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Research Article

In silico Exploration on The Potency of Basil (*Ocimum basilicum*) as an Anti-Aging Skin Agent

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Abstract
New and improved skin care products and procedures have been established by technological advances and scientific investigation. By increasing the skin's moisture, firmness, and elasticity, anti-aging skin care can enhance the skin's overall condition. The objective of this study was to examine the potential of basil's chemical compounds as an *in silico* anti-aging agent. Exploration of online databases, scholarly articles from national and international journals, and analysis using docking software are selected as examples of data collection methods. Matrix metalloproteinase 1 (MMP1), with PDB code 966C, is one of the targeted proteins related to skin anti-aging. Ladanein, acacetin, luteolin, 5-hydroxy-7,4'-dimethoxyflavone and genkwanin are five basil compounds that are predicted to exhibit anti-aging agents based on the presence of the binding affinity score indicator and the similarity of the appropriate attachment sites compared to the native ligand used. The scores for the binding affinity of luteolin, ladanein, acacetin, 5 -hydroxy-7,4'-dimethoxyflavone, and genkwanin are -10, -9.9, -9.9, -9.8, and -9.6 kcal/mol, respectively. At the attachment positions of five basil compounds, the interactions with ASN 180, LEU 181 and ALA 182 key amino acids, which are the attachment sites for the native ligands, were also formed.

Keywords: basil, anti-aging, *in silico*

1. INTRODUCTION

Significant advancements in skincare have been developed recently. Natural cosmetics have shown a significant increase in popularity nowadays due to consumer and industry interest in these substances [1]. It is crucial for the cosmetics industry to reassess these substances in light of the rising consumer desire for natural ingredients, and more crucially the demand for effective natural ingredients like plant oils. Skin is the location of visible indications of aging as a result of intrinsic and extrinsic damage, making anti-aging skin care essential [2]. By boosting moisture, firmness, and elasticity, anti-aging skin care can enhance the condition of the skin as a whole.

Despite the fact that anti-aging cosmetics containing chemical compounds can have a positive influence on the skin, there are also potential adverse effects to be considered. Potential side effects of anti-aging skin care products containing chemical compounds include skin irritation and allergic reactions. Some chemical compounds in anti-aging skin care products can irritate, redden, and aggravate sensitive skin types [2]. In addition, certain chemical compounds used in anti-aging skin care products may cause allergic reactions such as hives, edema, and difficulty breathing in some individuals [3].

One of the important factors in photoaging is matrix metalloproteinase (MMP). MMP expression is induced and activated when the skin has been exposed to ultraviolet (UV) and reactive oxygen species (ROS) are formed. Oxidative stress upregulates MMPs including MMP-1 through binding of AP-1 to MMPs [4]. MMP-1 is a subgroup of collagenase that plays a role in degrading type I and III collagen in the skin [5]. An increase in MMP-1 causes degradation of extracellular matrix components which will result in the buildup of disorganized collagen fibrils and a decrease in the production of new collagen and procollagen biosynthesis. [6]. Therefore, one promising strategy for antiaging therapy is to develop MMP inhibitors.

Basil (*Ocimum basilicum*) is among the foliage that has been believed to have numerous health benefits for centuries. Alkaloids, flavonoids, saponins, and tannins are among the secondary

Table 1. Results of exploration of a collection of basil compounds via the KNApSAck database web server.

