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ORIGINAL ARTICLE **OPEN ACCESS**

Molecular Docking Analysis of Bioactive Compounds from *Ocimum basilicum* Aqueous Leaf Extract against Estrogen Receptor

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Abstract
Molecular docking studies have been performed on three bioactive compound presents in Ocimum basilicum Aqueous Leaf Extract, which play a vital role in the treatment of breast cancer. These three compounds drug molecules have the same target called Estrogen Receptor which acts as a DNA-binding transcription factor that regulates gene expression. In silico docking studies were analysis by Auto dock Vina which provided a better understanding of the binding interactions of the three compounds. The general properties, lipophilicity, hydrophilicity, and medication similarity properties were gotten from the Swiss ADME online server instrument. Among the three drugs taken, Andrographolide had the lowest Binding affinity, i.e. -8.87, which shows that it had better binding interaction with the Receptor.
Keywords: *Breast Cancer, Estrogen Receptor, Molecular Docking, Auto dock Vina, Binding Interactions, Swiss ADME.*

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INTRODUCTION

Estrogens [1] are one among the five steroidal hormones which happen normally as the female regenerative hormone. Indeed, even before the hormone estrogen is spent by the body, it needs to tie to the proteins called estrogen receptors. Breast malignant growths are having a tendency to be touchy to the hormone estrogen which will improve the development of the tumor [2]. The carcinogenic cells which have the estrogen receptor on their surface are in this manner called as, estrogen receptor-positive malignant growth or ER-positive disease. Breast cancer growth is a disease which begins in the tissues of the breast, for the most part from the internal coating of the lobules or the milk pipes which supply milk [3].The malignant growth which is identified with the channels is called as ductal carcinoma, whereas the disease identified with the lobules is called as lobular carcinoma [4].

O. basilicum Linn. a plant which finishes its lifecycle inside one year and discovered wild in the tropical, subtropical and mild areas of the world particularly Ceylon, hot West Asia, Africa, Malayan and Pacific Islands. It has begun in Punjab and is additionally broadly dispersed in tropical and mild districts of India and Pakistan [5]. A wide range of naturally occurring compounds has been studied extensively for their immense potential in the prevention of cancer over the last few decades. Phytoconstituents are metabolites found solely in *O. basilicum* in experimental systems which confer protection against various environmental and ingested carcinogens by provoking our antioxidant enzymes, promoting DNA repair pathways and thereby directly effecting the progression of cancer and metastasis. Chemotherapy is one of the treatment strategies employed wherein natural or synthetic drugs are administered to slow down or delay the various steps involved in metastasis which includes initiation, promotion and progression of cancer. Common causes for most of the cancers that occur today are the environment and life-style factors. It has been suggested that the primary and root cause of most of the cancers is associated with

inherited genetic aberrations (5%-10%) and acquired genetic abnormality (90%-95%) caused by various exogenous and/or endogenous environmental agents [6].

In silico procedure is a modest method that abbreviates the time span spending in testing the adequacy drugs. Hence, the present study focused on the identification of bioactive compounds present in *Ocimum basilicum* Aqueous Leaf Extract through gas chromatography-mass spectrometry (GC-MS) analysis and to screen the potential bioactive compounds for breast cancer by molecular docking against estrogen receptor

MATERIAL AND METHODS

Plant Collection and Identification

New leaves of O. basilicum were gathered from the Palakarai Zone, Tiruchirappalli, Tamil Nadu, India and ordered ID of the gathered plant material was affirmed at Department of Botany, St. Joseph's College, Tiruchirappalli.The leaves were then concealed dried for a time of about fourteen days. The dried leaves were powdered and put away for additional examination.

Preparation of Extracts

Soxhlet extraction of the plant materials was carried out with aqueous solvents. 50 grams of the powdered plant material was packed in Whatman No.1 filter paper and were extracted separately with 300 ml of the solvents for 48 hours. The extracts were then concentrated at room temperature and stored at 40ºC for further use.

GC-MS analysis

The Phytochemical analysis of aqueous extracts of *Ocimum basilicum* was demonstrated in GC-MS equipment. The analysis was performed in SHIMADZU/ QP2020. Then the results were comparing by using National Institute of Standards and Technology Mass Spectral database (NIST-MS,1998)library.

Preparation of receptor

The three-dimensional (3D) structures of drug targets selected in this study available in the RCSB database. The ESTROGEN RECEPTOR PDB ID: 1X7R was downloaded in pdb format from the protein data bank.the structure was prepared and refined by Charges and bond orders were doled out, hydrogens were added to the overwhelming molecules, selenomethionines were changed over to methionines, and all waters were erased.

