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Research Article

In silico molecular docking study of phytochemicals obtained from *Holigarna caustica* (Dennst.) for cancer treatment

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Abstract

Holigarna caustica, commonly known in Bangladesh as "Katebel," is used in traditional medicine to treat tumors, malignancies, skin problems, obesity, inflammation, eye irritation, and arthritis. The goal of this work was to use computational models like molecular docking to find the bioactive phytochemicals in this plant that are responsible for the anticancer potential. The molecular docking experiment was carried out using Glide of Schrödinger Maestro (version 10.1). Our computational research revealed that a total of eighteen phytocompounds may be responsible for the plant's anticancer properties, which should be further studied in experimental models.

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1. Introduction

The Anacardiaceae family contains *Holigarna caustica* (Dennst.) Oken. In Bangladeshi, it's called as "Borola" or "Katebel," while in English, it's known as the black varnish tree. The Chittagong, Cox's Bazar, and Chittagong Hill Tract regions of Bangladesh are home to this species. Traditional medicine uses the plant to treat hemorrhoids, tumors, malignancies, skin disorders, obesity, inflammation, eye irritation, and arthritis, among other ailments. This plant's chloroform extract has been shown to have antibacterial and cytotoxic characteristics, and it's also been used as an antiseptic for cuts and wounds. Additionally, the previous study has shown that this herb contains antinociceptive, anti-inflammatory, and nematicidal properties. The plant includes alkaloids, carbohydrates, flavonoids, proteins, terpenoids, cardiac glycosides, saponins, sterols, steroids, coumarins, and fixed oils, according to a preliminary the phytochemical investigation and a GC-MS analysis found that it has 40 phytocompounds [1][2]. However, no evidence or report of its anticancer effect has been found, nor has it been determined which phytocompounds in this plant were responsible for that activity. Keeping this view, the current study's purpose was to investigate it utilizing molecular docking.

2. Methods

2.1. Selection of compounds for *in silico* molecular docking study

Thirty-six phytocompounds (selected by ADME analysis)were chosen as major phytocompounds based on their availability in the literature [1], and the

chemical structures of the compounds were retrieved from the PubChem compound library.

2.2. Molecular docking study

2.2.1. Preparation of ligands

As previously stated, the structures of the phytocompounds were acquired from the PubChem database. The ligands were synthesized in Maestro 2015 with the LigPrep tool, neutralized with Epik at pH 7.0±2.0, and minimized with the OPLS_2005 force field.

2.2.2. Preparation of enzymes or receptors

The following enzymes' 3D crystal structures were retrieved from the Protein Data Bank RCSB PDB [3]: CYP3A4 protein (PDB ID: 1TQN). [4], anti-apoptotic protein Bcl-2 (PDB ID: 2O2F) [5], navitoclax and Bcl-2 complex (PDB ID: 4LVT) [6] for anti-cancer (lung cancer) activity, and human estrogen receptor (PDB ID: 2IOK) [7] for anti-cancer (breast cancer) activity. Before removing all water molecules, the Protein Preparation Wizard in Schrödinger Maestro 10.1 was used to prepare and refine the crystal structure, which included assigning charges, bond orders, hydrogens to heavy atoms, and converting selenomethionines and selenocysteines into methionines and cysteines, respectively. Minimization was achieved by setting the maximum heavy atom RMSD to 0.30 Å using the force field OPLS 2005.

2.2.3. Receptor grid generation and glide standard precision ligand docking

To create receptor grids and conduct molecular docking experiments, researchers used Glide Schrödinger Maestro v10. Using the OPLS_2005 force field and default settings of van der Waals scaling factor 1.00 and charge cut-off value 0.25, a grid was constructed for each enzyme. A cubic box with precise dimensions centered on the centroid of the active site residues was also built for receptor docking, with the size of the box set at 14 Å × 14 Å × 14 Å. Glide's standard precision (SP) scoring function was used to conduct the docking tests, and only the best scoring pose with docking score for each ligand was recorded [3,8–10].

