class III)
Curcumin	COC1=C(C=C(C=C1)C=C(C=O)CC(=O)C=C2=CC(=C(C=C2)O)OC)O)CCCCCCCCC=C(C=C1)O)C	969516	368.38	2	6	1.47	High	No	0	High (Class III)	High (Class III)
trans-[10]-Shogaol	CCCCCCCCC=C(C=C1)O)C	6442612	332.48	1	3	3.82	High	Yes	0	Low (Class I)	Low (Class I)
Gergerenone A	COC1=C(C=CC=C1)CCC=CC(=O)CCCC2=CC(=C(C=C2)O)OC)O	5281775	356.41	2	5	2.44	High	Yes	0	High (Class III)	High (Class III)
Dihydrocurcumin	COC1=C(C=CC(=C1)CCC(=O)CC(=O)C=C2=CC(=C(C=C2)O)OC)O	10429233	370.40	2	6	1.55	High	No	0	High (Class III)	High (Class III)
Demethoxycurcumin	COC1=C(C=CC=C1)C=C(C=O)CC(=O)C=CC2=CC(=C(C=C2)O)O)CCCCCCCCC=C(C=C1)O)C	5469424	338.35	2	5	1.80	High	No	0	High (Class III)	High (Class III)
[8]-Shogaol	CCCCCCCCC=C(C=C1)O)C	6442560	304.42	1	3	3.37	High	Yes	0	Low (Class I)	Low (Class I)
[6]-Shogaol	CCCCC=C(C=C1)O)C	5281794	276.37	1	3	2.90	High	Yes	0	Low (Class I)	Low (Class I)
[11]-Paradol	CCC(=O)CCC1=CC(=C(C=C1)O)OC	51352033	208.25	1	3	1.70	High	Yes	0	Low (Class I)	Low (Class I)
Bisdemethoxycurcumin	C1=CC(=CC=C1C=CC(=O)CC(=O)C=CC2=CC(=C(C=C2)O)O)CCC(=C(C=C1)C(C(CCC=C(C(C)C	5315472	308.33	2	4	2.13	High	Yes	0	High (Class III)	High (Class III)
alpha-Zingiberene	CC1=CCC(C=C1)C(C(CCC=C(C(C)C	11127403	204.35	0	0	4.53	Low	No	1	Low (Class I)	Low (Class I)

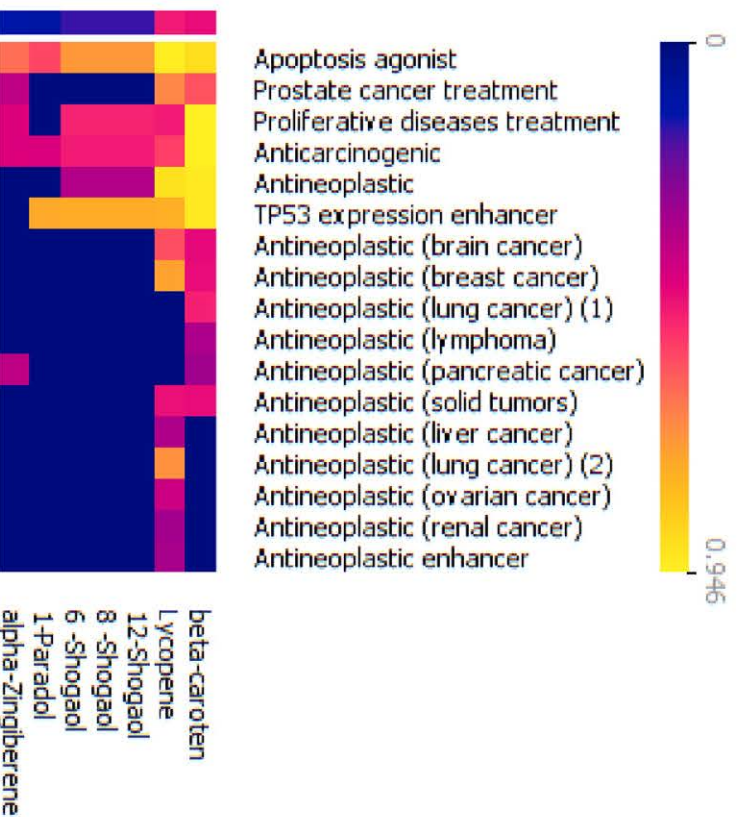


Fig. 5. Bioactivity prediction from compounds selected from ADME and toxic prediction.

MAPK2 protein reference ligand 2'-(2-fluorophenyl)-1-methyl-6',8',9',11'-tetrahydrospiro [azetidine-3,10'-pyrido [3,4':4,5]] pyrrrolo [2,3-f] isouquinolin], -7 (5'H)-one (PubChem code: 42646698) has the highest similarity with 5-Hydroxy-7,4'-dimethoxyflavone (9%). None of the compounds selected have a similarity greater than 10%. The model can choose the possible active compound even with a smaller similarity fingerprint of compounds from ginger with an active compound of training and testing data (Table 7).

