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Original Research Article

Unraveling the potential of *Ocimum gratissimum* and *Curcuma longa* phytoconstituents in managing non-alcoholic fatty liver disease (NAFLD): An *in silico* approach

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Abstract

Introduction: Non-alcoholic fatty liver disease (NAFLD) is a prevalent metabolic disorder with limited effective pharmacological treatments. Recent studies suggest that *Ocimum gratissimum* (OG) and *Curcuma longa* (CL) contain bioactive phytochemicals with reported hepatoprotective, antidiabetic, and hypolipidemic properties.
Purpose: The study used a computational approach to investigate the potential of turmeric (CL) and scent leaf (OG) in treating NAFLD.
Methods: Phytochemicals of OG and CL were obtained from literature sources, their 3D SDF structures were obtained from PubChem, and the target proteins 5LX9, 1PKW, 1DQ9, and 6TSG were retrieved from the Protein Data Bank (PDB). Molecular docking was done using PyRx software. Post-docking analysis was performed using BioDiscovery Studio 2.0, and ADMET properties were evaluated using the Swiss ADME web server and ProTox II.
Results: Molecular docking analysis of the 24 phytochemicals, from each plant, revealed several compounds with stronger binding affinities than standard drugs (metformin, pioglitazone, and rosuvastatin). *β*-Sitosterol, Apigenin, Chrysin, and rosmarinic acid in OG exhibited high ΔG Energy ranging from -7.3 to -10.1 kcal/mol, respectively, across the 4 target proteins (5LX9, 1PKW, 1DQ9 and 6TSG). Compounds from CL (Demethoxycurcumin, turmeronol, and humulene) showed potent activities against NALFD with ΔG ranging from -6.1 to -10.1 kcal/mol across the 4 protein targets used in this study.
Conclusion: The molecules from both plants satisfy the drug-likeness properties criteria of Lipinski (RO5) with one or no violations, and are further confirmed by ADMET pharmacokinetics profile analysis. Further optimization and validation through *in vitro* and *in vivo* studies are recommended to enhance the safety and therapeutic efficacy of these phytochemicals as potential agents for the treatment of NAFLD.

Keywords: NAFLD, *Curcuma longa, Ocimum gratissimum*, ADMET properties, phytochemicals

Indexing: Index Copernicus, African Index Medicus

Introduction

Non-alcoholic fatty liver disease (NAFLD), also known as Metabolic dysfunction-associated Fatty Liver Disease, is the presence of fat in the liver on imaging and/or liver biopsy after the exclusion of other apparent causes of liver damage which could be due to excessive alcohol consumption, hepatotoxic medication, toxins, microbial infections or genetic hepatic diseases [1]. NAFLD is a worldwide public health problem that affects about 30% of the adult population and causes considerable liver-related morbidity and mortality, and is the leading cause of mortality in patients with cardiovascular disease (CVD), apart from extra-hepatic cancers [2]. NAFLD is a cluster of metabolic dysfunctions of the liver with risk factors such as

obesity and type 2 diabetes or other chronic liver diseases [3].

NAFLD has become a significant non-communicable disease in Sub-Saharan Africa, and available data indicate that this region has one of the fastest-growing burdens worldwide, accounting for an estimated 24% of the global burden [4]. With an increase in prevalence, its complications (Non-Alcoholic Steatohepatitis [NASH], decompensated cirrhosis, hepatocellular carcinoma, etc.) are also estimated to increase progressively [1].

NAFLD can be caused by several factors, including type 2 diabetes mellitus, genetics, sedentary lifestyle, obesity, metabolic syndrome, and dyslipidemia. Symptoms include fatigue and malaise resulting from higher levels of liver inflammation and oxidative stress [5], as well as abdominal discomfort or pain, which may be attributed to underlying liver fat accumulation [6]. Different pharmacological interventions and management strategies have been employed to manage the condition, including the use of antidiabetic agents such as metformin and Pioglitazone, as well as Vitamin E [7,8,9]. Additionally, antihypertensives and statins (atorvastatin and rosuvastatin) have been utilized [10].

Recently, there has been an increased use of medicinal plants in managing various disease conditions, possibly due to their availability, low cost, and the belief that they have low or no toxicity. One such plant is *Ocimum gratissimum* (Linn.) (also known as scent leaf or African Basil). It is native to Africa and tropical Asia and belongs to the Lamiaceae family. In Nigeria, it is widely used for culinary and medicinal purposes, called *efirin* in Yoruba*, nchanwu* in Igbo, and *daidoya* in Hausa [11].

The medicinal value of scent leaf is attributed to its rich chemical composition, which includes essential oils such as thymol, eugenol, and camphor, that contribute to its aroma and therapeutic effects. Other notable components include alkaloids, flavonoids, tannins, and phenolic compounds [12]. These phytochemicals have been studied for their antioxidant, anti-inflammatory, antimicrobial, and hypoglycemic activities [13]. Scent leaf has been shown to impact cardiovascular health positively due to its flavonoids and phenols, which promote vasodilation and prevent lipid oxidation [14].

Another vital and valuable medicinal plant is *Curcuma longa* (Linn), family *Zingiberaceae*, commonly known as turmeric, and referred to as Ata ile pupa in Yoruba [15]. It has gained global recognition for its medicinal and therapeutic properties. It thrives in tropical climates, particularly in India, Southeast Asia, and Central America [16]. Turmeric's health benefits are primarily attributed to its content, which includes curcumin, demethoxycurcumin, and bisdemethoxycurcumin [17]. Turmeric also has antioxidant, anti-inflammatory, and anticancer effects [18]. Bioactive compounds, including turmerone, atlantone, and zingiberone, have been identified in turmeric [19]. It has been shown to exhibit neuroprotective and mental health [20,21], and cardioprotective effects [22].

Current pharmacological treatments for NAFLD are limited, with no specific drugs approved for direct disease management, and the few ones in use (antidiabetics and dyslipidemia) often come with side effects. Therefore, there is an urgent need for novel, effective, and safer treatment options for NAFLD. Computational methods provide a cost-effective and efficient means of identifying potential drug candidates. *Curcuma longa* and *Ocimum gratissimum* are utilized in traditional medicine for their anti-inflammatory, antioxidant, and hepatoprotective properties, which have been demonstrated in both preclinical and clinical studies [19].

This study aimed to unravel bioactive compounds derived from *Curcuma longa* and *Ocimum gratissimum* with the potential to treat NAFLD by docking them against some putative protein targets 5LX9, 1PKW, 1DQ9, and 6TSG, respectively, which are vital for the regulation of glucose and lipid metabolism, detoxification of environmental toxins and drugs, cholesterol biosynthesis, promotion of wound healing and suppression of inflammation using a molecular docking approach.

Methods

Protein Preparation

Crystal structures of target proteins (PDB IDs: 5LX9, 1PKW, 1DQ9, 6TSG) were retrieved from the Protein Data Bank (https://www.rcsb.org/). The crystal structures of the proteins were downloaded in PDB format using the PDB search interface and processed with Discovery Studio 2021 Client (Dassault Systèms, BIOVIA, San Diego, CA, USA). Each

structure was imported, visually inspected for missing residues or heteroatoms, and cleaned by removing water molecules and irrelevant ligands. Hydrogen atoms were added to ensure accurate protonation and molecular geometry. Prepared structures were saved in a Discovery Studio-compatible format for docking simulations.

Ligand preparation

The ligands (phytochemicals) from Ocimum gratissimum and Curcuma longa were obtained in SDF format from the PubChem database (https://pubchem.ncbi.nlm.nih.gov/) and imported into PyRx software (version 0.8, https://pyrx.sourceforge.io/) using the Open Babel plugin for structural optimization and energy minimization. Optimized ligands were converted to AutoDock-compatible PDBQT format for molecular docking.