C ID	Names of Compounds	C ID	Names of Compounds
C00000136	1,8-Cineole	C00001386	*L*-Phenylalanine
C00000149	Espatulenol	C00001528	Chlorophyll a
C00000152	*p*-Coumaric acid	C00002374	Cyanidin 3-*O*-glucoside
C00000155	*m*-Thymol	C00002378	Cyanin
C00000156	Carvacrol	C00002636	Anisaldehyde
C00000164	beta-Eudesmol	C00002663	2-Phenylethanol
C00000165	gamma-Eudesmol	C00002683	Vanillin
C00000170	Cinnamate	C00002723	Chicoric acid
C00000184	alpha-Thujene	C00002740	Estragol
C00000206	Salicylic acid	C00002741	Methyleugenol
C00000219	Methyl jasmonate	C00002757	4-Methoxycinnamaldehyde
C00000356	*cis*-3-Hexen-1-ol	C00002770	Labiatenic acid
C00000613	*p*-Coumaryl alcohol	C00002771	Safrole
C00000614	Coniferyl alcohol	C00003028	Borneol
C00000615	Caffeic acid	C00003029	Camphene
C00000619	Eugenol	C00003035	*trans*-Citral
C00000620	Isoeugenol	C00003040	*p*-Cymene
C00000621	Chavicol	C00003045	Fenchone
C00000674	Luteolin	C00003046	Geranyl acetate
C00000804	(-)-3-Isothujone	C00003047	Linalool
C00000805	alpha-Pinene	C00003048	Linalyl acetate
C00000816	beta-Pinene	C00003051	alpha-Phellandrene
C00000819	(+)-Camphor	C00003054	Piperitone
C00000823	Limonene	C00003060	alpha-Terpinene
C00000827	Pulegone	C00003061	gamma-Terpinene
C00000830	*cis*-Sabinene hydrate	C00003065	Thymol acetate
C00000839	3-Carene	C00003106	beta-Cadinene
C00000843	*cis*-beta-Ocimene	C00003110	beta-Caryophyllene
C00000845	(*E*)-geraniol	C00003111	alpha-Cedrene
C00000850	Menthyl acetate	C00003116	beta-Chamigrene
C00000853	beta-Myrcene	C00003118	alpha-Copaene
C00000855	beta-Nerol	C00003120	alpha-Cubebene
C00000861	alpha-Terpinolene	C00003121	beta-Cubebene
C00000862	*trans*-beta-Ocimene	C00003130	alpha-Farnesene
C00000907	Farnesyl pyrophosphate	C00003131	(*E*)-beta-farnesene
C00000931	Zeaxanthin	C00003147	alpha-Caryophyllene (obsol.)
C00001016	5-Hydroxy-7,4'-dimethoxyflavone	C00003166	Nerolidol
C00001043	Genkwanin	C00003186	beta-Eudesmene
C00001075	Nevadensin	C00003204	alpha-Zingiberene
C00001144	Planteose	C00003467	Phytol
C00001203	Shikimic acid	C00003650	Cycloartenol
C00001233	Palmitic acid	C00003737	alpha-Amyrin
C00001260	Nonacosane	C00003738	beta-Amyrin
C00003741	Betulinic acid	C00020065	(-)-alpha-Cadinol