The Pharmacophore similarity of amino acids interacting with the compound selected as a ligand is also calculated. Beta-carotene only shares about 12.9% pharmacophore similarity with reference ligands for KIT protein. This means there are substantial differences between amino acids from proteins, which are amino acids from proteins that interact with beta-carotene compared to reference ligands. On the other hand, we found Gingerone A share about 33.3% similarity with reference ligand for MAPK2 protein, Isogingerone B, and [1]-Paradol also shows higher pharmacophore similarity with MAPK2 reference ligand with a similarity of 27.8% and 22.2%

(Table 8). It is clear that even though 5-Hydroxy-7,4'-dimethoxyflavone ligands have the highest structure similarity (9%) with reference ligands, the compound does not always show the same result in pharmacophore similarity; the compound interaction only shares about 11.1% similarity.

#### 4. Conclusion

Machine learning has been used to help classify anticancer compounds derived from ginger. Lycopene, [12]-shogaol, [8]-shogaol, [6]-shogaol, [1]-shogaol -Paradol and alpha-Zingiberene are two compounds chosen after ADME and toxicity testing. All of the compounds mentioned previously have the potential to be anticarcinogenic, with a different score assigned to each compound. Beta-carotene, although showing two violations of the Lipinski rule, and lycopene have shown potential activity in various cancers. Each compound also acts as an apoptosis agonist, apart from alpha-Zingiberene, which does function as a TP53 expression enhancer.

Table 7  
Structure similarity (%) between reference ligand and selected compound

Molecule	PubChem ID	PubChem ID reference ligand	Structure similarity (%)	Protein target
Beta-carotene	10556789	5291	6.5	KIT
Lycopene	446925	42646698	1.2	MAPK2
5-Hydroxy-7,4'-dimethoxyflavone	44258362	42646698	9.0	MAPK2
[12]-Shogaol	9975813	42646698	6.5	MAPK2
Isogingerenone B	5318568	42646698	6.6	MAPK2
Curcumin	969516	42646698	8.6	MAPK2
trans-[10]-Shogaol	6442612	42646698	6.5	MAPK2
Gingerenone A	5281775	42646698	6.9	MAPK2
Dihydrocurcumin	10429233	42646698	7.6	MAPK2
Demethoxycurcumin	5469424	42646698	8.2	MAPK2
[8]-Shogaol	6442560	42646698	6.5	MAPK2
[6]-Shogaol	5281794	42646698	6.5	MAPK2
[1]-Paradol	51352033	42646698	7.2	MAPK2
Bisdemethoxycurcumin	5315472	42646698	5.3	MAPK2
alpha-Zingiberene	11127403	42646698	4.6	MAPK2

Table 8  
Pharmacophore similarity (%) between reference ligand and selected compound

Molecule	PubChem ID	PubChem ID reference ligand	Pharmacophore similarity (%)	Protein target
Beta-carotene	10556789	5291	12.9	KIT
Lycopene	446925	42646698	10	MAPK2
5-Hydroxy-7,4'-dimethoxyflavone	44258362	42646698	11.1	MAPK2
[12]-Shogaol	9975813	42646698	9.5	MAPK2
Isogingerenone B	5318568	42646698	27.8	MAPK2
Curcumin	969516	42646698	12.5	MAPK2
trans-[10]-Shogaol	6442612	42646698	11.8	MAPK2
Gingerenone A	5281775	42646698	33.3	MAPK2
Dihydrocurcumin	10429233	42646698	10.5	MAPK2
Demethoxycurcumin	5469424	42646698	11.8	MAPK2
[8]-Shogaol	6442560	42646698	9.5	MAPK2
[6]-Shogaol	5281794	42646698	25	MAPK2
[1]-Paradol	51352033	42646698	22.2	MAPK2
Bisdemethoxycurcumin	5315472	42646698	7.7	MAPK2
alpha-Zingiberene	11127403	42646698	18.8	MAPK2

### Conflict of interest

The authors declare no conflicts of interest.

### Data availability statement

The data supporting the findings of this study are available on request from the corresponding author.

### Author contribution

MEG and MRR wrote the original study design and protocol. MEG did the data collection. MRR

participated in the data analysis and interpretation. The paper was written by MRR and was revised and edited by all authors who have approved the final version. We would like to acknowledge the equal contributions of MEG and MRR to this project.

### References

- [1] Liu C-X, Overview on development of ASEAN traditional and herbal medicines, *Chin Herb Med*, 13: 441–450, 2021.
- [2] Park H-L, Lee H-S, Shin B-C et al., Traditional medicine in China, Korea, and Japan: A brief introduction and comparison, *Evid-Based Complement Alternat Med ECAM*, 2012: 429103, 2012.