Molecular docking

Docking simulations were performed using AutoDock Vina within the PyRx environment [23]. Prepared protein structures (PDB IDs: 5LX9, 1PKW, 1DQ9, 6TSG) were configured as macromolecules. Ligands from Ocimum gratissimum and Curcuma longa in PDBQT format were docked using a blind docking approach, with grid boxes set to encompass the entire protein structure. Grid box dimensions for Ocimum gratissimum ligands were: 5LX9 (X: 46.37, Y: 76.48, Z: 39.43 Å), 1PKW (X: 44.07, Y: 63.11, Z: 53.34 Å), 1DQ9 (X: 77.41, Y: 66.44, Z: 70.03 Å), and 6TSG (X: 58.83, Y: 54.72, Z: 60.01 Å). Also, for Curcuma longa the grid box dimensions were: 5LX9 (X: 44.89, Y: 75.43, Z: 39.45 Å), 1PKW (X: 44.02, Y: 60.43, Z: 53.85 Å), 1DQ9 (X: 76.67, Y: 67.91, Z: 68.39 Å), and 6TSG (X: 57.75, Y: 49.09, Z: 58.45 Å).

Pharmacophore modeling

Ligands with the highest binding affinities were selected for pharmacophore modeling using Discovery Studio 2021. Receptor-ligand interaction models (2D and 3D) were generated to identify key pharmacophoric features, including hydrogen bond donors, acceptors, and hydrophobic regions.

ADMET and toxicity profiling

Pharmacokinetic and physicochemical properties were evaluated using the SwissADME web platform (http://www.swissadme.ch). The parameters investigated included lipophilicity (consensus log P from XLOGP, WLOGP, MLOGP, iLOGP, and SILICOS-IT models), water solubility (log S, SILICOS-IT model), drug-likeness (Lipinski's rule of five), bioavailability, gastrointestinal absorption (GIA), blood-brain barrier (BBB) penetration, and interactions with permeability glycoprotein (P-gp) and cytochrome P450 enzymes. Toxicity profiles were predicted using ProTox-3.0. The ligand structures or SMILES notations were analyzed for endpoints, including acute toxicity (LD50), mutagenicity (AMES test), carcinogenicity, cytotoxicity, neurotoxicity, nephrotoxicity, and hepatotoxicity, with predictions interpreted based on confidence scores.

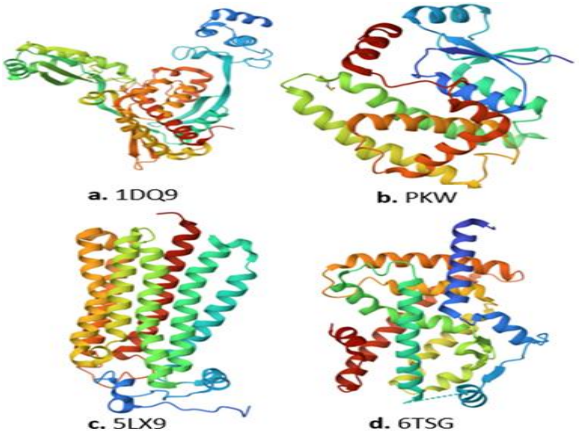

Figure 1: PDB structures of target proteins used in this experiment, with their PDB IDs

Results

Amino acid binding sites

The enzyme active binding site results for proteins with PDB IDs 5LX9, 1PKW, 1DQ9, and 6TSG (identified using Discovery Studio 2021 software) are shown in Table 1.

Binding affinities

The binding affinities of the selected ligands (24) of *Ocimum gratissimum* with protein targets 5LX9, LPKW, 1DQ9, and 6TSG using PyRx software are presented in Tables 2a – 2d, respectively. According to the results presented in Table 2a, the binding affinities of the phytochemicals from *Ocimum gratissimum* with protein 5LX9 ranged from -5.9 kcal/mol to -9.4 kcal/mol. Notably, all the phytochemicals from *Ocimum gratissimum*, except for two ligands with PubChem CIDs 2758 and 370, exhibited higher binding affinities than the standard drug metformin (-6.2 kcal/mol).

Table 1: Binding sites of amino acids of proteins 5LX9, 1PKW, 1DQ9, and 6TSG identified by Discovery Studio 2021.

5LX9							
SER131	PHE132	ARG133	PHE136	LEU153	CYS156	VAL157	PHE158
GLY163	PHE165	MET167	PHE168	ARG169	PRO170	ASN171	CYS161
GLN179	LEU186	SER196	PHE197	LEU200	HIS202	GLY210	LEU214
LEU218	ASP219	TYR220	ILE223	LEU225	SER230	VAL232	TYR236
TYR240	GLN265	GLN273	TYR274	GLY276	GLY280	PHE282	GLY284
LEU285	GLY286	LEU287	VAL297	GLY301	PHE302	LEU303	MET317
TRY321	ILE323	TRY328	ALA329	ARG335	HIS348	PHE351	HIS352
PHE354	GLY358	HIS362					
1PKW							
TYR9	SER18	ARG45	GLN54	VAL55	GLN67	TYR9	
THR68	LEU72	ILE96	ALA100	ASP101	ARG131	THR68	
1DQ9							
TYR479	GLU528	GLU559	ALA564	SER565	ASN567	ARG568	ARG571
ARG590	SER684	ASP690	LYS691	LYS692	VAL720	LYS722	LYS735
ALA751	HIS752	SER852	LEU853	ALA856	LEU862	SER865	
6TSG							
CYS385	ARG288	SER289	TYR327	LEU330	HIS449		
ILE341	SER342	GLU343	MET364	LYS367			

Table 2a: Binding affinities of selected ligands (24) of *Ocimum gratissimum* with 5LX9

S/N	Ligand Names	PubChem CIDs	ΔG Energy (Kcal/mol)	RMSD
1	2-(3,4-Dihydroxyphenyl)chroman-3,5,7-triol	1203	-8.5	0
2	Alpha-pinene	6654	-6.4	0
3	Alpha-Terpineol	17100	-6.8	0
4	Alpha-thujene	637518	-6.5	0
5	Apigenin	5280443	-9.2	0
6	beta-ocimene	5281553	-6.9	0
7	Beta-Sitosterol	222284	-7.3	0
8	Caryophyllene	5281515	-8.8	0
9	Chrysin	5281607	-9.4	0
10	Cineole (Eucalyptol)	2758	-6.0	0
11	Eugenol	3314	-6.4	0
12	Gallic acid	370	-5.9	0
13	Kaempferol	5280863	-9.3	0
14	Linalool	6549	-6.5	0
15	Luteolin	5280445	-8.4	0
16	Mrycene	31253	-6.3	0
17	Oleanolic acid	10494	-7.8	0
18	Orientin	5281675	-8.1	0
19	Procyanidins	107876	-6.8	0
20	Quercetin	5280343	-8.4	0
21	Rosmarinic acid	5281792	-8.1	0
22	Rutin	5280805	-8.3	0
23	Ursolic acid	64945	-7.9	0
24	Vitexin	5280441	-8.3	0
*	Metformin	4019	-6.2	0

NOTE: * Metformin (standard NALD medicine).

Table 2b: Binding free energy of OG phytomechemicals with 1PKW

S/N	Ligand Names	PubChem CIDs	ΔG Energy (Kcal/mol)	RMSD
1	2-(3,4-Dihydroxyphenyl)chroman-3,5,7-triol	1203	-8.8	0
2	Alpha-pinene	6654	-5.9	0
3	Alpha-Terpineol	17100	-6.5	0
4	Alpha-thujene	637518	-5.9	0
5	Apigenin	5280443	-9.4	0
6	beta-OCIMENE	5281553	-6.0	0
7	Beta-Sitosterol	222284	-10.8	0
8	Caryophyllene	5281515	-7.8	0
9	Chrysin	5281607	-9.3	0
10	Cineole (Eucalyptol)	2758	-6.0	0
11	Eugenol	3314	-6.0	0
12	Gallic acid	370	-6.1	0
13	Kaempferol	5280863	-9.3	0
14	Linalool	6549	-5.8	0
15	Luteolin	5280445	-9.0	0
16	Mrycene	31253	-5.7	0
17	Oleanolic acid	10494	-8.6	0
18	Orientin	5281675	-8.1	0
19	Procyanidins	107876	-7.7	0
20	Quercetin	5280343	-9.1	0
21	Rosmarinic acid	5281792	-9.0	0
22	Rutin	5280805	-8.7	0
23	Ursolic acid	64945	-8.9	0
24	Vitexin	5280441	-8.4	0
*	Pioglitazone	4829	-9.4	0

NOTE: * Pioglitazone (standard NALD medicine).