Ligand Preparation

Compounds were retrieved from PubChem databases, i.e. Palustric acid, Abietic acid and Andrographolide. Then Ligands are prepared by The SDF files were converted into PDB file format using OPEN BABEL software.

Protein-ligand docking

Protein ligand docking was completed in Auto dock Vina, [7] which is an intuitive sub-atomic designs program for figuring and showing the practical docking methods of protein and ligand sets displayed in a chain of command dependent on their binding affinities.

Lead-likeliness properties

The SWISS ADME, a free web device was utilized to create the physicochemical, therapeutic and drug likeness properties of these Compounds. Lipinski's standard likewise called the Rule of five (RO5) is to assess the drug likeness or decide whether a synthetic compound with a specific pharmacological or organic movement has properties that might be dynamic peroral [8] [9].

RESULTS AND DISCUSSION

Gas chromatography-mass spectrometry analysis Figure 1 depicts the various compounds present in the leaves of *Ocimum basilicum*. The compounds present in *Ocimum basilicum* extracts are demonstrated in Table 1. The chromatogram revealed the presence of 45 compoundsin the investigated polyherbal preparation. The three compounds, namely Palustric acid, Abietic acid and Andrographolide, were selected for further study on the basis of the Rule of five and Retention time are 33.21, 33.10, and 32.05.

Molecular Docking

The target proteins, namely estrogen receptor, were docked with 2 Palustric acid, Abietic acid and Andrographolide by Auto dock Vina. The binding affinities values are showed in the table 1.

The binding affinity values obtained by Auto dock Vina for 2 Palustric acid, Abietic acid and Andrographolide were -6.75,-8.19,-8.87 Kcal/mol, respectively.

General Properties

Table 3 introduces the general properties of mixes 2 Palustric acid, Abietic acid and Andrographolide, for example, molecular formula, chemical structure, simplified molecular input line entry specification, and international union of pure and applied chemistry name.

Table 4 tabulates the Physiochemical properties of the three compounds such as molecular weight, number of atoms, fraction CSP3, number of rotatable bonds, molar refractivity, and topological polar surface area. The molecular weights, Number of H-bond acceptors, Number of H-bond donors are less than 500, 10 and 5 in 2 Palustric acid, Abietic acid and Andrographolide representing a good oral bioavailability active drug.