Table 1. *Cont.*

C ID	Names of Compounds	C ID	Names of Compounds
C00003755	*trans*-squalene	C00020066	epi-alpha-Cadinol
C00003760	Antheraxanthin	C00020072	(+)-Calamenene
C00003787	Violaxanthin	C00020074	Calamenene
C00003820	Acacetin	C00020130	gamma-Muurolene
C00003839	Ladanein	C00020150	(-)-delta-Cadinol
C00003840	Salvigenin	C00020154	tau-Muurolol
C00003879	Xanthomicrol	C00020376	beta-Guaiene
C00003880	Pedunculin	C00020377	alpha-Guaiene
C00003883	Gardenin B	C00020379	alpha-Bulnesene
C00005373	Hirsutrin	C00021213	(-)-Globulol
C00006614	Cyanidin	C00021217	Viridiflorol
C00006728	Petunin	C00021229	allo-Aromadendrene
C00007242	beta-Bisabolene	C00021230	(+)-Aromadendrene
C00007264	Feruloyl-CoA	C00021236	Isosparthulenol
C00007280	*p*-Coumaroyl CoA	C00021309	alpha-Himachalene
C00007282	(*S*)-2,3-Epoxysqualene	C00021720	beta-Cedrene
C00007376	Chlorophyll b	C00021884	beta-Bourbonene
C00007453	beta-Elemene	C00021903	trans-alpha-Bergamotene
C00007558	Syringaldehyde	C00029334	trans-Anethol
C00007566	1-Aminocyclopropane-1-carboxylate	C00029335	(*E*)-beta-Ocimene
C00007630	beta-Sesquiphellandrene	C00029339	(*E*)-Nerolidol
C00007636	delta-Cadinene	C00029350	cis-beta-Farnesene
C00010868	(+)-Limonene	C00029423	1-Octen-3-ol
C00010934	*p*-Menth-3-en-1-ol	C00029524	4-Carene
C00010967	beta-Cymene	C00029544	4-Terpineol
C00011720	(-)-Germacrene D	C00029633	Acetylursolic acid
C00012005	(-)-Elemol	C00029671	alpha-Muurolene
C00012012	(-)-gamma-Elemene	C00029672	(-)-alpha-Selinene
C00012425	(+)-Bicyclogermacrene	C00029674	alpha-Terpineol
C00012443	Humulene epoxide	C00029679	alpha-Bisabolol
C00012474	Isocaryophyllene	C00029790	Basilimoside
C00012483	(-)-beta-Caryophyllene epoxide	C00029791	Basilol
C00016959	(+)-Maaliol	C00029811	Benzenemethanol
C00019064	Oleanolic acid	C00029816	beta-Ionone
C00019065	Erythrodiol	C00029844	Borneol acetate
C00019545	NADPH	C00029866	Cadina-1,4-diene
C00020051	alpha-Cadinene	C00029881	Calarene
C00020063	1-Epibicyclosesquiphellandrene	C00029970	*cis*-alpha-Bergamotene
C00031258	4(10)-Thujene	C00030345	gamma-Cadinene
C00031765	(-)-ent-Spathulenol	C00030471	Heptacosane
C00032467	Uvaol	C00030767	Methyl salicylate
C00033734	Cubenol	C00030880	Octanal
C00034452	Benzaldehyde	C00031014	*p*-Coumaraldehyde

Table 1. *Cont.*

C ID	Names of Compounds	C ID	Names of Compounds
C00034456	beta-Gurjunene	C00052671	3,7-Dimethyl-1,5-octadiene-3,7-diol
C00034496	*trans*-Furanoid linalool oxide	C00052803	alpha-Bisabolene
C00034575	Lavandulol	C00052870	Bergamotene
C00034746	(*Z*)-Furanoid linalool oxide	C00052882	Elixene
C00034818	Cichoric acid	C00053014	delta-Gurjunene
C00034989	(*E*)-Ocimene	C00053057	*cis*-Rose oxide
C00035062	Carvone	C00053095	MVAPP
C00035138	Neryl acetate	C00053122	*cis*-ocimene
C00035341	Menthone	C00053324	Hotrienol
C00035451	1,10-Diepicubenol	C00053436	FEMA 2646
C00035480	(2*E*)-Hex-2-enal	C00053486	Methyl cinnamate
C00035495	3-Octanol	C00053520	Myrcenylacetate
C00035520	alpha-Amorphene	C00053538	Neoisomenthol
C00035536	beta-Damascenone	C00053584	Ocimene
C00035557	Caprylyl acetate	C00053588	1-Octen-3-yl acetate
C00035801	alpha-Fenchylalcohol	C00053595	Oleanolic aldehyde
C00036174	Nepetoidin A	C00053847	*trans*-Cadina-1(6),4-diene
C00036175	Nepetoidin B	C00053856	*trans*-Sabinene hydrate
C00036271	(-)-beta-Elemene	C00053972	Aceteugenol
C00036308	*D*-germacrene	C00055703	Aciphyllene
C00036546	3-Hexen-1-ol	C00055774	*cis*-Cadina-1(6),4-diene
C00036907	*cis*-Calamenene	C00055810	(*E*)-Methyl cinnamate
C00037113	Epizonarene	C00057669	Ocimol
C00037332	Isoledene	C00058860	Terpinene-4-acetate
C00038883	Cyanidin 3,5-di-*O*-glucoside	C00059005	alpha-Muurolol
C00040605	Ursolic aldehyde	C00059181	Cadinol
C00045131	Ursane	C00059948	Veridiflorol
C00048311	alpha-Bergamotene	C00060409	Cyanidin-3-*O*-coumaroylglucoside-5-*O*-glucoside
C00048335	Bisabolene	C00060644	*cis*-Methyl cinnamate
C00048486	Neo-allo-ocimene	C00060724	5-(beta-*D*-Glucopyranosyloxy)-7-hydroxy-2-(4-hydroxy-3-methoxyphenyl)-3-[[6-*O*-[(2E)-3-(4-hydroxyphenyl)-1-oxo-2-propen-1-yl]-beta-*D*-glucopyranosyl]oxy]-1-
C00050783	*D*-Mannuronic acid	C00060725	Cyanidin 3-(6"-*O*-trans-*p*-coumaroyl)-beta-D-glucoside
C00051532	Menthol	C00060825	Butyl 3-(3,4-dihydroxyphenyl) acrylate
C00052035	DMAPP	C00060997	Campholenal
C00052039	IPP	C00061239	2-Hexen-4-yn-1-ol
C00052276	Fenchol	C00061587	3-Hydroxy-beta-damascone
C00052277	Fenchyl acetate	C00061639	2-Butenoic acid
C00052446	Cadinene	C00061895	Peonidin-3,5-*O*-di-beta-glucopyranoside