The docking results presented in Table 2c indicate that the phytochemicals demonstrated binding affinities with 1DQ9 ranging from -4.1 kcal/mol to -8.6 kcal/mol. Thirteen ligands, identified by their PubChem CIDs (1203, 5280443, 5281607, 5280863, 5280445, 10494, 5281675, 107876, 5280343, 5281792, 5280805, 64945, and 5280441), exhibited binding affinities between -7.5 kcal/mol and -8.6 kcal/mol, all of which were higher than Rosuvastatin (-7.4 kcal/mol).

Table 2c: Binding affinities of selected ligands of *Ocimum gratissimum* with 1DQ9.

S/N	Ligand Names	PubChem CIDs	ΔG Energy (Kcal/mol)	RMSD
1	2-(3,4-Dihydroxyphenyl)chroman-3,5,7-triol	1203	-7.6	0
2	Alpha-pinene	6654	-4.8	0
3	Alpha-Terpineol	17100	-5.4	0
4	Alpha-thujene	637518	-5.1	0
5	Apigenin	5280443	-7.7	0
6	beta-OCIMENE	5281553	-4.2	0
7	Beta-Sitosterol	222284	-7.4	0
8	Caryophyllene	5281515	-5.9	0
9	Chrysin	5281607	-7.7	0
10	Cineole (Eucalyptol)	2758	-4.9	0
11	Eugenol	3314	-5.2	0
12	Gallic acid	370	-5.7	0
13	Kaempferol	5280863	-7.7	0
14	Linalool	6549	-4.4	0

15	Luteolin	5280445	-7.6	0
16	Mrycene	31253	-4.1	0
17	Oleanolic acid	10494	-8.4	0
18	Orientin	5281675	-7.9	0
19	Procyanidins	107876	-7.6	0
20	Quercetin	5280343	-7.5	0
21	Rosmarinic acid	5281792	-7.5	0
22	Rutin	5280805	-8.3	0
23	Ursolic acid	64945	-8.6	0
24	Vitexin	5280441	-7.5	0
*	Rosuvastatin	446157	-7.4	0

NOTE: * Rosuvastatin (standard NALD medicine).

In Table 2d, the phytochemicals demonstrated binding affinities with 6TSG ranging from -4.9 kcal/mol to -8.3 kcal/mol. Nine ligands (PubChem CIDs 5280443, 5281607, 5280445, 10494, 107876, 5280343, 5281792, 5280805, and 64945) displayed binding affinities between -7.8 kcal/mol and -8.3 kcal/mol, all of which were higher than Pioglitazone (-7.7 kcal/mol).

Table 2d: Binding affinities of selected ligands of *Ocimum gratissimum* with 6TSG

S/N	Ligand Names	PubChem CIDs	ΔG Energy (Kcal/mol)	RMSD
1	2-(3,4-Dihydroxyphenyl)chroman-3,5,7-triol	1203	-7.5	0
2	Alpha-pinene	6654	-5.8	0
3	Alpha-Terpineol	17100	-5.9	0
4	Alpha-thujene	637518	-5.7	0
5	Apigenin	5280443	-8.1	0
6	beta-OCIMENE	5281553	-5.3	0
7	Beta-Sitosterol	222284	-7.5	0
8	Caryophyllene	5281515	-7.3	0
9	Chrysin	5281607	-7.9	0
10	Cineole (Eucalyptol)	2758	-5.8	0
11	Eugenol	3314	-5.8	0
12	Gallic acid	370	-5.6	0
13	Kaempferol	5280863	-7.5	0
14	Linalool	6549	-5.1	0
15	Luteolin	5280445	-8.0	0
16	Mrycene	31253	-4.9	0
17	Oleanolic acid	10494	-8.0	0
18	Orientin	5281675	-7.6	0
19	Procyanidins	107876	-7.8	0
20	Quercetin	5280343	-8.0	0
21	Rosmarinic acid	5281792	-8.2	0
22	Rutin	5280805	-8.3	0
23	Ursolic acid	64945	-8.1	0
24	Vitexin	5280441	-7.5	0
*	Pioglitazone	4829	-7.7	0

NOTE: *Pioglitazone (Standard agent for NALD treatment).

The binding affinities of the selected ligands of *Curcuma longa* with protein targets 5LX9, LPKW, 1DQ9, and 6TSG are presented in Tables 3a – 3d, respectively.

Table 3a presents the results of the binding affinity scores of phytochemicals identified in *Curcuma longa* interacting with the human adiponectin receptor 2 (5LX9). The binding affinity ranged from -5.0 to -10.1 kcal/mol, and in most cases exceeded that of the standard drug metformin (-6.2 kcal/mol).

Table 3a: Binding affinities of selected ligands of *Curcuma longa* with 5LX9

S/N	Ligand Names	PubChem CIDs	ΔG Energy (Kcal/mol)	RMSD
1	(-)-beta-Curcumene	14014430	-8.7	0
2	2-Heptanol	10976	-5.0	0
3	beta-Bisabolene	10104370	-8.6	0
4	Bisacumol	5315469	-7.1	0
5	Carvacrol	10364	-7.1	0
6	Cineole (Eucalyptol)	2758	-8.1	0
7	Cinnamyl cinnamate	1550890	-7.5	0
8	Curlone	196216	-8.4	0
9	Curzerenone	3081930	-8.6	0
10	Demethoxycurcumin	5469424	-10.1	0
11	Elemicin	10248	-6.7	0
12	Eugenol	3314	-6.0	0
13	gamma-Terpinene	7461	-6.8	0
14	Germacrene B	5281519	-7.3	0
15	Germacrone	6436348	-8.8	0
16	Humuladienone	101297706	-6.5	0
17	Humulene	5281520	-8.4	0
18	Mrycene	31253	-6.0	0
19	Myrtenol	10582	-6.6	0
20	O-Cymene	10703	-7.0	0
21	Sesquisabinene	25202482	-7.7	0
22	Thymol	6989	-6.9	0
23	Turmeronol	11117927	-8.9	0
24	Zingiberene	92776	-9.1	0
*	Metformin	4019	-6.2	0

NOTE: * Metformin (Standard antidiabetic agent)

The binding affinity scores of phytochemicals of CL with 1PKW protein are presented in Table 3b. The scores revealed that Cinnamyl cinnamate (-9.0 kcal/mol) and -9.3 kcal/mol gave comparative binding affinity scores with the standard drug Pioglitazone (-9.4 kcal/mol). Other phytochemicals equally showed promising binding affinity with the protein target.

The binding affinities of the phytochemicals of CL with 1DQ9 are presented in Table 3c, which shows binding affinities of the representative compounds lower than that of the standard drug (-7.4 kcal/mol).

The binding affinities of the phytochemicals of CL with 6TSG are presented in Table 3d. The table revealed that Demethoxycurcumin and humuladienone had the highest binding score affinity of -8.4 and -7.8 kcal/mol, compared to the standard agent Pioglitazone (-7.7 kcal/mol).

2D and 3D interactions between the proteins and ligands

The molecular docking results of the 2D and 3D images of hydrogen bond interactions between proteins (5LX9, LPKW, 1DQ9, AND 6TSG) and the selected ligands of *Ocimum gratissimum* are presented in Figures 4a-h, with their binding affinity scores.