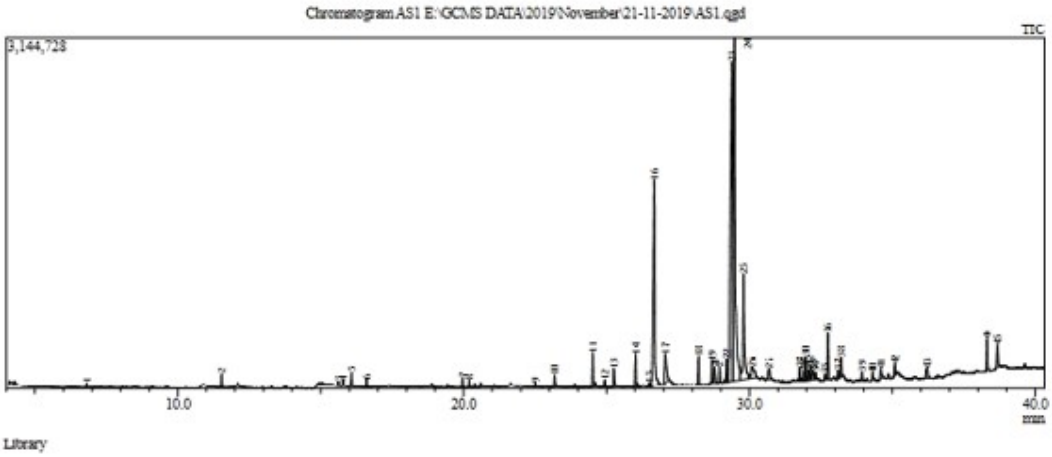


Figure 1: Gas chromatography-mass spectrometry analysis of Ocimum basilicum

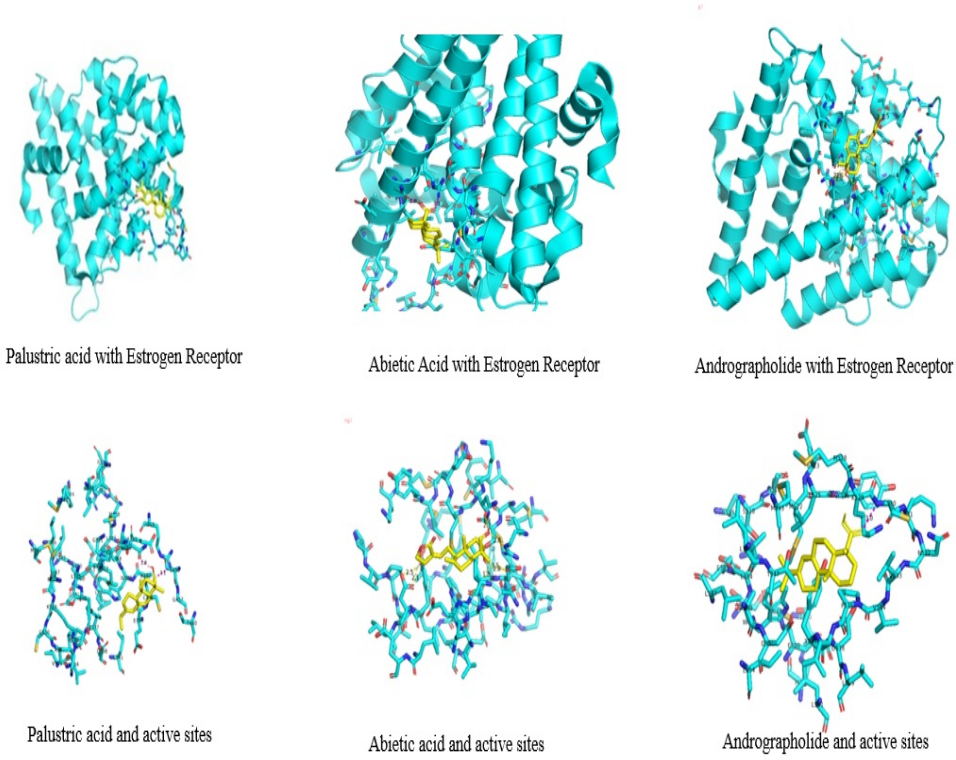


Figure 2: Docking analysis of 2 Palustric Acid, Abietic Acid and Andrographolide in the Estrogen Receptor (PDB ID: 1x7r)

Table 1: Compounds obtained from the gas chromatography-mass spectrometry analysis of Ocimum basilicum.