3. Results and Discussion

3.1. Molecular docking study for anticancer activity

In the present study, four primary proteins (CYP3A4 protein, PDB ID: 1TQN; anti-apoptotic protein Bcl-2, PDB ID: 2O2F; navitoclax and Bcl-2 complex, PDB ID: 4LVT; human estrogen receptor, PDB ID: 2IOK) responsible for anti-cancer activity (lung and breast) were chosen to examine the possible mechanism action of the traditional uses of *H. causitica* plant. At this point, 32 major compounds of *H. causitica* were docked against all proteins, and the results of molecular docking are presented in **Table 1. Fig. 1** represented **the** chemical structure of the eighteen compounds found most potential in the molecular docking study and the molecular interactions of ligand compounds are shown in **Tables 2-3 and Fig. 2**. Here, for CYP3A4 protein, thirty-two compounds have been docked with kappa receptor in which seventeen compounds have given the highest scores viz. C1, C2, C3, C4, C10, C19, C20, C21, C22, C23, C24, C25, C26, C27, C28, C29, C31 (**Table 1**). The most common amino acid residue for hydrogen bond interactions is Ala305, Arg105, Pro434, Arg212, Ala305, and hydrophobic interactions are Arg106, Phe57, Phe108, Phe215, Ala305, Ile118, Ile443, Phe302, Ala370, Leu364, Ile369, Cys442, Phe435, Phe271, Ile184, Phe271, Phe447, Arg372, Ala370, and Met371 (**Table 2**). Additionally, for anti-apoptotic protein Bcl-2, thirty-two compounds have been docked with kappa receptor in which eighteen compounds have given the highest scores viz. C1, C2, C3, C4, C10, C19, C20, C21, C22, C23, C24, C25, C26, C27, C28, C29, C30, C31, and C32 (**Table 1**). The most common amino acid residue for hydrogen bond interactions is Arg143, Arg104, Asp100, Val130, and hydrophobic interactions are Met112, Leu134, Ala146, Val130, Leu134, Phe150, Phe101, Tyr105, Phe150, Val145, Trp141, Tyr199, Ala146, Ala97, Phe101, Arg143, and Tyr105 (**Table 2**). Moreover, for navitoclax and Bcl-2 complex protein, thirty-two compounds have been docked with kappa receptor in which eighteen compounds have given the highest scores viz. C1, C2, C3, C4, C10, C19, C20, C21, C22, C23, C24, C25, C26, C27, C28, C29, C30, C31, and C32 (**Table 1**). The most common amino acid residue for hydrogen bond interactions is Arg124, Arg143, Ala97, Leu198, Glu133, and hydrophobic interactions are Met112, Ala146, Val130, Leu134, Phe101, Phe150, Val153, Phe109, Val153, Phe109, Val145, Ala97, Tyr199, Tyr105, Leu198, Phe195, and Arg143 (**Table 3**).

Table 1. Docking score of the identified compounds in MEHC against CYP3A4 protein (PDB ID: 1TQN), anti-apoptotic protein Bcl-2 (PDB ID: 2O2F), and navitoclax and Bcl-2 complex (PDB ID: 4LVT) for anti-cancer (lung cancer) activity, respectively, and against human estrogen receptor (PDB ID: 2IOK) for anti-cancer (breast cancer) activity