- [3] Sumarni W, Sudarmin S, Sumarti SS, The scientification of jamu: A study of Indonesian's traditional medicine, *J Phys Conf Ser*, 1321: 032057, 2019.
- [4] Ekor M, The growing use of herbal medicines: Issues relating to adverse reactions and challenges in monitoring safety, *Front Pharmacol*, 4: 177, 2014.
- [5] Mashhadi NS, Ghiasvand R, Askari G et al., Anti-oxidative and anti-inflammatory effects of ginger in health and physical activity: Review of current evidence, *Int J Prev Med*, 4: S36–S42, 2013.
- [6] Prasad S, Tyagi AK, Ginger and its constituents: Role in prevention and treatment of gastrointestinal cancer, *Gastroenterol Res Pract*, 2015: e142979, 2015.
- [7] Akimoto M, Iizuka M, Kanematsu R et al., Anticancer effect of ginger extract against pancreatic cancer cells mainly through reactive oxygen species-mediated autotic cell death, *PLoS One*, 10: e0126605, 2015.
- [8] Vemuri SK, Banala RR, Subbaiah GPV et al., Anti-cancer potential of a mix of natural extracts of turmeric, ginger and garlic: A cell-based study, *Egypt J Basic Appl Sci*, 4: 332–344, 2017.
- [9] Rahmani AH, shabrmi FMA, Aly SM, Active ingredients of ginger as potential candidates in the prevention and treatment of diseases via modulation of biological activities, *Int J Physiol Pathophysiol Pharmacol*, 6: 125–136, 2014.
- [10] Kumari M, Tiwari N, Chandra S et al., Comparative analysis of machine learning based QSAR models and molecular docking studies to screen potential anti-tubercular inhibitors against InhA of mycobacterium tuberculosis, *Int J Comput Biol Drug Des*, 11: 209, 2018.
- [11] Genç B, Tunc H, Optimal training and test sets design for machine learning, *Turk J Electr Eng Comput Sci*, 27: 1534–1545, 2019.
- [12] Mysinger MM, Carchia M, Irwin John J et al., Directory of useful decoys, enhanced (DUD-E): Better ligands and decoys for better benchmarking, *J Med Chem*, 55: 6582–6594, 2012.
- [13] Lotfaliansaremi S, Sabio M, Comwell S et al., The role of the Mitogen-Activated Protein Kinase (MAPK) signaling pathway in cancer, *Med Res Arch*, 8,2020. . Epub ahead of print 24 April 2020. doi:10.18103/mra.v8i4.2086.
- [14] Sheikh E, Tran T, Vranic S et al., Role and significance of c-KIT receptor tyrosine kinase in cancer: A review, *Bosn J Basic Med Sci*, 22: 683–698, 2022.
- [15] Shinbo Y, Nakamura Y, Altaf-UI-Amin M et al. KNApSACk: A comprehensive species-metabolite relationship database, in: Saito K, Dixon RA, Willmitzer L (eds), *Plant Metabolomics*. 1 ed. Springer (Berlin, Heidelberg), 165–181, 2006. ISBN: 978-3-540-29782-6.
- [16] Klekota J, Roth FP, Chemical substructures that enrich for biological activity, *Bioinforma Oxf Engl*, 24: 2518–2525, 2008.
- [17] Pedregosa F, Varoquaux G, Gramfort A et al., Scikit-learn: Machine learning in Python, *J Mach Learn Res*, 12: 2825–2830, 2011.
- [18] Kluyver T, Ragan-Kelley B, Pérez Fernando et al. Jupyter Notebooks – A publishing format for reproducible computational workflows, in: Schmidt B, Loizides F (eds), *Positioning and Power in Academic Publishing: Players, Agents and Agendas*. IOS Press, 87–90, 2016. ISBN: 978-1-61499-649-1.
- [19] Korb O, Stützel T, Exner TE, Empirical scoring functions for advanced protein–ligand docking with PLANTS, *J Chem Inf Model*, 49: 84–96, 2009.
- [20] Korb O, Stützel T, Exner TE et al. PLANTS: Application of ant colony optimization to structure-based drug design, in: Dorigo M, Gambardella LM, Birattari M (eds), *Ant Colony Optimization and Swarm Intelligence*. Springer (Berlin, Heidelberg), 247–258, 2006.
- [21] Xue LC, Rodrigues JP, Kastitis PL et al., PRODIGY: A web server for predicting the binding affinity of protein–protein complexes, *Bioinformatics*, 32: 3676–3678, 2016.
- [22] Vangone A, Schaarschmidt J, Koukos P et al., Large-scale prediction of binding affinity in protein-small ligand complexes: The PRODIGY-LIG web server, *Bioinforma Oxf Engl*, 35: 1585–1587, 2019.
- [23] Daina A, Michielin O, Zoete V, SwissADME: A free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules, *Sci Rep*, 7: 42717, 2017.
- [24] Patlewicz G, Jeliaskova N, Safford RJ et al., An evaluation of the implementation of the Cramer classification scheme in the Toxtree software, *SAR QSAR Environ Res*, 19: 495–524, 2008.
- [25] Lipinski CA, Drug-like properties and the causes of poor solubility and poor permeability, *J Pharmacol Toxicol Methods*, 44: 235–249, 2000.
- [26] Damião MCFCB, Pasqualoto KFM, Polli MC et al., To be drug or prodrug: Structure-property exploratory approach regarding oral bioavailability, *J Pharm Pharm Sci Publ Can Soc Pharm Sci Soc Can Sci Pharm*, 17: 532–540, 2014.
- [27] Filimonov DA, Lagunin AA, Glorizova TA et al., Prediction of the biological activity spectra of organic compounds using the pass online web resource, *Chem Heterocycl Compd*, 50: 444–457, 2014.
- [28] Istyastono EP, Radifar M, Yuniarti N et al., PyPLIF HIPPOS: A molecular interaction fingerprinting tool for docking results of AutoDock Vina and PLANTS, *J Chem Inf Model*, 60: 3697–3702, 2020.
- [29] Liu K, Kokubo H, Exploring the stability of ligand binding modes to proteins by molecular dynamics simulations: A cross-docking study, *J Chem Inf Model*, 57: 2514–2522, 2017.
- [30] Demšar J, Curk T, Erjavec A et al., Orange: Data mining toolbox in python, *J Mach Learn Res*, 14: 2349–2353, 2013.
- [31] Pfeffer CM, Singh ATK, Apoptosis: A target for anticancer therapy, *Int J Mol Sci*, 19: 448, 2018.
- [32] Kim KM, Ahn A-R, Park HS et al., Clinical significance of p53 protein expression and TP53 variation status in colorectal cancer, *BMC Cancer*, 22: 940, 2022.
- [33] Powell E, Piwnica-Worms D, Piwnica-Worms H, Contribution of p53 to metastasis, *Cancer Discov*, 4: 405–414, 2014.
- [34] Gloria NF, Soares N, Brand C et al., Lycopene and beta-carotene induce cell-cycle arrest and apoptosis in human breast cancer cell lines, *Anticancer Res*, 34: 1377–1386, 2014.
- [35] Kim MJ, Kim H, Anticancer effect of lycopene in gastric carcinogenesis, *J Cancer Prev*, 20: 92–96, 2015.
- [36] Qi WJ, Sheng WS, Peng C et al., Investigating into anti-cancer potential of lycopene: Molecular targets, *Biomed Pharmacother Biomedecine Pharmacother*, 138: 111546, 2021.