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Table 3b: Binding affinities of selected ligands of *Curcuma longa* with 1PKW

S/N	Ligand Names	PubChem CIDs	ΔG Energy (Kcal/mol)	RMSD
1	(-)-beta-Curcumene	14014430	-7.9	0
2	2-Heptanol	10976	-4.5	0
3	beta-Bisabolene	10104370	-7.7	0
4	Bisacumol	5315469	-7.7	0
5	Carvacrol	10364	-6.3	0
6	Cineole (Eucalyptol)	2758	-6.0	0

7	Cinnamyl cinnamate	1550890	-9.0	0
8	Curlone	196216	-7.8	0
9	Curzerenone	3081930	-7.6	0
10	Demethoxycurcumin	5469424	-9.3	0
11	Elemicin	10248	-6.4	0
12	Eugenol	3314	-6.0	0
13	gamma-Terpinene	7461	-6.4	0
14	Germacrene B	5281519	-7.6	0
15	Germacrone	6436348	-7.8	0
16	Humuladienone	101297706	-8.3	0
17	Humulene	5281520	-7.7	0
18	Mrycene	31253	-5.7	0
19	Myrtenol	10582	-6.0	0
20	O-Cymene	10703	-6.1	0
21	Sesquisabinene	25202482	-7.3	0
22	Thymol	6989	-6.6	0
23	Turmeronol	11117927	-7.7	0
24	Zingiberene	92776	-6.8	0
*	Pioglitazone	4829	-9.4	0

NOTE: Pioglitazone (Standard antidiabetic agent)

Table 3c: Binding affinities of selected ligands of *Curcuma longa* with 1DQ9

S/N	Ligand Names	PubChem CIDs	ΔG Energy (Kcal/mol)	RMSD
1	(-)-beta-Curcumene	14014430	-5.6	0
2	2-Heptanol	10976	-4.3	0
3	beta-Bisabolene	10104370	-5.2	0
4	Bisacumol	5315469	-5.5	0
5	Carvacrol	10364	-5.6	0
6	Cineole (Eucalyptol)	2758	-4.9	0
7	Cinnamyl cinnamate	1550890	-6.6	0
8	Curlone	196216	-5.9	0
9	Curzerenone	3081930	-6.0	0
10	Demethoxycurcumin	5469424	-6.7	0
11	Elemicin	10248	-5.1	0
12	Eugenol	3314	-5.2	0
13	gamma-Terpinene	7461	-5.0	0
14	Germacrene B	5281519	-6.1	0
15	Germacrone	6436348	-6.6	0
16	Humuladienone	101297706	-6.4	0
17	Humulene	5281520	-6.1	0
18	Mrycene	31253	-4.1	0
19	Myrtenol	10582	-5.2	0
20	O-Cymene	10703	-5.1	0
21	Sesquisabinene	25202482	-5.1	0
22	Thymol	6989	-5.5	0
23	Turmeronol	11117927	-6.7	0
24	Zingiberene	92776	-5.2	0
*	Rosuvastatin	446157	-7.4	0

NOTE: Rosuvastatin (Standard antidiabetic agent)

Table 3d: Binding affinities of selected ligands of *Curcuma longa* with 6TSG

S/N	Ligand Names	PubChem CIDs	ΔG Energy (Kcal/mol)	RMSD
1	(-)-beta-Curcumene	14014430	-6.2	0
2	2-Heptanol	10976	-4.3	0
3	beta-Bisabolene	10104370	-6.7	0
4	Bisacumol	5315469	-6.6	0
5	Carvacrol	10364	-6.2	0
6	Cineole (Eucalyptol)	2758	-5.8	0
7	Cinnamyl cinnamate	1550890	-7.3	0

8	Curlone	196216	-6.3	0
9	Curzerenone	3081930	-6.7	0
10	Demethoxycurcumin	5469424	-8.4	0
11	Elemicin	10248	-5.8	0
12	Eugenol	3314	-5.8	0
13	gamma-Terpinene	7461	-6.0	0
14	Germacrene B	5281519	-6.8	0
15	Germacrone	6436348	-6.8	0
16	Humuladienone	101297706	-7.8	0
17	Humulene	5281520	-7.0	0
18	Mrycene	31253	-5.0	0
19	Myrtenol	10582	-5.7	0
20	O-Cymene	10703	-5.7	0
21	Sesquisabinene	25202482	-7.1	0
22	Thymol	6989	-6.2	0
23	Turmeronol	11117927	-7.3	0
24	Zingiberene	92776	-6.8	0
*	Pioglitazone	4829	-7.7	0

NOTE: Pioglitazone (Standard antidiabetic agent)

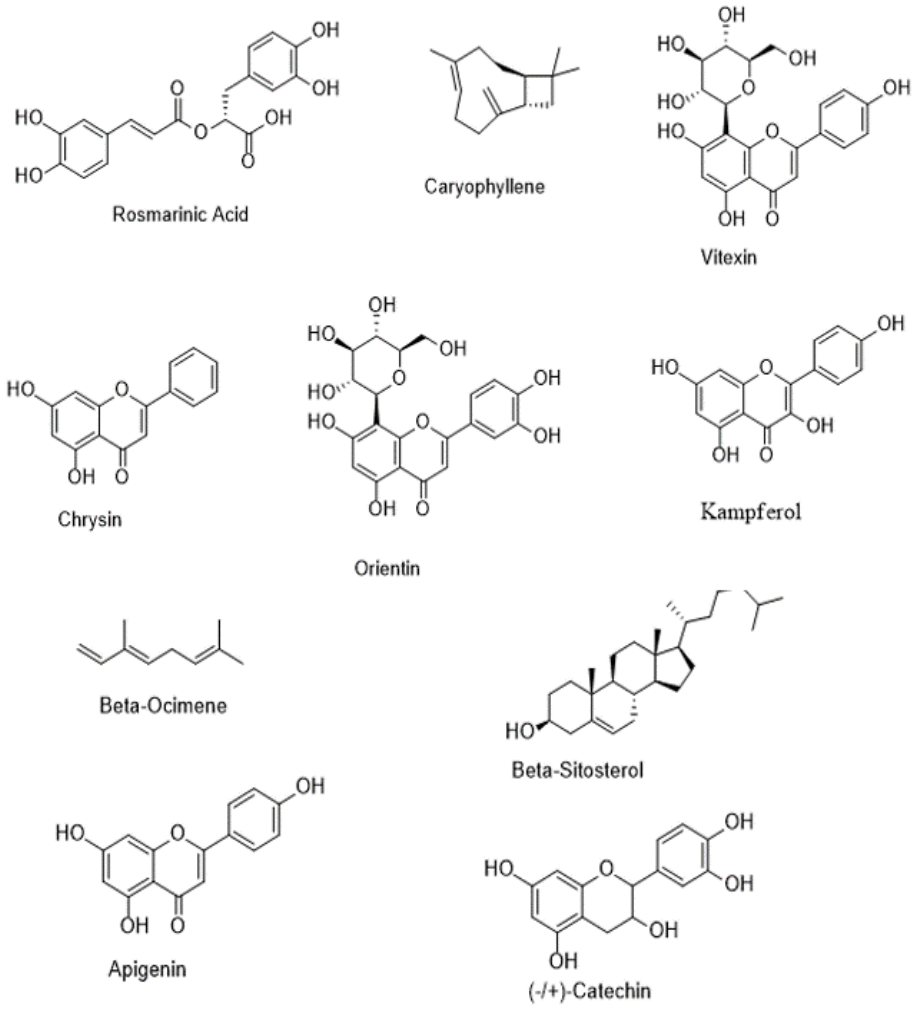

Figure 2: Chemical structures of some ligands of *Ocimum gratissimum* with relatively high binding affinities, drawn using ChemDraw version 12 (Revvity, PerkinElmer, USA).