Compounds	Com. No.	Docking Score (kcal/mol)			
		1TQN	2O2F	4LVT	2IOK
Santalol, *E*-cis,epi-β-	C1	-3.458	-4.906	-5.237	-6.625
β-D-Glucopyranoside, methyl	C2	-6.729	-4.527	-4.37	-5.482
6-Hydroxy-4,4,7α-trimethyl-5,6,7,7a tetrahydrobenzofuran-2(4H)-one	C3	-4.682	-5.526	-5.31	-7.071
1-(7-Hydroxy-1,6,6-trimethyl-10-oxatricyclo[5.2.1.0(2,4)]dec-9-yl)ethanone	C4	-4.093	-4.042	-4.459	-7.686
Neophytadiene	C5	-0.466	-2.053	-0.91	-2.293
2-Pentadecanone, 6,10,14-trimethyl-	C6	-1.45	-0.304	-1.573	-3.739
3,7,11,15-Tetramethyl-2-hexadecen-1-ol	C7	-1.03	-1.967	-1.933	-1.71
Hexadecanoic acid, methyl ester	C8	-0.933	-0.918	-0.33	-0.173
n-Hexadecanoic acid	C9	0.96	0.264	0.139	-2.353
2(3H)-Furanone, dihydro-5-(2-octenyl)-, (*Z*)-	C10	-6.259	-5.121	-4.082	-5.541
9,12-Octadecadienoic acid (*Z,Z*)-, methyl ester	C11	-2.033	-1.506	-1.303	-1.671
9-Octadecenoic acid, methyl ester, (*E*)-	C12	-0.492	-1.019	-0.961	-1.15
Phytol	C13	-2.352	-1.198	-1.787	-3.756
Methyl stearate	C14	-0.649	-0.531	-1.163	-0.723
9,12-Octadecadienoic acid (*Z,Z)*-	C15	-1.726	-0.496	-1.167	-3.54
9-Octadecenoic acid, (*E*)-	C16	-1.145	-0.845	-0.979	-1.582
Stearic acid	C17	-0.155	-0.66	-0.208	-1.262
3-Tridecylphenol	C18	-2.295	-2.967	-1.711	-4.813
9-Octadecenamide, (*Z*)-	C19	-1.418	-1.56	-0.794	-3.642
(*Z*)-3-(pentadec-8-en-1-yl)phenol	C20	-4.601	-6.13	-5.152	-8.538
Phenol, 3-pentadecyl-	C21	-3.835	-5.891	-4.672	-6.723
Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester	C22	-6.00	-4.413	-3.993	-4.453
Bis(2-ethylhexyl) phthalate	C23	-4.325	-4.408	-4.429	-4.473
(*Z)*-3-(Heptadec-10-en-1-yl)phenol	C24	-4.49	-6.158	-6.232	-5.809
3-((4*Z*,7*Z*)-Heptadeca-4,7-dien-1-yl)phenol	C25	-5.104	-6.798	-5.778	-8.689
α-Tocospiro A	C26	-5.236	-5.38	-5.408	-5.84
γ-Tocopherol	C27	-4.682	-5.71	-4.766	-6.037
Cholesta-4,6-dien-3-ol, (3β)-	C28	-5.157	-4.299	-3.868	-9.358
α-Tocopherol	C29	-3.16	-5.865	-4.949	-6.607
Campesterol	C30	-	-3.287	-3.749	-7.909
Stigmasterol	C31	-5.119	-4.22	-3.601	-6.002
γ-Sitosterol	C32	-	-4.167	-3.975	-

Com. No.: Compound number

Table 2. Binding interactions of the selected eighteen compounds with CYP3A4 protein (PDB ID: 1TQN), anti-apoptotic protein Bcl-2 (PDB ID: 2O2F), and navitoclax and Bcl-2 complex (PDB ID: 4LVT) for anti-cancer (lung cancer) activity, respectively

Compounds	**CYP3A4 protein (PDB ID: 1TQN)**		**Anti-apoptotic protein Bcl-2 (PDB ID: 2O2F)**		**Navitoclax and Bcl-2 complex (PDB ID: 4LVT)**	
	Hydrogen bond interactions	**Hydrophobic interactions**	**Hydrogen bond interactions**	**Hydrophobic interactions**	**Hydrogen bond interactions**	**Hydrophobic interactions**
Santalol, *E*-cis,epi-β-	Arg372 (2), Phe57	Arg105 (2), **Arg106**, **Phe57**, **Phe108** (2), **Phe215** (4)	Tyr105	**Met112** (2), **Leu134**, **Ala146** (2), **Val130**, **Leu134** (2), **Phe150**	Asp108	**Met112** (3), **Ala146**, **Val130**, **Leu134**, **Phe101** (2), **Phe150**
β-D-Glucopyranoside, methyl	Ile369, Pro434 (3), **Ala305**	-	Asp100 (2), Gln96	-	**Arg124** (2), Ala128 (2), Trp173 (2), Glu176	-
6-Hydroxy-4,4,7*α*-trimethyl-5,6,7,7a tetrahydrobenzofuran-2(4H)-one	**Arg105**, Arg130 (2)	**Ala305**, Ile301 (2), **Ile118**, **Ile443**, **Phe302**	**Arg143**	Met112, Leu134, **Phe101**	Val130	Ala146, Met112, Leu134, Phe101
1-(7-Hydroxy-1,6,6-trimethyl-10-oxatricyclo[5.2.1.0(2,4)]dec-9-yl)ethanone	Thr310, Ala305, Thr309	Val313 (2), **Ala370**, **Leu364**, **Ile369** (4), **Cys442**, **Phe435** (2)	Arg143	Met112 (2), Leu134, Phe101, Phe109	Arg124 (2)	Ala128, Phe127, His181 (2)
2(3H)-Furanone, dihydro-5-(2-octenyl)-, (*Z*)-	Phe302	Ala305, **Phe271**, Phe302 (2)	Arg143 (3)	Val130, Leu134, **Tyr105**, **Phe150**	**Arg143** (2)	Leu134, Met112, **Val153**, **Phe109**
9-Octadecenamide, (*Z*)-	**Pro434**	**Ile184**, Ile303, Phe271	Ala97, **Arg104** (2)	Ala146, Val130, Leu134, Phe150	Phe101, Arg104	**Val153**, Phe101, **Phe109**
(*Z*)-3-(pentadec-8-en-1-yl)phenol	Phe213, **Arg212**	Phe108, Arg212	Ala146	**Val145**, **Trp141**, **Tyr199**, Met112, Val130, Leu134,	**Ala97**	Val153, Phe101, Phe109, **Val145**
Phenol, 3-pentadecyl-	Pro434	Ile118, Ile443, Ala370	Val130	Val145, Trp141, Tyr199, Met112, Val13, Leu134, Ala146	Ala97	Val153, Phe101, Phe109