# Breast Disease

AN INTERNATIONAL JOURNAL



ISSN 0888-6008



Intended for healthcare professionals

**Sage Journals**

## Breast Disease

[Journal indexing and metrics](#)

### Editorial board

 [Hide all](#)

#### Founding Editor



**Edison T. Liu**

The Jackson Laboratory, USA

#### Editorial Board Members



**William G. Cance**

University of Florida, USA

**Charles V. Clevenger**

Virginia Commonwealth University, USA

**Stan Lipkowitz**

National Cancer Institute, USA

**Diana M. Lopez**

University of Miami School of Medicine, USA

**Kathy D. Miller**

Indiana Cancer Pavilion, USA

**Etta Pisano**

University of North Carolina, USA



**Barbara Rimer**

National Cancer Institute, USA

**Andrew Seidman**

Memorial Sloan-Kettering Cancer Center, USA

**Wei-Zen Wei**

Wayne State University, USA

**Yosef Yarden**

Weizmann Institute of Science, Israel

**Doug Yee**

University of Minnesota, USA

## Browse journal

---

Current issue

All issues

## Journal Information

---

Journal overview and metrics

### Editorial board

---

Submission Guidelines

Reprints

Journal permissions

Recommend to library

Advertising & promotion



## Keep up to date



Facebook



X



LinkedIn



YouTube



RSS feed



Email alerts

[View all options](#)

## Also from Sage

### CQ Library

Elevating debate

### Sage Data

Uncovering insight

### Sage Business Cases

Shaping futures

### Sage Campus

Unleashing potential

### Sage Knowledge

Multimedia learning resources

### Sage Research Methods

Supercharging research

### Sage Video

Streaming knowledge

### Technology from Sage

Library digital services





## Breast Disease

[Journal indexing and metrics](#)

[← Previous issue](#)

[Next issue →](#)

Volume 43, March 2024

[View issue contents](#) ▾

☐ Select all

[Export selected citations](#)

### Research Article



Open Access

Research article

First published January 24, 2024

[Clinicopathological analysis of 38 male patients diagnosed with breast cancer](#)

Seniha Irem Sahin , Serdar Balci , Gulnur Guler , Kadri Altundag

[Preview Abstract](#) ▾

PDF / EPUB



Open Access

Research article

First published January 11, 2024



[Impact of the COVID-19 pandemic on breast cancer pathological stage at diagnosis in Tunisian patients](#)

Meriam Triki, Mouna Zghal, Houda Ben Ayed, Saadia Makni, Maroua Bouhamed, Semi Fendri [...]

[View all](#) ✓

[Preview Abstract](#) ✓

PDF / EPUB



Open Access

Research article

First published January 27, 2024

[Use of axillary ultrasound to guide breast cancer management in the genomic assay era](#)

Geok Hoon Lim, John Carson Allen, Yien Sien Lee, Sze Yiun Teo, Li Ching Lau, Thida Win, Lester Chee Hao Leong

[Preview Abstract](#) ✓

PDF / EPUB



Open Access

Research article

First published November 29, 2023

[Cancer associated fibroblasts modulate the cytotoxicity of anti-cancer drugs in breast cancer: An in vitro study](#)

Dharambir Kashyap, Shalmoli Bhattacharya, Santosh Irinike, Siddhant Khare, Ashim Das [...]

[View all](#) ✓

[Preview Abstract](#) ✓

PDF / EPUB



Open Access

Research article

First published February 7, 2024



[Anti-IL-8 monoclonal antibodies inhibits the autophagic activity and cancer stem cells maintenance within breast cancer tumor microenvironment](#)

Seham Abou Shousha, Eman M. Osman, Suzan Baheeg, Yasmine Shahine

[Preview Abstract](#) ▾

PDF / EPUB



Open Access

Research article

First published February 1, 2024

[Primary breast sarcomas: A 13 case-series study treated in university hospital in central Tunisia over a 25-year period](#)

Fadoua Bouguerra , Samia Kanoun Belajouza, Emna Mziou , Rym Zanzouri, Hayfa Chahdoura[...]