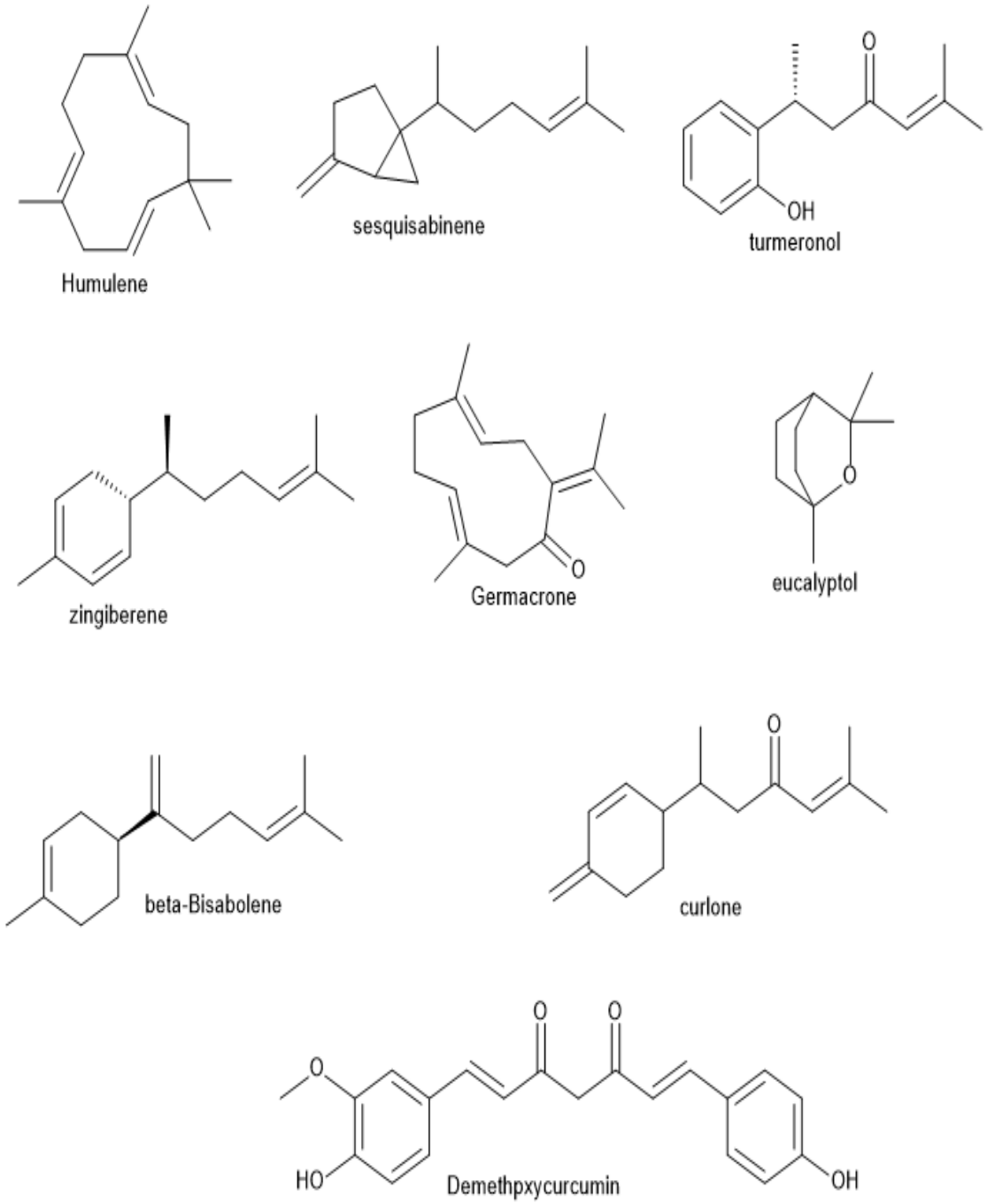

Figure 3: Chemical structures of some ligands of *Curcuma longa* with relatively high binding affinities**,** drawn using ChemDraw version 12 (Revvity, PerkinElmer, USA).

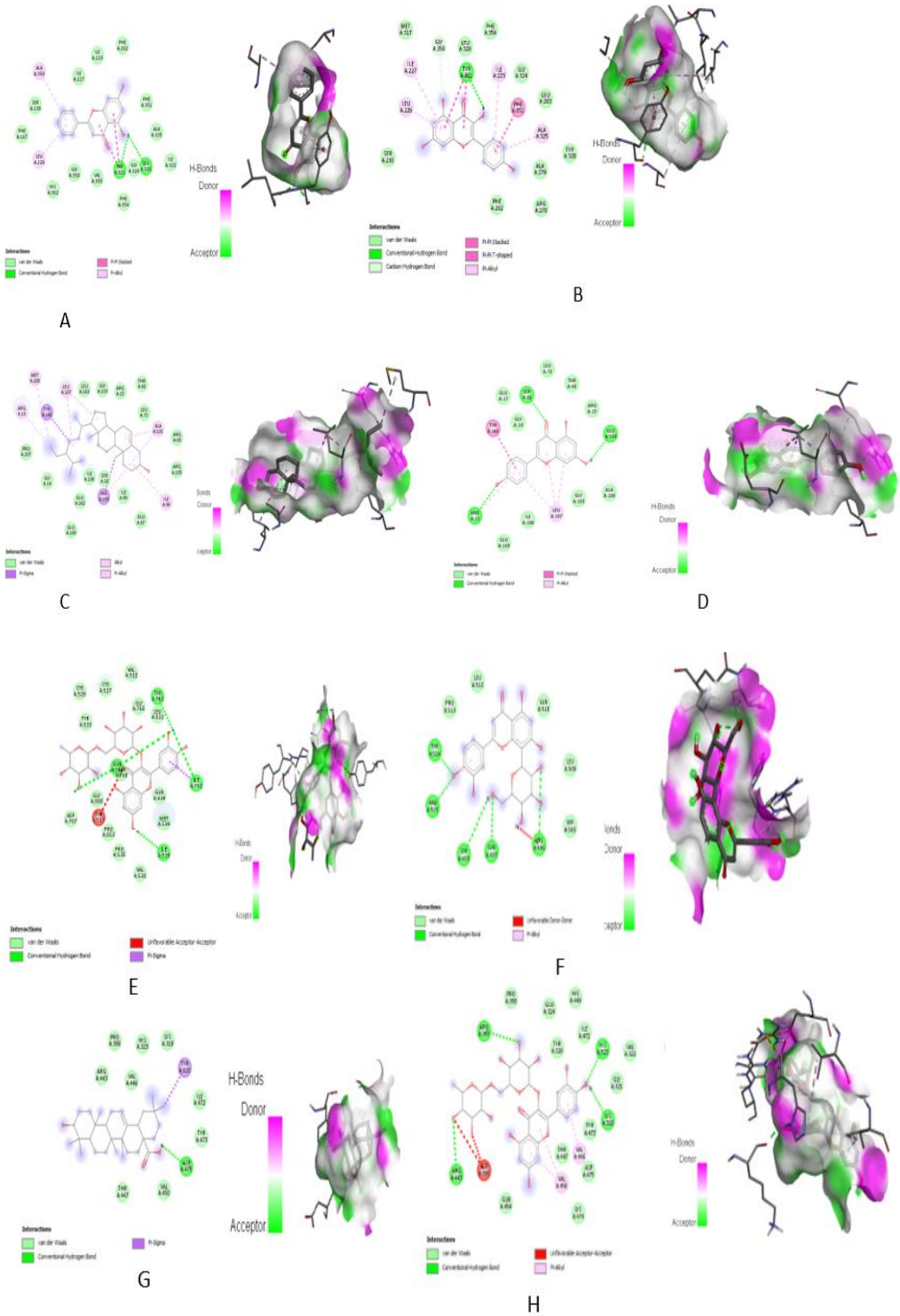

Figure 4 (A-H): 2D and 3D visualizations of the molecular interactions between protein 5LX9, LPKW, 1DQ9, and 6TSG with ligands 5281607, 5280863, 222284, 528044, 5280805, 5281675, 10494 and 52808 (A-H) with binding affinity of -9.4, -9.3, -10.8, -9.4, -8.3, -7.9, -8.0 and -8.3 kcal/mol, respectively.

The images display the binding interactions of prominent molecules, including Chrysin, Kaempferol, β-Sitosterol, and Apigenin from Ocimum gratissimum, with 5LX9, LPKW, 1DQ9, and 6TSG proteins.

Also, the images of the 2D and 3D H-bond interactions between protein 5lx9, lpkw, 1dq9, and 6tsg and the selected ligands of *Curcuma longa* are shown in Figures 5A-F.