Table 1. *Cont.*

C ID	Names of Compounds	C ID	Names of Compounds
C00052504	8-Hydroxylinalool	C00061920	Cyclofenchene
C00062435	4-Hexen-1-ol	C00062272	Isopulegyl acetate
C00062519	Diethylene glycol diacetate		

metabolite compounds found in basil, as demonstrated by scientific evidence [7]. Studies have identified that this group of compounds in basil leaves can be used in the production of hand disinfectants [8]. Other studies indicate that basil leaves are used as insecticides against mosquitoes that transmit dengue fever and there are still a large number of identical studies on the benefits of basil leaves [9].

Numerous studies have been conducted on the cosmetic advantages of basil leaves. Basil leaf extract at a concentration of 3% and white rice at a concentration of 10% are the optimal components for the formulation of a body scrub cream for skin care [10]. Other studies have confirmed that the flavonoids and polyphenols in basil leaves can be formulated as transdermal gel preparations and have been tested for their high antioxidant activity and beneficial effects on the skin. Unfortunately, there is still not much research regarding the use of basil as an anti-aging agent targeting the MMP1 protein. As a result, the purpose of this work is to investigate the possibility of using basil chemicals as an *in silico* anti-aging drug.

2. MATERIALS AND METHODS

This study utilized a laptop with 4GB RAM, Windows 10 operating system, PyRx software, Biovia Discovery Studio software, Datawarrior software, KNApSAck database webserver (http://www.knapsackfamily.com), PubChem database webserver (https://pubchem.ncbi.nlm.nih.gov/), and Protein Data Bank database webserver (PDB, https://www.rcsb.org/). During the docking test, the three-dimensional structure of the target protein MMP1 and the structure of the bioactive compounds in basil will be processed.

In this descriptive study, an *in silico* approach is utilized. The investigation was conducted at the Department of Biology, Faculty of Mathematics and Natural Sciences, Surabaya State University. The web server of the PDB database was used to obtain the 3D structure of the protein MMP1 (PDB Code: 966C). Separating the experimental co-crystals from the downloaded PDB data yielded the native ligand [11]. In addition, basil's bioactive compounds will be employed as test ligands during the docking test procedure. Basil's bioactive compounds are identified and known based on the KNApSAck web server database (Table 1). The structure of the basil compounds was then downloaded using the PubChem database webserver [12].