[View all](#) ▾

[Preview Abstract](#) ▾

PDF / EPUB



## Case Report



Open Access

Case Report

First published March 12, 2024

[Telangiectasias induced by combination tucatinib and ado-trastuzumab emtansine in a patient with metastatic breast cancer](#)

Gabriella F. Rodriguez, Anuj Shah, Andrea D. Maderal

[Preview Abstract](#) ▾

PDF / EPUB



## Research Article



Open Access

Research article

First published March 14, 2024

[Sentinel node in breast cancer as an indicator of quality in medical care: Evaluation of statistics in Colombia](#)

Mario Arturo González Mariño

[Preview Abstract](#) ▾

PDF / EPUB



Open Access

Research article

First published April 19, 2024

[The relationship of changes in molecular subtypes with metastases and progression-free survival in breast cancer](#)

Fitran Amansyah, Prihantono Prihantono , Firdaus Hamid , Salman Ardi Syamsu 

[...]

[View all](#) ▾

[Preview Abstract](#) ▾

PDF / EPUB



## Review Article



Open Access

Review article

First published April 19, 2024

[PD-1/PD-L1 pathway: Current research in breast cancer](#)

Salman Ardi Syamsu , Muhammad Faruk , Nilam Smaradania, Elridho Sampepajung

[...]

[View all](#) ▾

[Preview Abstract](#) ▾

PDF / EPUB



## Research Article



Open Access

Research article

First published April 19, 2024

[Pleiotrophin serum level and metastasis occurrence in breast cancer patients](#)

Muhamad Ikhlās, Djonny Ferianto, Salman Ardi Syamsu , Idham Jaya Ganda, Nilam Smaradania[...]

[View all](#) 

[Preview Abstract](#) 

PDF / EPUB



Open Access

Research article

First published April 19, 2024

[In-silico prediction of anti-breast cancer activity of ginger \(Zingiber officinale\) using machine learning techniques](#)

Marisca Evalina Gondokesumo , Muhammad Rezki Rasyak 

[Preview Abstract](#) 

PDF / EPUB



Open Access

Research article

First published March 8, 2024

[The role of platelet rich plasma enriched fat graft for correction of deformities after conservative breast surgery](#)

Ahmed Shaaban , Medhat Anwar , Rabie Ramadan 

[Preview Abstract](#) 

PDF / EPUB



Review Article



Open Access

Review article

First published April 19, 2024



[Massage on the prevention of breast cancer through stress reduction and enhancing immune system](#)

Zilhana Siregar, Andi Nilawati Usman , Mardiana Ahmad , Andi Ariyandy[...]

[View all](#) ▾

[Preview Abstract](#) ▾

PDF / EPUB



---

## Systematic Review






Open Access

Review article

First published April 19, 2024

[Contraceptive use with breast cancer incidence in Indonesia](#)

Sulfiana Sulfiana, Prihantono Prihantono , Andi Nilawati Usman , Mardiana Ahmad   
[...]

[View all](#) ▾

[Preview Abstract](#) ▾

PDF / EPUB






Open Access

Review article

First published April 19, 2024

[Early detection of self-breast examination using smartphone breast application](#)

Nur Indah, Andi Nilawati Usman , Yusring Sanusi Baso , Syafruddin Syarif   
[...]

[View all](#) ▾

[Preview Abstract](#) ▾

PDF / EPUB






Open Access

Review article

First published April 19, 2024



[Influence of variables on breast self-examination: Potential barrier or enhancement of breast cancer prevention](#)

Hijrah Hijrah, Andi Nilawati Usman , Yusring Sanusi Baso , Syafruddin Syarif   
[...]

[View all](#) 

[Preview Abstract](#) 

PDF / EPUB



---

## Erratum



Free access

| Correction

| First published April 30, 2024

[Erratum to: Anti-IL-8 monoclonal antibodies inhibits the autophagic activity and cancer stem cells maintenance within breast cancer tumor microenvironment](#)

Seham Abou Shousha, Eman M. Osman, Suzan Baheeg, Yasmine Shahine

PDF / EPUB



Free access

| Correction

| First published April 30, 2024

[Erratum to: Clinical significance of Notch receptors in triple negative breast cancer](#)

Heer Shah, Mittal Mistry, Nupur Patel, Hemangini Vora

PDF / EPUB



---

## Systematic Review




Open Access

| Review article

| First published April 19, 2024



## [Physical activity and quality of life in breast cancer survivors](#)

Nurul Qisti Agussalim, Mardiana Ahmad , Prihantono Prihantono , Andi Nilawati Usman   
[...]

[View all](#) 

[Preview Abstract](#) 

PDF / EPUB



Open Access

Review article

First published April 19, 2024

## [The quality of life assessment of breast cancer patients](#)

Uswatun Hasanah, Mardiana Ahmad , Prihantono Prihantono , Andi Nilawati Usman   
[...]