(continued on next page)

Table 2. (*Continued*)

Compounds	**CYP3A4 protein (PDB ID: 1TQN)**		**Anti-apoptotic protein Bcl-2 (PDB ID: 2O2F)**		**Navitoclax and Bcl-2 complex (PDB ID: 4LVT)**	
	Hydrogen bond interactions	**Hydrophobic interactions**	**Hydrogen bond interactions**	**Hydrophobic interactions**	**Hydrogen bond interactions**	**Hydrophobic interactions**
Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester	**Ala305**	Ile184, **Phe271**	Arg104 (2), **Asp100**	Val130, Leu134, Phe150	Asp137 (3), Leu134 (2), Glu133 (2)	**Ala97**, **Tyr199**
Bis(2-ethylhexyl) phthalate	Arg105, asn441	Asn441, Ala305, Ala448, Ile118, Leu364, Ile369, Trp126, Phe302, Phe435, Ala370, Cys442	Arg143 (2)	Val130, Leu134 (2), Met112, Val145, Tyr105, Phe150	Arg143 (2)	Met112, Val130, Leu134 (2), Val153, Phe101 (2), **Tyr105**, Phe109, Phe150
(*Z*)-3-(Heptadec-10-en-1-yl)phenol	Ala305	Phe271, **Phe447**, Ala370, Cys442	Val130	Phe150, Val145, Tyr199, Met112, Val130, Leu134, **Ala146**	**Leu198**	Tyr199, Val153, Phe101, Phe109, Ala97
3-((*4Z,7Z*)-Heptadeca-4,7-dien-1-yl)phenol	Asp76	Phe215, Ile369	**Val130**	**Ala97**, Val145, Tyr199, Met112, Val130, Leu134, Ala146	Leu198	Tyr199, Met112, Ala97
α-Tocospiro A	Cys442	Ala370, Leu373, Cys442, Ile369, **Arg372**, Phe57, Phe215, Phe435	Phe101, Gly142	Val130, Leu134, Met112, Val130, Leu134, **Phe101**, Phe150(2), Tyr199	Gly142	Ala146, **Leu198**, Met112, Phe101 (2), Tyr105 (3), **Phe195**, Tyr199
γ-Tocopherol	Arg212	**Ala370** (3), **Met371**, Ile369, Phe57, Phe215 (2)	-	Val145, Ala146, Met112, Val130, Leu134, Phe109, Phe150 (2), Ala97	**Glu133**	Ala97, Leu134 (2), Ala146, Leu198, Phe101 (2), Tyr105 (2), Phe195 (2), Tyr199
Cholesta-4,6-dien-3-ol, (3β)-	Ser119	Arg106 (3), Arg105, Met371 (2), Arg372, Phe57 (2), Phe108 (3), Phe215 (4), Phe304	Asp100	Ala97 (2), Val145, Ala146, Leu134, **Arg143**, Phe101, **Tyr105** (2), Tyr199 (2)	Glu133	Leu134 (2), **Arg143**, Val145, Phe101, Tyr105 (2)

(continued on next page)

Table 2. (*Continued*)