Using Datawarrior software, the identified compounds were then selected based on the parameters of Lipinski's five principles. Lipsinki's rule of five (RO5) is used to estimate the level of solubility of a compound in lipids and water, membrane permeability, and pharmacological effectiveness specifically for drug discovery and design through programming and computational methods. The RO5 are used as a guide in efforts to find drugs for several reasons, one of which is because drug manufacturers that comply with the five Lipinski rules tend to have a lower attrition rate than drug discovery that is not based on the Lipinski rules [13]. The 5 Lipinski rules include: drugs to be consumed orally must not violate more than one of the following five provisions: no more than five hydrogen bond donors (the total number of nitrogen-hydrogen, and oxygen-hydrogen bonds); no more than ten hydrogen bond acceptors; molecular mass less than five hundred Daltons; and the octanol-water partition coefficient (Log-P) does not exceed the value of five.

The binding affinity values for the MMP1 protein and the test ligand in the form of a bioactive compound of basil were then calculated using PyRx software [14]. Table 2 shows the location of the docking positions carried out on the MMP1 protein. The interaction of the protein-ligand complex formed between MMP1 and each test ligand was determined using the Biovia Discovery Studio software to visualize the results of the docking test [15].

3. RESULTS AND DISCUSSIONS

The presence of cell signalling and communication systems is intimately related to all categories of bodily activities. Relay molecules and receptor proteins are two essential components that play a role in the cell signalling system and communication within the body. The main function of relay molecules and receptor proteins is to transmit signal messages (signal transduction) that are conveyed until the target cell or tissue can respond to the stimulus. Each signal message received by a particular receptor protein is relayed by activating other relay molecules until it reaches the response or final target of the signalling cascade in the body [16]. The MMP1 protein can be used as a protein target in anti-aging processes uet o its function in collagen hydrolysis. Collagen hydrolysis events degrade and reduce collagen in the skin, making it susceptible to causing skin creases [11]. Therefore, inhibiting the mechanism of action mediated by the MMP1 protein can be a viable anti-aging strategy for the skin.

The alignment of the native ligand is assessed in terms of its resemblance to the pre-docking position of the native ligand, with the aim of validating the molecular docking methodology employed. The flexibility of ligands enables them to undergo structural alterations in order to attain a stable conformation upon binding to the receptor [17]. The root mean square deviation (RMSD) is a metric commonly employed in docking validation to assess the accuracy and reliability of a docking methodology. It serves as a measure to evaluate the validity of the docking method under consideration. A docking approach is considered valid if it yields a RMSD value of 2 Å or below. The RMSD value is a measure used to quantify the deviation of errors that arise during the process of docking. A decrease in the RMSD number corresponds to a decrease in the magnitude of the error deviation in docking [18]. Based on the results of the docking test in figure 1, the MMP1 protein has a validation RMSD value of 1.60 Å so the docking approach used for the MMP1 protein can be considered valid.

Exploration of basil's active compounds led to the identification of 153 active compounds. Then, these compounds were selected based on Lipinski's rule of five parameters. The result of the selection process yielded seven basil compounds that were suitable and secure under the specified conditions. These seven compounds will be the test ligands in the docking test with the MMP1 protein. In Table 3, the binding affinity values of the seven tested ligand compounds for the target protein MMP1 are displayed. The binding affinity values of five basil compounds, specifically ladanein, acacetin, luteolin, 5-hydroxy-7,4'-dimethoxyflavone, and genkwanin, exhibit lower values in comparison to the native ligands. *p*-Coumaric acid and shikimic acid, the remaining compounds, have values that are greater than the original ligand's binding affinity values. When the binding affinity value is greater or more positive, the resulting bond is weaker [19]. In contrast, the more negative or the lower the binding affinity value, the stronger the bond. The binding affinity between the ligand compound and the target protein is a measure of the binding strength [20]. The tested ligand compound with the lowest binding affinity was luteolin at -10 kcal/mol, followed by ladanein, acacetin, and 5-hydroxy-7,4'-dimethoxyflavone with -9.9, -9.9, and -9.7 kcal/mol. The fact that the binding affinity values of these five compounds are higher than that of the native ligand demonstrates that they have tremendous potential as anti-aging drug candidates.

According to the visualization results in table 4, each of the five basil compounds with a binding affinity value less than the native ligand has an attachment similarity of 75% for ladanein and 5-hydroxy-7,4'-dimethoxyflavone, 62.5% for luteolin and acacetin, and 50% for genkwanin. The comparison of attachment locations is conducted by assessing the amount of similarity between the

Table 2. Gridbox position of MMP1 protein docking process with basil compounds.