[View all](#) 

[Preview Abstract](#) 

PDF / EPUB



## Case Report



Open Access

Case Report

First published May 16, 2024

## [Metaplastic breast cancer masquerading as a recurrent haematoma: A case report](#)

Nicholas Chen Yi Png, Winfred Xi Tai Goh, Clement Wenhao Chan

[Preview Abstract](#) 

PDF / EPUB



## Review



Open Access

Review article

First published May 22, 2024





## [Lectins as a promising therapeutic agent for breast cancer: A review](#)

Keerti Singh, Lokita Agrawal, Rhea Gupta, Divyam Singh, Meghavi Kathpalia, Navkiran Kaur

[Preview Abstract](#) ▾

PDF / EPUB



### Research Article



Open Access

Research article

First published May 29, 2024

## [A novel PIK3CA hot-spot mutation in breast cancer patients detected by HRM-COLD-PCR analysis](#)

Saoussen Debouki-Joudi, Wala Ben Kridis, Fatma Trifa, Wajdi Ayadi, Abdelmajid Khabir

[...]

[View all](#) ▾

[Preview Abstract](#) ▾

PDF / EPUB



### Case Report



Open Access

Case Report

First published June 6, 2024

## [Development of neuro-Behcet's disease in a patient with operable HER2-positive breast cancer during neoadjuvant chemotherapy: A case report](#)

Taketo Nakai, Hirohito Seki, Akitsugu Makino, Yoshie Kadota, Takuji Kaburagi, Takehiro Okumura[...]

[View all](#) ▾

[Preview Abstract](#) ▾

PDF / EPUB



Open Access

Case Report

First published June 21, 2024

[Nipple-sparing mastectomy and immediate breast reconstruction by prepectoral implant for the management of giant phyllodes tumors: A case series](#)

Khaled M. Abdelwahab, Sara Elsaed, Omar Hamdy, Mahmoud M. Saleh, Amr Hosam

[Preview Abstract](#) ▾

PDF / EPUB



---

## Research Article



Open Access

Research article

First published May 16, 2024

[Genomic signatures in breast cancer in a real-world setting: Experience in a Brazilian Northeastern Center](#)

Sabas Carlos Vieira, Cristiane Amaral dos Reis, Mariana Elvas Feitosa Holanda[...]

[View all](#) ▾

[Preview Abstract](#) ▾

PDF / EPUB



Open Access

Research article

First published July 23, 2024

[Breast gel based on Boswellia serrata, Betaine and myo-Inositol improves cyclic mastodynia in fertile women: A retrospective clinical study](#)

Moira Burratti, Giuseppina Morano, Chiara Pasquale, Grazia Di Fonso, Loredana Costabile

[Preview Abstract](#) ▾

PDF / EPUB



Open Access

Research article

First published August 2, 2024



[Chemotherapy induced alopecia in breast cancer patients: A monocentric prospective study](#)

Wala Ben Kridis, Olfa Boudawara, Afef Khanfir

[Preview Abstract](#) ▾

PDF / EPUB



Open Access

Research article

First published August 20, 2024

[Parametric optimization and comparative study of machine learning and deep learning algorithms for breast cancer diagnosis](#)

Parul Jain, Shalini Aggarwal, Sufiyan Adam, Mohsin Imam

[Preview Abstract](#) ▾

PDF / EPUB



## Brief Report



Open Access

Brief Report

First published August 28, 2024

[Synchronous primary breast angiosarcoma with invasive ductal carcinoma](#)

Wala Ben Kridis, Mayssa Lajnef, Afef Khanfir

[Preview Abstract](#) ▾

PDF / EPUB



## Research Articles



Open Access

Research article

First published November 15, 2024



## [A low-cost breast cancer prognosis tool using machine learning](#)

Iván Romarico Gonzalez-Espinoza, Abraham Castro-Ponce, María Castelló-Pons[...]

[View all](#) ▾

[Preview Abstract](#) ▾

PDF / EPUB



## Brief Reports



Open Access

Brief Report

First published November 11, 2024

### [Desmoid fibromatosis of breast masquerading as malignancy: Report of a rare case](#)

Syeda Iqra Usman, Khalaf Saba, Sadia Afreen, Karthik Dasari, Mohammad Akram, Kafil Akhtar [...]

[View all](#) ▾

[Preview Abstract](#) ▾

PDF / EPUB



Open Access

Brief Report

First published November 11, 2024

### [Spontaneous breast haemorrhagic necrosis: A case report](#)

Lina Pankratjevaite, Katrine Lind, Julie Tastesen, Marco Mele

[Preview Abstract](#) ▾

PDF / EPUB



## Review Articles



Open Access

Review article

First published November 11, 2024



[Paget disease of the breast: An often-overlooked malignancy](#)

Cherie M Kuzmiak, Romuald Ferre 

[Preview Abstract](#) 

PDF / EPUB



---

## Research Articles



Open Access

Research article

First published December 23, 2024

[Comparative proteomic landscape, gene expression profiling, and hotspot HER2 and PIK3CA alterations in trastuzumab-sensitive and resistant HER2-positive breast cancer cell line](#)

Tamanna Thakur, Shalmoli Bhattacharyya, Ashim Das, Ishita Laroia, Rajender Kumar, Amanjit Bal

[Preview Abstract](#) 

PDF / EPUB



Open Access

Research article

First published December 21, 2024

[Breast-graded prognostic assessment scores in prediction of breast cancer brain metastases survival](#)

Wala Ben Kridis , Emna Hadj Taib, Hanene Ben Salah, Jamel Daoud, Afef Khanfir

[Preview Abstract](#) 

PDF / EPUB



---

## Review Articles




Open Access

Review article

First published December 20, 2024

[Omission of axillary surgery in breast cancer: An overview](#)