Compounds	CYP3A4 protein (PDB ID: 1TQN)		Anti-apoptotic protein Bcl-2 (PDB ID: 2O2F)		Navitoclax and Bcl-2 complex (PDB ID: 4LVT)	
	Hydrogen bond interactions	**Hydrophobic interactions**	**Hydrogen bond interactions**	**Hydrophobic interactions**	**Hydrogen bond interactions**	**Hydrophobic interactions**
α-Tocopherol	Glu374	Phe215 (3), Ala305, Ala370, Met371, Ile118, Ile443, Arg372, Arg106, Phe108, Phe137, Phe215 (2), Phe271, Phe447	-	Ala97 (2), Val145 (3), Arg104, Val130 (2), Leu134 (2), Met112, Phe101, Tyr105, Phe150 (2), Tyr199	Leu198, Gly142 (2)	Ala146, Val145, Arg143, Leu198, Leu134, Phe101 (2), Phe150
Stigmasterol	-	Ala370 (2), Arg372, Arg106, Phe57, Phe215 (3)	-	Ala97 (2), Ala146, Val145, Arg143, Phe101, Tyr199 (3)	Glu133	Leu134 (3), Ala146, Met112, Val130, Arg143, Phe101, Tyr105
γ-Sitosterol	-	-	-	Ala97 (2), Ala146, Val145, Leu134, Phe101 (2), Tyr105 (2), Tyr199 (3)	Tyr199	Phe101, Tyr105 (2), Tyr199 (2)
Campesterol	-	-	-	Ala97, Ala146, Phe101,	Glu133	Leu134 (3), Ala146, Phe101 (3),

Table 3. Binding interactions of the selected eighteen compounds with human estrogen receptor (PDB ID: 2IOK) for anti-cancer (breast cancer) activity

Compounds	Human estrogen receptor (PDB ID: 2IOK)	
	Hydrogen bond interactions	**Hydrophobic interactions**
Santalol, *E*-cis,epi-β-	**Glu353**	**Leu384** (2), **Leu346**, **Leu525**, **Met388**, **Met421**, **Ile424**, **Leu387**, **Leu391**
β-D-Glucopyranoside, methyl	Leu346 (2), Glu353, Ala350, Glu353	-
6-Hydroxy-4,4,7α-trimethyl-5,6,7,7a tetrahydrobenzofuran-2(4H)-one	Met388, Gly521	**Ala350**, Leu346 (2), Leu384, Leu387, Met421, **Phe404**(2)
1-(7-Hydroxy-1,6,6-trimethyl-10-oxatricyclo[5.2.1.0(2,4)]dec-9-yl)ethanone	-	Ala350,Leu384 (2), Ile424, Leu525 (4), Met421, Ile424, **Leu428**, Leu346 (2),

(continued on next page)

Table 3. (*Continued*)

Compounds	**Human estrogen receptor (PDB ID: 2IOK)**	
	Hydrogen bond interactions	**Hydrophobic interactions**
2(3H)-Furanone, dihydro-5-(2-octenyl)-, (Z)-	**Arg394**	Ala350, **Leu349**, Leu387, Ile424, Leu525
9-Octadecenamide, (Z)-	Glu353	Met421, **His524**
(Z)-3-(pentadec-8-en-1-yl)phenol	Glu353	Phe404, Leu525, Leu349, Ala350, Leu387, Leu391
Phenol, 3-pentadecyl-	Glu353	Phe404, Leu354, **Leu539**, Leu349, Ala350, Leu387
Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester	Trp383, Leu536, Glu380, Met522	Met388, Leu391, Leu428
Bis(2-ethylhexyl) phthalate	**Thr347**, Asp351	Leu384, Leu525 (2), Leu354 (2), **Leu536**, Met421, Leu539, **Trp383** (3), His524
(Z)-3-(Heptadec-10-en-1-yl)phenol	Glu353	Phe404, **Met522**, Trp383 (2), Leu349, Ala350, Leu387
3-((4Z,7Z)-Heptadeca-4,7-dien-1-yl)phenol	Thr347	**Met343**, Leu387, Leu391, Phe404, Leu346, Leu525
α-Tocospiro A	-	Ala350, Leu346, Met388, Leu391, Leu428, Ile424, Leu525, Leu346, Met421, His524, Tyr526 (2)
γ-Tocopherol	His524, Met421	Leu525 (3), Leu346, Met343, **Met528** (2), Leu536, Met522, Trp383 (3), His524, Tyr526, Met421
Cholesta-4,6-dien-3-ol, (3β)-	Glu353	Leu346 (2), **Ala350** (2), Leu387 (3), Met388, Leu391, Met421, Ile424, Leu384, Leu525 (2), Leu387, Met343, Val418, Met528, Phe404, His524
α-Tocopherol	-	Ala350 (2), Leu384, Leu346, Leu525 (3), Leu391, Leu428, Met421, Ile424, Leu536 (2), Trp383 (2), Phe404
Campesterol	Arg394, Leu387	Leu346 (3), Ala350, Leu391, Met421, Leu525 (4), Leu384, Leu387, Met528 (2), Met343 (2), Phe404 (2)
Stigmasterol		Leu346 (2), Ala350 (4), Leu525 (3), Leu387, Met421 (2), Ile424 (2), Leu384, Met388, Leu402, Leu428, Trp383 (2), Phe404, Phe425