Protein Name	PDB ID	Dimensional Coordinates			Center Coordinates		
		x	y	z	x	y	z
Matrix Metalloproteinase 1 (MMP1)	966C	25	25	25	9.24	-10.42	38.38

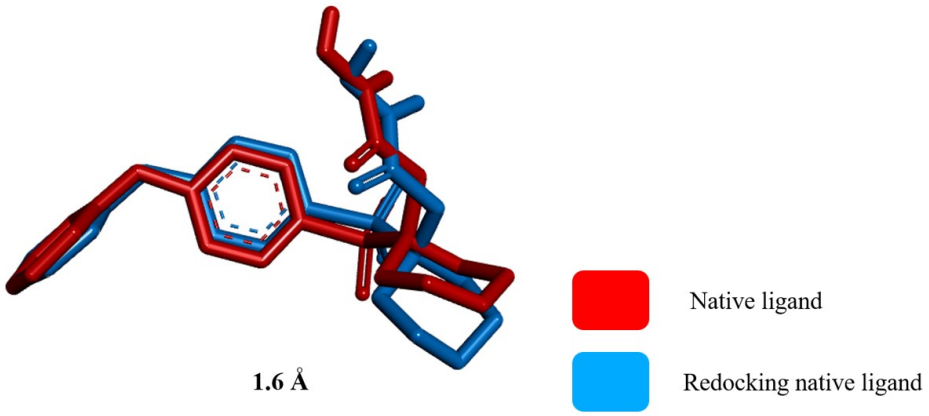


Figure 1. Results of validation analysis of the native ligand redocking test method.

attachment site produced between the native ligand and the target protein, and the attachment position of the test ligand molecule. The primary binding sites of the native ligands are comprised of ASN 180, LEU 181, and ALA 182 amino acids [21]. These three attachment points will contribute to altering the conformation of the MMP1 protein's active site, which will impede the action's mechanism, particularly the collagen hydrolysis process.

Ladanein and 5-hydroxy-7,4'-dimethoxyflavone exhibit binding affinity towards the MMP1 protein at the 8 same amino acid residue attachment site. Both of these compounds also exhibit three attachment places for crucial amino acid residues in MMP1, namely ASN 180, LEU 181, and ALA 181, among all eight attachment positions. This may suggest that these two compounds may play a role in altering the conformation of the activated MMP1 and thereby inhibiting its mechanism of action. Ladanein compounds have an anti-aging effect on the skin as well as a role in skin depigmentation, whereas 5-hydroxy-7,4'-dimethoxyflavone has an anti-aging effect on the skin by promoting collagen synthesis in the skin [22]-[24]. On the basis of the value of the binding affinity, the similarity of the positions of the formed bonds, and empirical studies conducted on ladanein and 5-hydroxy-7,4'-dimethoxyflavone, it is predicted that these two compounds will serve as anti-aging drug ingredients.

On the other hand, genkwanin creates four connections with the MMP1 protein, whereas luteolin and acacetin create six. These three compounds exhibit binding to LEU 181 and ALA 182 amino acid residues, which are among the three attachment sites for the crucial amino acids of MMP1. Consequently, these two compounds have the potential to influence alterations in the regulation of MMP1's active site. Studies conducted indicate that the development of luteolin-based anti-aging drugs is extremely promising [25][26]. It is believed that acacetin plays a significant role in preventing photoaging caused by UV-B exposure [27]. However, there is still no comparable research on genkwanin for anti-aging, either *in vivo* or *in vitro*, so with the docking test data from this study, the genkwanin compound may be developed in subsequent studies as an anti-aging agent. Based on the appropriateness of the comparison of binding affinity values, the similarity of the formed bond sites, and empirical studies conducted on these compounds, it can be predicted that luteolin, acetin, and genkwanin will become components of anti-aging medications.