Aleessa Azmi, Omar Hamdy 

[Preview Abstract](#) 

PDF / EPUB



## Browse journal

Current issue

All issues

## Journal Information

Journal overview and metrics

Editorial board

Submission Guidelines

Reprints

Journal permissions

Recommend to library

Advertising & promotion



## Keep up to date



Facebook



X



LinkedIn



YouTube



RSS feed



Email alerts

[View all options](#)

## Also from Sage

### CQ Library

Elevating debate

### Sage Data

Uncovering insight

### Sage Business Cases

Shaping futures

### Sage Campus

Unleashing potential

### Sage Knowledge

Multimedia learning resources

### Sage Research Methods

Supercharging research

### Sage Video

Streaming knowledge

### Technology from Sage

Library digital services



Breast Disease

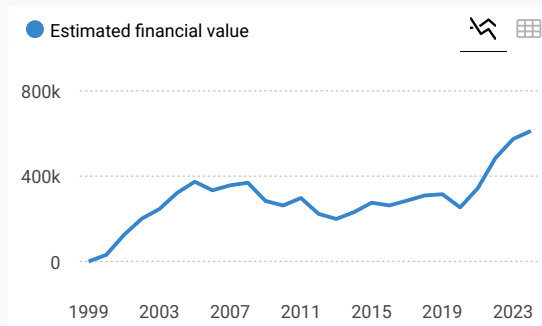
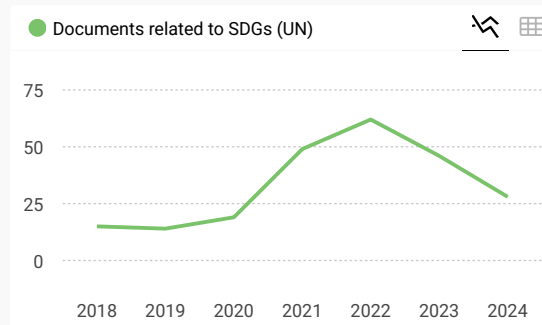
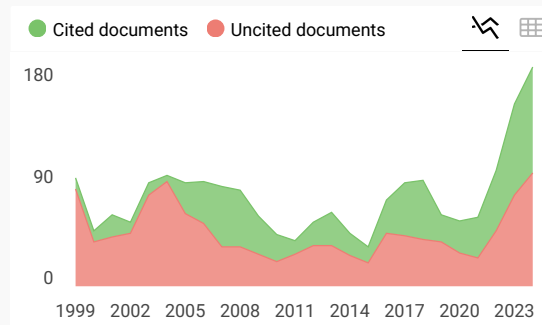
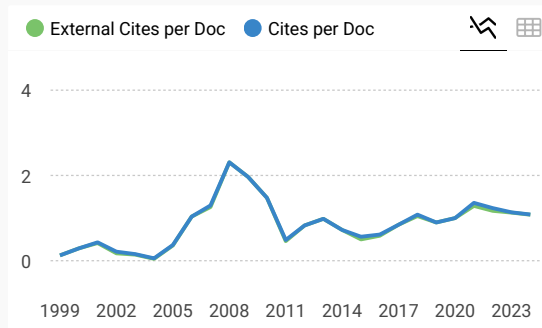
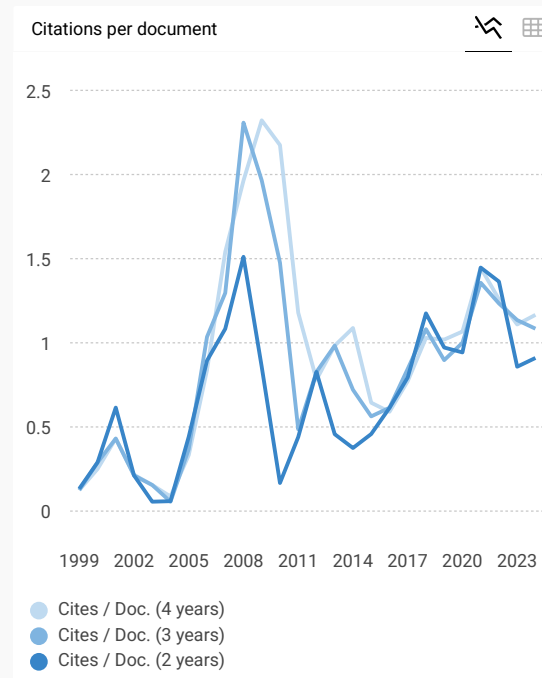
<div>COUNTRY</div> <div>Netherlands</div> <div>Universities and research institutions in Netherlands</div> <div>Media Ranking in Netherlands</div>	<div>SUBJECT AREA AND CATEGORY</div> <div>Biochemistry, Genetics and Molecular Biology</div> <div>Cancer Research</div> <div>Medicine</div> <div>Medicine (miscellaneous)</div> <div>Oncology</div>	<div>PUBLISHER</div> <div>SAGE Publications Ltd</div>	<div>SJR 2024</div> <div>0.342Q3</div> <div>H-INDEX</div> <div>37</div>
<div>PUBLICATION TYPE</div> <div>Journals</div>	<div>ISSN</div> <div>08886008, 15581551</div>	<div>COVERAGE</div> <div>1987-1996, 1998, 2000-2008, 2010-2024</div>	<div>INFORMATION</div> <div>Homepage</div> <div>How to publish in this journal</div> <div>breastdisease@iospress.com</div>