On the other hand, for human estrogen receptor, thirty-two compounds have been docked with kappa receptor in which eighteen compounds have given the highest scores viz. C1, C2, C3, C4, C10, C19, C20, C21, C22, C23, C24, C25, C26, C27, C28, C29, C30, and C31 (**Table 1**). The most common amino acid residue for hydrogen bond interactions is Glu353, Arg394, Thr347, and hydrophobic interactions are Leu384, Leu346, Leu525, Met388, Met421, Ile424, Leu387, Leu391, Ala350, Phe404, Leu428, Leu349, His524, Leu539, Leu536, Trp383, Met522, Met343, Met528, and Ala350 (**Table 2**).

According to the results of the molecular docking analysis, eighteen phytocompounds (C1, C2, C3, C4, C10, C19, C20, C21, C22, C23, C24, C25, C27, C28, C29, C30, C31, C32) might well be responsible for the plant's analgesic effects by forming multiple molecular contacts with target proteins. And the name of the chemical structure of the eighteen compounds found most potential in the molecular docking study

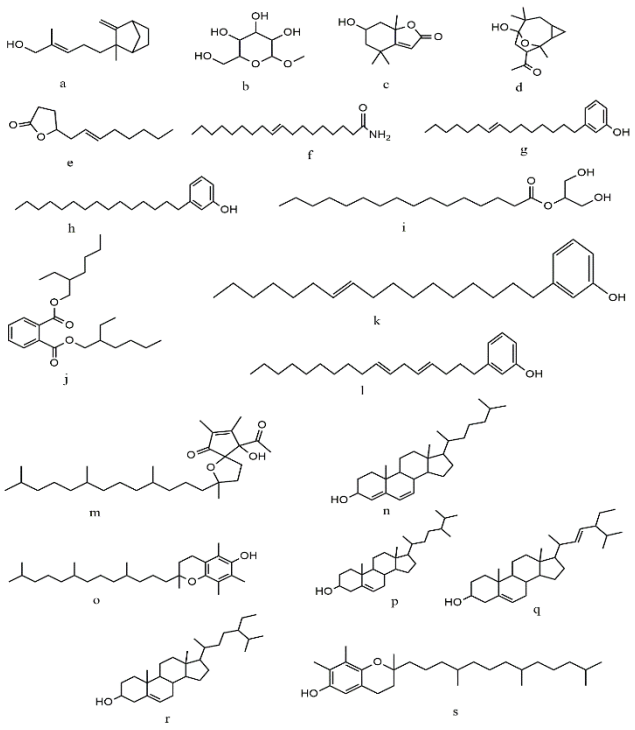

Fig. 1. Chemical structure of the compounds found most potential in the molecular docking study. (a) Santalol, *E*-cis,epi-β- (b) β-D-Glucopyranoside, methyl (c) 6-Hydroxy-4,4,7β-trimethyl-5,6,7,7a tetrahydrobenzofuran-2(4H)-one (d) 1-(7-Hydroxy-1,6,6-trimethyl-10-oxatricyclo[5.2.1.0(2,4)]dec-9-yl)ethanone (e) 2(3H)-Furanone, dihydro-5-(2-octenyl)-, (*Z*)- (f) 9-Octadecenamide, (*Z*)- (g) (*Z*)-3-(pentadec-8-en-1-yl)phenol (h) Phenol, 3-pentadecyl- (i) Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester (j) Bis(2-ethylhexyl) phthalate (k) (*Z*)-3-(Heptadec-10-en-1-yl)phenol (l) 3-((*4Z,7Z*)-Heptadeca-4,7-dien-1-yl)phenol (m) α-Tocospiro A (n) Cholesta-4,6-dien-3-ol, (3β)- (o) α-Tocopherol (p) Campesterol (q) Stigmasterol (r) γ-Sitosterol (s) γ-Tocopherol