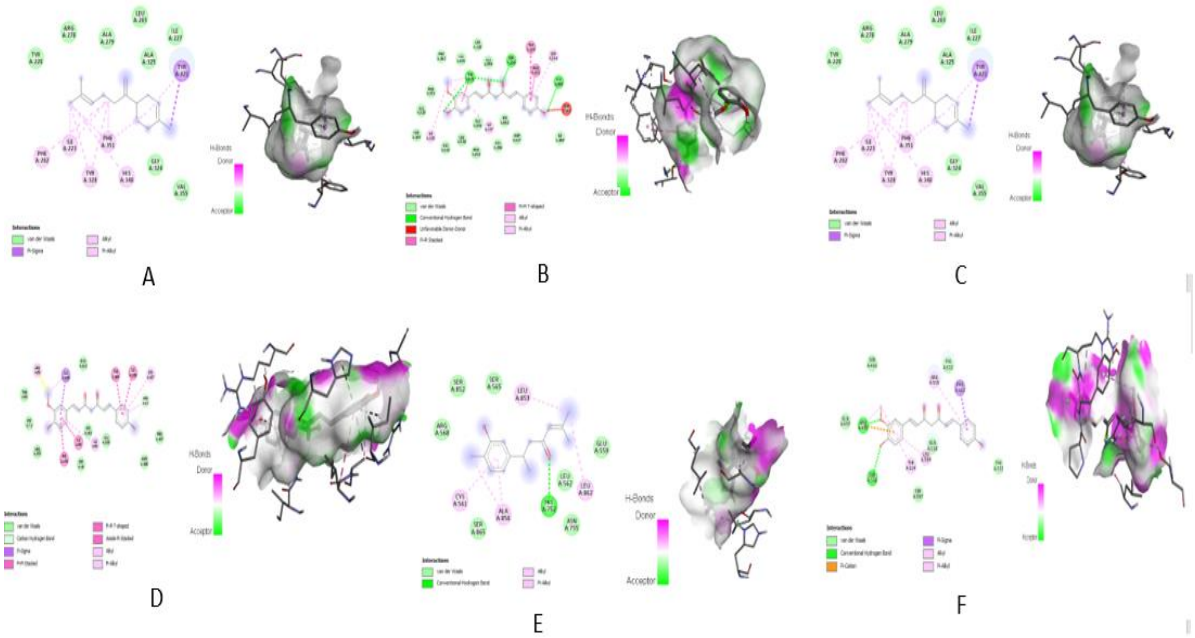

Figure 5A-F: 2D and 3D visualizations of the molecular interactions between protein 5lx9, lpkw, 1dq9, and 6tsg ligands 10104370, 5469424, 1550890, 5469424, 11117922, and 5469424, with binding affinities of -8.6**,** -10.1, -9.0, -9.3, -6.7, and -6.7 kcal/mol, respectively.

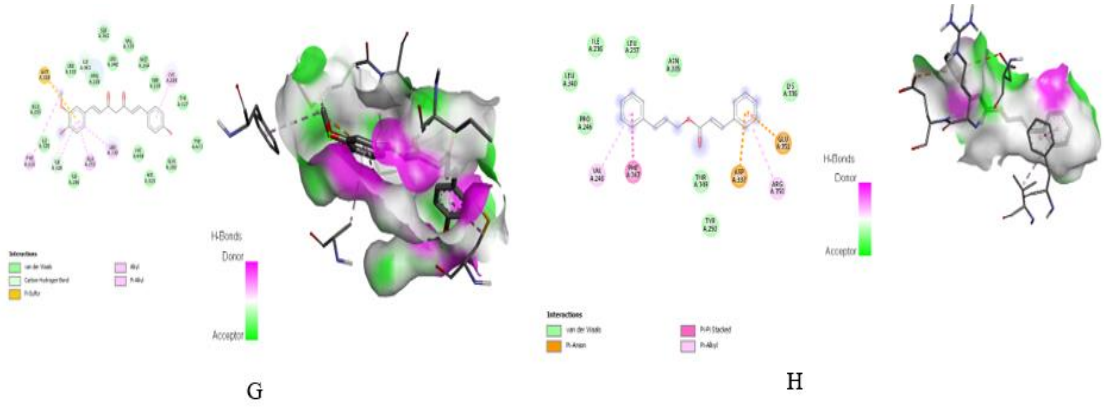

Figure 5G-H: 2D and 3D visualizations of the molecular interactions between protein 6tsg and ligands (1550890 and 5469424) with binding affinity scores of -7.3 and -8.4 kcal/mol.

Post-docking analysis

The physicochemical properties and pharmacokinetic parameters of the selected ligands of *Ocimum gratissimum* obtained using SwissADMET are shown in Tables 4a and 4b, respectively, while the lipophilicity, drug-likeness and toxicity profiles of the ligands are shown in Tables 4c and 4d, respectively. From the results, the MW of all phytochemicals of *Ocimum gratissimum* ranged from 141 to 663, with 2 ligands greater than the allowable limit of 500 Daltons. Similarly, all the ligands have fewer than 10 rotatable hydrogen bonds, with all but three hydrogen bond donors and acceptors. Five ligands have a Topological Polar Surface Area (TPSA) greater than 140 Å, and three have a lipophilicity (Log P) greater than 5. The ligands also had 4 violations of the Lipinski rule of 5 for drug-likeness.

The physicochemical properties and pharmacokinetic parameters of the selected ligands (phytochemicals) of *Curcuma longa* obtained using SwissADMET are shown in Tables 5a and 5b, respectively, while the lipophilicity, drug-likeness and toxicity profiles of the ligands are shown in Tables 5c and 5d, respectively. The physicochemical and pharmacokinetic parameters of the phytoconstituents of Ocimum gratissimum are presented in Tables 4a and 4b, while the druglikeness and toxicity properties are presented in Tables 4c and 4d.

Table 4a: Physicochemical and pharmacokinetic parameters of phytoconstituents of *Ocimum gratissimum*

S/N	Phytochemicals	Molecular Formula	Molecular Weight (g/mol)	Num. Heavy Atoms	Fraction CSP3	Num. Rotatable Bonds	Num. H Bond Acceptors	Num. H Bond Donors	Molar Refractivity	TPSA (Å2)
1	(-)-beta-Curcumene	$C_{15}H_{14}O_6$	290.27	21	0.2	1	6	5	74.33	110.38
2	2-Heptanol	$C_{10}H_{16}$	136.23	10	0.8	0	0	0	45.22	0
3	beta-Bisabolene	$C_{10}H_{18}O$	154.25	11	0.8	1	1	1	48.8	20.23
4	Bisacumol	$C_{10}H_{16}$	136.23	10	0.8	1	0	0	45.22	0
5	Carvacrol	$C_{15}H_{10}O_5$	270.24	20	0	1	5	3	73.99	90.9
6	Cineole (Eucalyptol)	$C_{10}H_{16}$	136.23	10	0.4	3	0	0	48.76	0
7	Cinnamyl cinnamate	$C_{29}H_{50}O$	414.71	30	0.93	6	1	1	133.23	20.23
8	Curlone	$C_{15}H_{24}$	204.35	15	0.73	0	0	0	68.78	0
9	Curzerenone	$C_{15}H_{10}O_4$	254.24	19	0	1	4	2	71.97	70.67
10	Demethoxycurcumin	$C_{10}H_{18}O$	154.25	11	1	0	1	0	47.12	9.23
11	Elemicin	$C_{10}H_{12}O_2$	164.2	12	0.2	3	2	1	49.06	29.46
12	Eugenol	$C_7H_6O_5$	170.12	12	0	1	5	4	39.47	97.99
13	gamma-Terpinene	$C_{15}H_{10}O_6$	286.24	21	0	1	6	4	76.01	111.13
14	Germacrene	$C_{10}H_{18}O$	154.25	11	0.6	4	1	1	50.44	20.23
15	Germacrone	$C_{15}H_{10}O_6$	286.24	21	0	1	6	4	76.01	111.13
16	Humuladienone	$C_{10}H_{16}$	136.23	10	0.4	4	0	0	48.76	0
17	Humulene	$C_{30}H_{48}O_3$	456.7	33	0.9	1	3	2	136.65	57.53
18	Mrycene	$C_{21}H_{20}O_{11}$	448.38	32	0.29	3	11	8	108.63	201.28
19	Myrtenol	$C_{30}H_{26}O_{13}$	594.52	43	0.2	4	13	10	147.52	229.99
20	O-Cymene	$C_{15}H_{10}O_7$	302.24	22	0	1	7	5	78.03	131.36
21	Sesquisabinene	$C_{18}H_{16}O_8$	360.31	26	0.11	7	8	5	91.4	144.52
22	Thymol	$C_{27}H_{30}O_{16}$	610.52	43	0.44	6	16	10	141.38	269.43
23	Turmeronol	$C_{30}H_{48}O_3$	456.7	33	0.9	1	3	2	136.91	57.53
24	Zingiberene	$C_{21}H_{20}O_{10}$	432.38	31	0.29	3	10	7	106.61	181.05