Compound No	Retention time	Area %	Height %	Name of the Compound
1	6.814	0.17	0.33	DECANE
2	11.533	0.46	0.89	Dodecane
3	15.619	0.17	0.29	3,5-Diisopropoxy-1,1,1,7,7,7-hexamethyl-3,5-bis(trimethylsiloxy)tetrasiloxane
4	15.78	0.24	0.35	2-PROPENOIC ACID, 3-PHENYL-, METHYL ESTER
5	16.081	0.5	0.86	TETRADECANE
6	16.604	0.29	0.54	BICYCLO[7.2.0]UNDEC-4-ENE, 4,11,11-TRIMETHYL-8-METHYLENE-, [1R-(1R*,4E,9S*)]-
7	19.968	0.4	0.68	(-)-5-OXATRICYCLO[8.2.0.0(4,6)]DODECANE,,12-TRIMETHYL-9-METHYLENE-, [1R-(1R*,4R*,6R*,10S*)]-
8	20.192	0.31	0.57	TETRADECANE
9	22.516	0.17	0.3	OCTADECANOIC ACID, METHYL ESTER
10	23.187	0.53	0.77	Tetradecanoic acid
11	24.522	1.29	2.23	Neophytadiene
12	24.942	0.27	0.44	Neophytadiene
13	25.257	0.84	1.15	3,7,11,15-Tetramethylhexadec-2-en-1-yl acetate
14	26.019	1.26	2.16	Hexadecanoic acid, methyl ester
15	26.496	0.14	0.3	Dibutyl phthalate
16	26.674	13.5	13.04	n-Hexadecanoic acid
17	27.06	2.16	1.88	1H-inden-1-one, 2-(2-furanylmethylene)-2,3-dihydro-
18	28.223	1.13	1.83	7-Isopropyl-1,1,4a-trimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene
19	28.691	0.81	1.4	9,12-Octadecadienoic acid (Z,Z)-, methyl ester
20	28.788	0.73	0.96	9,12-OCTADECADIENOIC ACID (Z,Z)-, METHYL ESTER
21	28.958	0.62	0.98	2-HEXADECEN-1-OL, 3,7,11,15-TETRAMETHYL-, [R-[R*,R*-(E)]]-
22	29.207	0.96	1.46	OCTADECANOIC ACID, METHYL ESTER
23	29.39	28	20.19	9,12-Octadecadienoic acid (Z,Z)-
24	29.479	23.8	21.68	Oleic Acid
25	29.798	7.05	6.69	OCTADECANOIC ACID
26	30.095	1.49	0.68	9,12-Octadecadienoic acid (Z,Z)-
27	30.682	0.76	0.67	9,12-Octadecadienoic acid (Z,Z)-
28	31.765	0.47	0.85	2-Propenoic acid, 3-phenyl-, methyl ester
29	31.899	0.44	0.61	(E)-ZIMTSAEURE, METHYLESTER
30	31.965	0.96	1.54	2-Propenoic acid, 3-phenyl-, methyl ester
31	32.056	0.42	0.6	Andrographolide
32	32.133	0.67	0.91	1-Phenanthrenemethanol, 1,2,3,4,4a,5,6,9,10,10a-decahydro-1,4a-dimethyl-7-(1-methylethyl)-, [1R-(1.alpha.,4a.beta.,10a.alpha.)]
33	32.229	0.57	0.59	9,12-Octadecadienoic acid (Z,Z)-
34	32.312	0.28	0.39	(2E,4E,12E)-13-(Benzo[d][1,3]dioxol-5-yl)-N-isobutyltrideca-2,4,12-trienamide
35	32.651	0.17	0.31	EICOSANOIC ACID
36	32.744	1.96	2.9	1-Phenanthrenemethanol, 1,2,3,4,4a,9,10,10a-octahydro-1,4a-dimethyl-7-(1-methylethyl)-, [1R-(1.alpha.,4a.beta.,10a.alpha.)]-
37	33.102	0.42	0.56	Abietic acid
38	33.21	0.85	1.28	Palustric acid
39	33.946	0.33	0.55	((1R,4aR,4bR,10aR)-7-Isopropyl-1,4a-dimethyl-1,2,3,4,4a,4b,5,6,10,10a-decahydrophenanthren-1-yl)methanol
40	34.315	0.21	0.37	Pregnan-17,21-diol-20-one, 3,9-epoxy-3-O-methyl-11-thiocyano-,
41	34.603	0.54	0.58	Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester
42	35.09	0.46	0.68	(1S,3aR,4R,8R,8aS)-1-Isopropyl-3a-methyl-7-methylenedecahydro-4,8-epoxyazulene
43	36.221	0.7	0.56	5.alpha.-Pregn-16-en-20-one, 12.beta.-hydroxy-, acetate
44	38.315	1.31	2.01	Squalene
45	38.675	1.16	1.4	2-Butene-1,4-dione, 1,2,3,4-tetraphenyl-, (Z)-

Table 2: Docking Results With 2 Palustric Acid, Abietic Acid and Andrographolide in the Estrogen Receptor (PDB ID: 1x7r)

Name of the ligand	Compound ID	Binding affinity
Palustric acid	443613	-6.75
Abietic acid	10569	-8.19
Andrographolide	5318517	-8.87

Table 3: General properties of 2 Palustric Acid, Abietic Acid and Andrographolide.

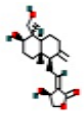
Name of the ligand/compound	Chemical formula	Structure	SMILES	IUPAC name
Palustric acid	C20H30O2		CC(C1=CC2=C(CC1)C1(C)CCCC(C1CC2)(C)C(=O)O)C	(1*R*,4a*S*,10a*R*)-1,4*a*-dimethyl-7-propan-2-yl-2,3,4,5,6,9,10,10*a*-octahydrophenanthrene-1-carboxylic acid
Abietic acid	C20H30O2		CC(C1=CC2=CCC3C(C2CC1)(C)CCCC3(C)C(=O)O)C	1*R*,4a*R*,4b*R*,10a*R*)-1,4*a*-dimethyl-7-propan-2-yl-2,3,4,4*b*,5,6,10,10*a*-octahydrophenanthrene-1-carboxylic acid
Andrographolide	C20H30O5		OCC1(C)C(O)CCC2(C1CCC(=C)C2CC=C1C(O)COC1=O)C	(3*E*,4*S*)-3-[2-[(1*R*,4a*S*,5*R*,6*R*,8a*S*)-6-hydroxy-5-(hydroxymethyl)-5,8*a*-dimethyl-2-methylidene-3,4,4*a*,6,7,8-hexahydro-1*H*-naphthalen-1-yl]ethylidene]-4-hydroxyoxolan-2-one

Table 4: Physiochemical properties of 2 Palustric Acid, Abietic Acid and Andrographolide

Name of the ligand	Molecular weight (g/mol)	Num. heavy atoms	Num.Arom. Heavy atoms	Fraction CSP3	Num. rotatable bonds	Num. H-bond acceptors	Num. H- bond donors	Molar refractivity	TPSA (°A2)
Palustric acid	302.45	22	0	0.75	2	2	1	92.22	37.3
Abietic acid	302.45	22	0	0.75	2	2	1	92.22	37.3
Andrographolide	350.45	25	0	0.75	3	5	3	95.21	86.99

Table 5: Lipophilicity and hydrophilicity of 2 Palustric Acid, Abietic Acid and Andrographolide.