are given as follows: (a) Santalol, *E*-cis, epi-β- (b) β-D-Glucopyranoside, methyl (c) 6-Hydroxy-4,4,7α-trimethyl-5,6,7,7a tetrahydrobenzofuran-2(4H)-one (d) 1-(7-Hydroxy-1,6,6-trimethyl-10 oxatricyclo [5.2.1.0 (2,4)] dec-9-yl)ethanone (e) 2(3H)-Furanone, dihydro-5-(2-octenyl)-, (*Z*)- (f) 9-Octadecenamide, (*Z*)- (g) (*Z*)-3-(pentadec-8-en-1-yl)phenol (h) Phenol, 3-pentadecyl- (i) Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester (j) Bis(2-ethylhexyl) phthalate (k) (*Z*)-3-(Heptadec-10-en-1-yl)phenol (l) 3-((*4Z,7Z*)-Heptadeca-4,7-dien-1-yl)phenol (m) α-Tocospiro A (n) Cholesta-4,6-dien-3-ol, (3β)- (o) α-Tocopherol (p) Campesterol (q) Stigmasterol (r) γ-Sitosterol (s) γ- Tocopherol.

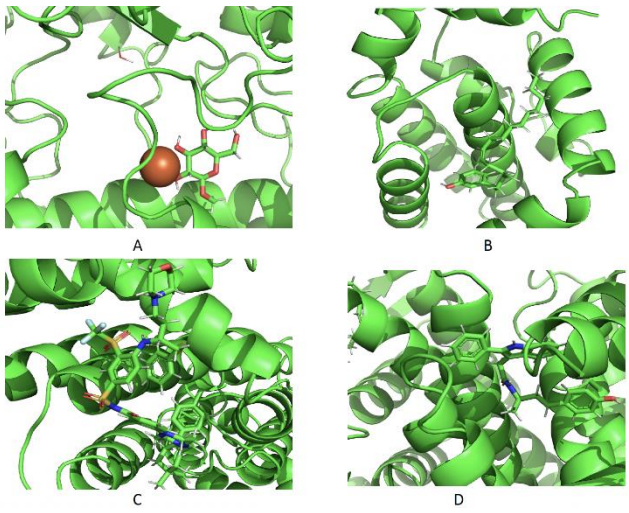

Figure 2. Best ranked pose of (A) β-D-Glucopyranoside, methyl in the binding pocket of CYP3A4 protein (PDB ID: 1TQN), Best ranked pose of (B) 3-((*4Z,7Z*)-Heptadeca-4,7-dien-1-yl)phenol in the binding pocket of anti-apoptotic protein Bcl-2 (PDB ID: 2O2F), Best ranked pose of (C) (*Z*)-3-(Heptadec-10-en-1-yl)phenol in the binding pocket of navitoclax and Bcl-2 complex (PDB ID: 4LVT) for anti-cancer (lung cancer) activity, and Best ranked pose of (D) 3-((*4Z,7Z*)-Heptadeca-4,7-dien-1-yl)phenol in the binding pocket of human estrogen receptor (PDB ID: 2IOK) for anti-cancer (breast cancer) activity.

4. Conclusions

In conclusion, the eighteen phytocompounds (C1, C2, C3, C4, C10, C19, C20, C21, C22, C23, C24, C25, C27, C28, C29, C30, C31, C32) revealed to be responsible for the plant's anticancer characteristics were shown to be safe during the ADME/T investigation. As a result, it is clear that those molecules could be a promising source for the development of new anticancer agents, and they merit further investigation in the experimental study to discover their exact molecular mechanism of action.

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6. Author's contributions

MA, MNUC and AIS. conceived and designed the experiments. MNUC, AIS, AR, and MHUC performed the computational study, analyzed the data and wrote the final manuscript. MA supervised this study.

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8. Conflicts of Interest

The authors declare that they have no conflict of interest

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