Table 4b: Pharmacokinetic parameters of phytochemicals of *Ocimum gratissimum*

S/N	Phytochemicals	GI Absorption	BBB Permeant	P-gp Substrate	CPY1A2 Inhibitor	CP2C19 Inhibitor	CP2D6 Inhibitor	CP3A4 Inhibitor	Log Kp (Skin permeation (cm/s)
1	(-)-beta-Curcumene	High	No	Yes	No	No	No	No	-7.82
2	2-Heptanol	Low	Yes	No	No	No	No	No	-3.95
3	beta-Bisabolene	High	Yes	No	No	No	No	No	-4.83
4	Bisacumol	Low	Yes	No	No	No	No	No	-5.11
5	Carvacrol	High	No	No	Yes	No	Yes	Yes	-5.8
6	Cineole (Eucalyptol)	Low	Yes	No	No	No	No	No	-4.11
7	Cinnamyl cinnamate	Low	No	No	No	No	No	No	-2.2
8	Curlone	Low	No	No	No	Yes	No	No	-4.44
9	Curzerenone	High	Yes	No	Yes	No	Yes	Yes	-5.35
10	Demethoxycurcumin	High	Yes	No	No	No	No	No	-5.3
11	Elemicin	High	Yes	No	Yes	No	No	No	-5.69
12	Eugenol	High	No	No	No	No	No	Yes	-6.84
13	gamma-Terpinene	High	No	No	Yes	No	Yes	Yes	-6.7
14	Germacrene	High	Yes	No	No	No	No	No	-5.13
15	Germacrone	High	No	No	Yes	No	Yes	Yes	-6.25
16	Humuladienone	Low	Yes	No	No	No	No	No	-4.17
17	Humulene	Low	No	No	No	No	No	No	-3.77
18	Mrycene	Low	No	No	No	No	No	No	-9.14
19	Myrtenol	Low	No	No	No	No	No	No	-8.54
20	O-Cymene	High	No	No	Yes	No	Yes	Yes	-7.05
21	Sesquisabinene	Low	No	No	No	No	No	No	-6.82
22	Thymol	Low	No	Yes	No	No	No	No	-10.26
23	Turmeronol	Low	No	No	No	No	No	No	-3.87
24	Zingiberene	Low	No	No	No	No	No	No	-8.79

Table 4c: Lipophilicity characteristics and drug Likeness of *Ocimum gratissimu*

S/N	Phyochemicals	Hepatotoxicity	Neurotoxicity	Nephro Toxicity	Respiratory Toxicity	Cardio toxicity	Carcino Genicity	Immuno toxicity	Mutagenicity	Cytotoxicity
1	(-)-beta-Curcumene	-	-	+	+	-	-	-	-	-
2	2-Heptanol	-	+	-	-	-	-	-	-	-
3	beta-Bisabolene	-	-	-	-	-	-	-	-	-
4	Bisacumol	-	+	-	-	-	-	-	-	-
5	Carvacrol	-	-	+	+	-	-	-	-	-
6	Cineole (Eucalyptol)	-	+	-	-	-	-	-	-	-
7	Cinnamyl cinnamate	-	+	-	+	-	-	+	-	-
8	Curlone	-	-	-	-	-	-	+	-	-
9	Curzerenone	-	-	+	+	-	-	-	-	-
10	Demethoxycurcumim	-	-	-	-	-	-	-	-	-
11	Elemicin	-	+	-	-	-	-	-	-	-
12	Eugenol	-	-	+	+	-	+	-	-	-
13	gamma-Terpinene	-	-	+	+	-	-	-	-	-
14	Germacrene	-	-	-	-	-	-	-	-	-
15	Germacrone	-	-	+	+	-	+	-	+	-
16	Humuladienone	-	+	-	-	+	-	-	-	-
17	Humulene	+	-	-	+	+	+	+	-	-
18	Mrycene	-	-	+	+	-	-	+	+	-
19	Myrtenol	-	-	+	+	-	-	-	-	-
20	O-Cymene	-	-	+	+	-	+	-	+	-
21	Sesquisabinene	-	-	+	-	-	-	+	-	-
22	Thymol	-	-	+	+	-	-	+	-	-
23	Turmeronol	+	-	-	+	+	+	+	-	-
24	Zingiberene	-	-	+	+	-	-	-	+	-

Table 4d: Toxicity profile of the selected Phytochemicals of scent leaf *(Ocimum gratissimum)*

S/N	Phytochemicals	Lipophilicity (Log Po/w (!LOGP))	Lipophilicity (Log Po/w (XLOGP3))	Lipophilicity (Log Po/w (MLOGP))	Lipophilicity (Log Po/w (SILICOS-IT))	Drug likeness (Lipinski)
1	(-)-beta-Curcumene	1.47	0.36	0.24	0.98	Yes, 0 violation
2	2-Heptanol	2.63	4.48	4.29	2.79	Yes; 1 violation: MLOGP>4.15
3	beta-Bisabolene	2.51	3.39	2.3	2.17	Yes, 0 violation
4	Bisacumol	2.67	2.85	4.29	2.95	Yes; 1 violation: MLOGP>4.15
5	Carvacrol	1.89	3.02	0.52	2.52	Yes; 0 violation
6	Cineole (Eucalyptol)	2.8	4.26	3.56	2.88	Yes; 0 violation
7	Cinnamyl cinnamate	5.05	9.34	6.73	7.04	Yes; 1 violation: MLOGP>4.15
8	Curlone	3.25	4.38	4.63	4.19	Yes; 1 violation: MLOGP>4.15
9	Curzerenone	2.27	3.52	1.08	3.02	Yes; 0 violation
10	Demethoxycurcumim	2.58	2.74	2.45	2.86	Yes; 0 violation
11	Elemicin	2.37	2.27	2.01	2.48	Yes; 0 violation
12	Eugenol	0.21	0.7	-0.16	-0.2	Yes; 0 violation
13	gamma-Terpinene	1.7	1.9	-0.03	2.03	Yes; 0 violation
14	Germacrene	2.7	2.97	2.59	2.35	Yes; 0 violation
15	Germacrone	1.86	2.53	-0.03	2.03	Yes; 0 violation
16	Humuladienone	2.89	4.17	3.56	3.05	Yes; 0 violation
17	Humulene	3.94	7.49	5.82	5.85	Yes; 1 violation: MLOGP>4.15
18	Mrycene	1	-0.15	-2.51	-0.14	No; 2 violations: NorO>10, NHorOH>5
19	Myrtenol	2.17	1.95	-0.6	0.66	No; 3 violations: MW>500, NorO>10, NhorOH>5
20	O-Cymene	1.63	1.54	-0.56	1.54	Yes; 0 violation
21	Sesquisabinene	1.48	2.36	0.9	1.5	Yes; 0 violation
22	Thymol	0.46	-0.33	-3.89	-2.11	No; 3 violations: MW>500, NorO>10, NhorOH>5
23	Turmeronol	3.95	7.34	5.82	5.46	Yes; 1 violation: MLOGP>4.15
24	Zingiberene	1.63	0.21	-2.02	0.33	Yes; 1 violation: Nhor OH>5

\+ Represents Active; - Represent Inactive

The physicochemical, pharmacokinetic, druglikeness, lipophilicity and toxicity parameters of phytoconstituents of *Curcuma longa* are presented in Tables 5a, 5b, 5c and 5d, respectively.