SCOPE

Breast Disease is a peer-reviewed journal publishing papers on topics such as basic cellular and molecular biology, epidemiology, genetics, clinical research, imaging, and social and legal issues. The journal publishes research articles and reviews. Breast Disease publishes review issues devoted to an in-depth analysis of the scientific and public implications of recent research on a specific problem in breast cancer. Thus, the reviews will not only discuss recent discoveries but will also reflect on their impact in breast cancer research or clinical management. The ongoing work in the field of breast cancer inevitably will hasten discoveries that will have impact on patient outcome. The breadth of this research that spans basic science, clinical medicine, epidemiology, and public policy poses difficulties for investigators. Not only is it necessary to be facile in comprehending ideas from many disciplines, but also important to understand the public implications of these discoveries.

Join the conversation about this journal





### Breast Disease


Q3

Medicine  
(miscellaneous)

best quartile

SJR 2024

0.34



powered by scimagojr.com

← Show this widget in your own website

Just copy the code below and paste within your html code:

```
<a href="https://www.scimagojr.com" data-bbox="588 718 884 788">
```

Metrics based on Scopus® data as of March 2025

Thank you verry much

← reply



Melanie Ortiz 2 months ago

SCImago Team

Dear Hasnah, thanks for your participation! Best Regards, SCImago Team



Hasnah M.Noor 2 months ago

I really enjoyed reading articles in los Pres, if possible I would like to publish my articles in this journal about maternal and child health

← reply



Melanie Ortiz 2 months ago

SCImago Team

Dear Hasnah,  
Thank you for contacting us.  
We suggest you visit the journal's homepage (See submission/author guidelines) or contact the journal's editorial staff , so they could inform you more deeply.  
Best Regards, SCImago Team



Dr Vijay Kulshrestha 3 years ago

Dear sir/madam  
I am dr Vijay Kulshrestha, Associate professor in radiodiagnosis department at GSMEDICAL College and Hospitals, Hapur ,U.P state ,India.  
I want to publish a paper related to ANDI breast .  
Are you providing hard copy of journal becZ hard copy is required for promotion by National Medical Commission, india ?  
Kindly let me know the paper publication charges .  
Thanks and regards  
Dr Vijay Kulshrestha

← reply



Melanie Ortiz 3 years ago

SCImago Team

Dear Dr Vijay,  
Thank you for contacting us.  
We suggest you visit the journal's homepage or contact the journal's editorial staff , so they could inform you more deeply.  
Best Regards, SCImago Team

Leave a comment

Name

Email   
(will not be published)

Submit

The users of Scimago Journal & Country Rank have the possibility to dialogue through comments linked to a specific journal. The purpose is to have a forum in which general doubts about the processes of publication in the journal, experiences and other issues derived from the publication of papers are resolved. For topics on particular articles, maintain the dialogue through the usual channels with your editor.

Developed by:



Powered by:



Follow us on @ScimagoJR

Scimago Lab, Copyright 2007-2025. Data Source: Scopus®

EST MODUS IN REBUS

Horatio (Satire 1,1,106)

[Legal Notice](#)

[Privacy Policy](#)

# Source details

## Breast Disease

Years currently covered by Scopus: from 1987 to 1996, 1998, from 2000 to 2008, from 2010 to 2025

Publisher: SAGE


ISSN: 0888-6008 E-ISSN: 1558-1551

Subject area: Medicine: Oncology Biochemistry, Genetics and Molecular Biology: Cancer Research

Source type: Journal


[View all documents >](#)

[Set document alert](#)

 [Save to source list](#)

CiteScore 2023

1.8



SJR 2023

0.361



SNIP 2023

0.449



CiteScore

CiteScore rank & trend

Scopus content coverage

CiteScore

2023

▼

1.8


=

351 Citations 2020 - 2023

199 Documents 2020 - 2023

Calculated on 05 May, 2024

CiteScoreTracker 2024



2.0

=

420 Citations to date

208 Documents to date

Last updated on 05 April, 2025 • Updated monthly

### CiteScore rank 2023

Category	Rank	Percentile
Medicine		
Oncology	#279/404	31st
Biochemistry, Genetics and Molecular Biology		
Cancer Research	#186/230	19th

[View CiteScore methodology >](#)

[CiteScore FAQ >](#)

[Add CiteScore to your site !\[\]\(d3e32d099174a7c248ec1f564ee4f69c\_img.jpg\)](#)

---

## About Scopus

[What is Scopus](#)

[Content coverage](#)

[Scopus blog](#)

[Scopus API](#)

[Privacy matters](#)

## Language

[日本語版を表示する](#)

[查看简体中文版本](#)

[查看繁體中文版本](#)

[Просмотр версии на русском языке](#)

## Customer Service

[Help](#)

[Tutorials](#)

[Contact us](#)

---

## ELSEVIER

[Terms and conditions ↗](#) [Privacy policy ↗](#) [Cookies settings](#)

All content on this site: Copyright © 2025 Elsevier B.V. ↗, its licensors, and contributors. All rights are reserved, including those for text and data mining, AI training, and similar technologies. For all open access content, the relevant licensing terms apply.  
We use cookies to help provide and enhance our service and tailor content.By continuing, you agree to the use of cookies ↗.