4. CONCLUSIONS

Five basil compounds, namely ladanein, acacetin, luteolin, 5-hydroxy-7,4'-dimethoxyflavone, and genkwanin were discovered to have the potential to act as skin-anti-aging agents based on the findings of the tethering experiments that were conducted. Based on the fulfilment of the binding affinity indicators and the similarity of the relevant attachment locations when compared to the native ligands utilized, these five compounds were predicted to be anti-aging agents. In the future, a molecular dynamics method, *in vitro*, and *in vivo* studies can be used to further validate basil's constituents that have the potential to act as anti-aging agents.

Table 3. Results of docking of MMP1 protein with basil compounds.

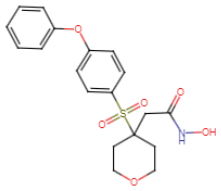
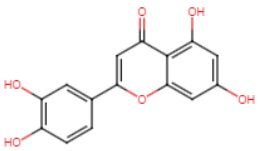
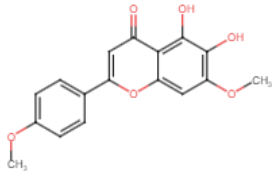
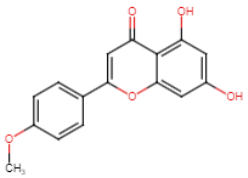
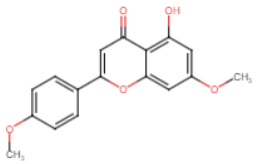
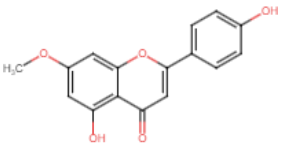
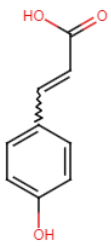
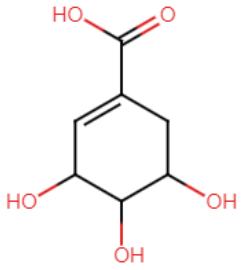
Ligand Compounds	Ligand Code	Binding Affinity Score (kcal/mol)	Compound Structure
Ligand RS2 (*Native ligand*)	NL	-9.5	
Luteolin	L1	-10	
Ladanein	L2	-9.9	
Acacetin	L3	-9.9	
5-Hydroxy-7,4'-dimethoxyflavone	L4	-9.8	
Genkwanin	L5	-9.6	
p-Coumaric acid	L6	-6.9	

Table 3. *Cont.*

Ligand Compounds	Ligand Code	Binding Affinity Score (kcal/mol)	Compound Structure
Shikimic acid	L7	-6.1	

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Author Contributions

W. N. A. did coordination of all research authors, administration of research writing activities, development of processing of research data results, and data inference. R. A. Z. A. did data collection and management, molecular docking testing and analysis, and the visualization of docking results. N. R. derived conclusions from the research results and developed abstracts. H. N. I. did the identification of basil (*Ocimum basilicum*) compounds through literature and Datawarrior studies, as well as composing and describing the employed research methodologies. M. D. I. I. did communication with research specialists and analysis of active compounds using literature and web databases. E. R. P. was responsible for selecting target proteins, directing, editing, and refining writing rules and article drafts.

Conflicts of Interest

The authors declare that there are no competing financial interests, personal relationships, or government politics in this study that could influence the work reported in this paper or negatively impact the public.

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Table 4. The type of bond formed after the docking process and the visualization results of the docking test between the target protein and the ligand compound.