	Lipophilicity	Hydrophilicity								
Name of the ligand	Consensus Log P	Log S (ESOL)	Solubility (mg/ml)	Class	Log S (Ali)	Solubility (mg/ml)	Class	LogSw (Silicos-IT)	Solubility (mg/ml)	Class
Palustric acid	4.39	-4.41	119;0.0000	Moderately soluble	-4.98	0.00314; 0.0000104	Moderately soluble	-4.19	0.0194;0.0000643	Moderately soluble
Abietic acid	4.37	-4.59	0769;0.0000	Moderately soluble	-5.29	0.00153; 0.00000507	Moderately soluble	-3.74	0.0547;0.000181	Soluble
Andrographolide	2.3	-3.18	234;0.0006	Soluble	-3.62	0.0842;0.00024	Soluble	-2.69	0.722;0.00206	Soluble

Table 6: Pharmacokinetics properties 2 Palustric Acid, Abietic Acid and Andrographolide.

Name of the ligand	GI absorption	BBB permeant	Pgp substrate	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor	log Kp (cm/s) (skin Permeation Cm/s)
Palustric acid	High	Yes	No	No	Yes	Yes	No	No	-4.96
Abietic acid	High	Yes	No	No	Yes	Yes	No	No	-4.75
Andrographolide	High	No	Yes	No	No	No	No	No	-6.9

Table 7: Drug likeness properties of 2 Palustric Acid, Abietic Acid and Andrographolide.

Name of the ligand	Lipinski	Ghose	Veber	Egan	Muegge	Bioavailability Score
Palustric acid	1	0	0	0	0	0.56
Abietic acid	1	0	0	0	0	0.56
Andrographolide	0	0	0	0	0	0.55

Table 8: Lead likeness properties of 2 Palustric Acid, Abietic Acid and Andrographolide.

Name of the ligand	Pains	Brenk	Lead likeness	Synthetic Accessibility
Palustric acid	0	0	1	5.03
Abietic acid	0	0	1	4.8
Andrographolide	0	2	1	5.06

Table 5 demonstrates the octanol-water partition coefficient values of 2 Palustric acid, Abietic acid and Andrographolide as indicated in this table, these values were within the permissible range of -0.4 to +5.6, implying a good lipophilic compound. 2 Palustric acid, Abietic acid and Andrographolide compounds were mostly soluble in aqueous medium.

Table 6 illustrates the pharmacokinetic properties of 2 Palustric acid, Abietic acid and Andrographolide. According to the results, the oral bioavailability was high for 2 Palustric acid, Abietic acid and Andrographolide. Both compounds of 2 Palustric acid, Abietic acid cross blood brain barrier, and Andrographolide does not cross blood brain barrier however, penetration through skin was better for all three of the compounds.

Based on Table 7, 2 Palustric acid, Abietic acid and Andrographolide followed the Lipinski's rule of 5 with one violation on 2 Palustric acid, Abietic acid and other filters, like Veber and Egan, Ghose, Muegge filter are no violations for 2 Palustric acid, Abietic acid and Andrographolide. For a new drug molecule, the bioavailability score is to predict the probability of a new drug that have at least 10% oral bioavailability in rodents.

Table 8 shows the filters for lead likeliness, like pains filter and brenk filter were obeyed for 2 Palustric acid, Abietic acid and Andrographolid

The findings are in support of Stephanie Sommer [10] estrogen receptor (ER) gave us an incredible prescient and prognostic marker, yet in addition a productive for the therapy of hormone-subordinate breast malignant growth with antiestrogens. *Ocimum basilicum* extract compounds were ability to kill and control the breast cancer cells. Arshad; Farooq *et al*.[11]

CONCLUSION

The GC-MS analysis of *Ocimum basilicum* Aqueous Leaf Extract revealed the presence of 45 compounds among that three compounds are choose by rule of five. The docking analysis has exhibited and binding affinities of 2 Palustric acid, Abietic acid and Andrographolide are -6.75,-8.19,-8.87 Kcal/mol,

respectively. The drug likeness properties showed Andrographolide was satisfied all rules. The results revealed out that the compounds present in *Ocimum basilicum* Aqueous Leaf Extract can inhibit the Estrogen receptor.

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