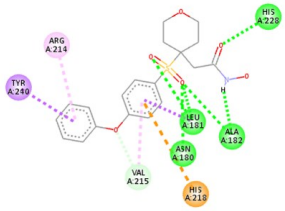
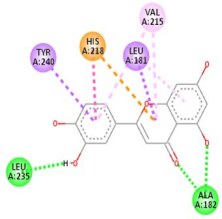
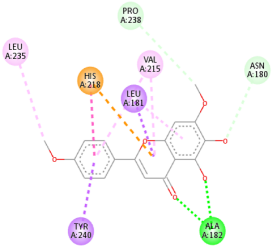
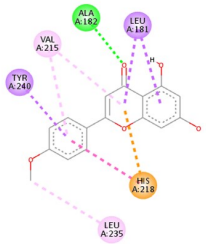
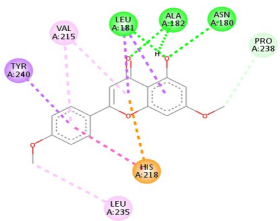
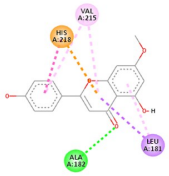
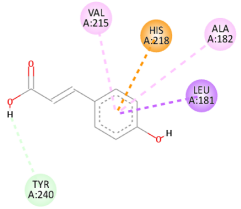
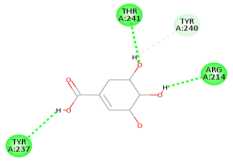
Ligand Code	Amino Acid Residues*		Bond Type	Distance (Å)	Percentage of Similarity to Native Ligand (%)	Visualization Result**
NL	ASN	180	Hydrogen	2.35	Native Ligand	
	LEU	181	Hydrogen	2.74		
	ALA	182	Hydrogen	2.24		
	ARG	214	Hydrophobic	5.41		
	VAL	215	Hydrogen	4.03		
	HIS	218	Electrostatic	4.90		
	HIS	228	Hydrogen	2.58		
	TYR	240	Hydrophobic	3.91		
L1	LEU	181	Hydrophobic	4.57	62.5	
	ALA	182	Hydrogen	2.05		
	VAL	215	Hydrophobic	5.24		
	HIS	218	Electrostatic	4.88		
	LEU	235	Hydrogen	1.77		
	TYR	240	Hydrophobic	3.87		
L2	ASN	180	Hydrogen	3.60	75.0	
	LEU	181	Hydrophobic	4.14		
	ALA	182	Hydrogen	2.33		
	VAL	215	Hydrophobic	5.21		
	HIS	218	Electrostatic	4.9		
	LEU	235	Hydrophobic	4.57		
	PRO	238	Hydrogen	3.63		
	TYR	240	Hydrophobic	3.91		
L3	LEU	181	Hydrophobic	3.81	62.5	
	ALA	182	Hydrogen	2.57		
	VAL	215	Hydrophobic	5.2		
	HIS	218	Electrostatic	4.9		
	LEU	235	Hydrophobic	4.58		
	TYR	240	Hydrophobic	3.92		
L4	ASN	180	Hydrogen	2.76	75.0	
	LEU	181	Hydrogen	3.23		
	ALA	182	Hydrogen	2.47		
	VAL	215	Hydrophobic	5.2		
	HIS	218	Electrostatic	4.85		
	LEU	235	Hydrophobic	4.57		
	PRO	238	Hydrogen	3.66		
	TYR	240	Hydrophobic	3.99		

Table 4. *Cont.*

Ligand Code	Amino Acid Residues*		Bond Type	Distance (Å)	Percentage of Similarity to Native Ligand (%)	Visualization Result**
L5	LEU	181	Hydrophobic	4.27	50.0	
	ALA	182	Hydrogen	2.79		
	VAL	215	Hydrophobic	5.19		
	HIS	218	Electrostatic	4.94		
L6	LEU	181	Hydrophobic	3.68	62.5	
	ALA	182	Hydrophobic	5.43		
	VAL	215	Hydrophobic	4.84		
	HIS	218	Electrostatic	4.99		
	TYR	240	Hydrogen	3.13		
L7	ARG	214	Hydrogen	1.98	25.0	
	TYR	237	Hydrogen	2.49		
	TYR	240	Hydrogen	2.74		
	THR	241	Hydrogen	2.12		

Notes
* : The same colored text (except black with underlined) shows the similarity of the positions of the amino acids formed between the test ligands and the native ligand.
** : The various sorts of bonds formed are shown by the variation in color. An electrostatic binding is shown by orange color, a hydrogen bond is indicated by cyan-green color, and a hydrophobic bond is indicated by pink-purple color.

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