Table 5a: Showing the physicochemical and pharmacokinetic parameters of phytoconstituents of *Curcuma longa*

S/N	Phytochemicals	Molecular Formula	Molecular Weight (g/mol)	Num. Heavy Atoms	Fraction CSP3	Num. Rotatable Bonds	Num. H Bond Acceptors	Num. H Bond Donors	Molar Refractivity	TPSA (Å2)
1	(-)-beta-Curcumene	$C_{15}H_{24}$	204.35	15	0.6	4	0	0	70.68	0
2	2-Heptanol	$C_7H_{16}O$	116.2	8	1	4	1	1	36.92	20.23
3	beta-Bisabolene	$C_{15}H_{24}$	204.35	15	0.6	4	0	0	70.68	0
4	Bisacumol	$C_{15}H_{22}O$	218.33	16	0.47	4	1	1	70.71	20.23
5	Carvacrol	$C_{10}H_{14}O$	150.22	11	0.4	1	1	1	48.01	20.23
6	Cineole (Eucalyptol)	$C_{10}H_{18}O$	154.25	11	1	0	1	0	47.12	9.23
7	Cinnamyl cinnamate	$C_{18}H_{16}O_2$	264.32	20	0.06	6	2	0	81.85	26.3
8	Curlone	$C_{15}H_{22}O$	218.33	16	0.53	4	1	0	70.88	17.07
9	Curzerenone	$C_{15}H_{18}O_2$	230.3	17	0.4	2	2	0	69.16	30.21
10	Demethoxycurcumin	$C_{20}H_{18}O_5$	338.35	25	0.1	7	5	2	96.31	83.83
11	Elemicin	$C_{12}H_{16}O_3$	208.25	15	0.33	5	3	0	60.02	27.69
12	Eugenol	$C_{10}H_{12}O_2$	164.2	12	0.2	3	2	1	49.06	29.46
13	gamma-Terpinene	$C_{10}H_{16}$	136.23	10	0.6	1	0	0	47.12	0
14	Germacrene B	$C_{15}H_{24}$	204.35	15	0.6	0	0	0	70.68	0
15	Germacrone	$C_{15}H_{22}O$	218.33	16	0.53	0	1	0	70.88	17.07
16	Humuladienone	$C_{15}H_{24}O$	220.35	16	0.67	0	1	0	71.1	17.07
17	Humulene	$C_{15}H_{24}$	204.35	15	0.6	0	0	0	70.42	0
18	Mrycene	$C_{10}H_{16}$	136.23	10	0.4	4	0	0	48.76	0
19	Myrtenol	$C_{10}H_{16}O$	152.23	11	0.8	1	1	1	46.38	20.23
20	O-Cymene	$C_{10}H_{14}$	134.22	10	0.4	1	0	0	45.99	0
21	Sesquisabinene	$C_{15}H_{24}$	204.35	15	0.73	4	0	0	68.78	0
22	Thymol	$C_{10}H_{14}O$	150.22	11	0.4	1	1	1	48.01	20.23
23	Turmeronol	$C_{15}H_{20}O_2$	232.32	17	0.4	4	2	1	71.77	37.3
24	Zingiberene	$C_{15}H_{24}$	204.35	15	0.6	4	0	0	70.68	0

Table 5b: Pharmacokinetic parameters of phytochemicals of *Curcuma longa*

S/N	Phyochemicals	GI Absorption	BBB Permeant	P-gp Substrate	CPY1A2 Inhibitor	CP2C19 Inhibitor	CP2D6 Inhibitor	CP3A4 Inhibitor	Log Kp (Skin permeation (cm/s)
1	(-)-beta-Curcumene	Low	No	No	No	No	No	No	-2.95
2	2-Heptanol	High	Yes	No	No	No	No	No	-5.37
3	beta-Bisabolene	Low	No	No	No	No	No	No	-2.98
4	Bisacumol	High	Yes	Yes	No	No	Yes	No	-4.74
5	Carvacrol	High	Yes	No	Yes	No	No	No	-4.74
6	Cineole (Eucalyptol)	High	Yes	No	No	No	No	No	-5.3
7	Cinnamyl cinnamate	High	Yes	No	Yes	Yes	No	No	-4.75
8	Curlone	High	Yes	No	No	Yes	No	No	-4.78
9	Curzerenone	High	Yes	No	Yes	Yes	No	No	-4.84
10	Demethoxycurcumin	High	No	No	Yes	No	No	Yes	-6.01
11	Elemicin	High	Yes	No	Yes	No	No	No	-5.77
12	Eugenol	High	Yes	No	Yes	No	No	No	-5.69
13	gamma-Terpinene	Low	Yes	No	No	No	No	No	-3.94
14	Germacrene B	Low	No	No	No	No	No	No	-3.45
15	Germacrone	High	Yes	No	No	No	No	No	-5.18
16	Humuladienone	High	Yes	No	No	No	No	No	-4.95
17	Humulene	Low	No	No	No	No	No	No	-4.32
18	Mrycene	Low	Yes	No	No	No	No	No	-4.17
19	Myrtenol	High	Yes	No	No	No	No	No	-4.94
20	O-Cymene	Low	Yes	No	No	No	Yes	No	-4.01
21	Sesquisabinene	Low	No	No	No	Yes	No	No	-3.96
22	Thymol	High	Yes	No	Yes	No	No	No	-4.87
23	Turmeronol	High	Yes	No	Yes	No	No	No	-4.84
24	Zingiberene	Low	No	No	No	Yes	No	No	-3.88

Table 5c: Lipophilicity Characteristics and Drug Likeness *Curcuma longa*

S/N	Phytochemicals	Lipophilicity (Log Po/w (LOGP))	Lipophilicity (Log Po/w (XLOGP3))	Lipophilicity (Log Po/w (MLOGP))	Lipophilicity (Log Po/w (SILICOS-IT))	Drug likeness (Lipinski)
1	(-)-beta-Curcumene	3.6	6.47	4.53	4.48	Yes; 1 violation: MLOGP>4.15
2	2-Heptanol	2.29	2.31	1.89	1.54	Yes; 0 violation
3	beta-Bisabolene	3.67	6.43	4.53	4.5	Yes; 1 violation: MLOGP>4.15
4	Bisacumol	2.87	4.08	3.76	4.05	Yes; 0 violation
5	Carvacrol	2.24	3.49	2.76	2.79	Yes; 0 violation
6	Cineole (Eucalyptol)	2.58	2.74	2.45	2.86	Yes; 0 violation
7	Cinnamyl cinnamate	2.66	4.45	3.98	4.42	Yes; 0 violation
8	Curlone	3.14	4.01	3.37	3.93	Yes; 0 violation
9	Curzerenone	2.87	4.04	2.32	4.38	Yes; 0 violation
10	Demethoxycurcumin	2.78	3.32	1.8	3.95	Yes; 0 violation
11	Elemicin	2.89	2.53	1.97	3.06	Yes; 0 violation
12	Eugenol	2.37	2.27	2.01	2.48	Yes; 0 violation
13	gamma-Terpinene	2.73	4.5	3.27	2.95	Yes; 0 violation
14	Germacrene B	3.26	5.77	4.53	4.25	Yes; 1 violation: MLOGP>4.15
15	Germacrone	2.88	3.46	3.37	3.93	Yes; 0 violation
16	Humuladienone	2.98	3.8	3.46	3.59	Yes; 0 violation
17	Humulene	3.29	4.55	4.53	3.91	Yes; 1 violation: MLOGP>4.15
18	Mrycene	2.89	4.17	3.56	3.05	Yes; 0 violation
19	Myrtenol	2.34	3.22	2.3	2.15	Yes; 0 violation
20	O-Cymene	2.43	4.38	4.47	3.29	Yes; 1 violation: MLOGP>4.15
21	Sesquisabinene	3.63	5.05	4.63	4.77	Yes; 1 violation: MLOGP>4.15
22	Thymol	2.32	3.3	2.76	2.79	Yes; 0 violation
23	Turmeronol	2.83	4.05	3.02	3.91	Yes; 0 violation
24	Zingiberene	3.63	5.17	4.53	4.09	Yes; 1 violation: MLOGP>4.15

Table 5d: Toxicity profile of the selected Phytochemicals of *(Curcuma longa)*

S/N	Ligand PubChem CID	Hepato-toxicity	Neuro-toxicity	Nephro-toxicity	Respiratory toxicity	Cardio toxicity	Carcino Genicity	Immuno-toxicity	Mutagenicity	Cytotoxicity
1	(-)-beta-Curcumene	-	-	-	-	-	-	-	-	-
2	2-Heptanol	-	-	-	-	-	-	-	-	-
3	beta-Bisabolene	-	-	-	-	-	-	+	-	-
4	Bisacumol	-	-	-	-	-	-	-	-	-
5	Carvacrol	-	+	-	+	-	-	-	-	-
6	Cineole (Eucalyptol)	-	-	-	-	-	-	-	-	-
7	Cinnamyl cinnamate	-	-	-	-	-	+	-	+	-
8	Curlone	-	-	-	-	-	-	-	-	-
9	Curzerenone	-	+	-	-	-	+	-	-	-
10	Demethoxycurcumin	-	-	+	-	+	-	+	-	-
11	Elemicin	-	-	-	-	-	+	-	+	-
12	Eugenol	+	-	-	-	-	-	-	-	-
13	gamma-Terpinene	-	+	-	-	-	-	-	-	-
14	Germacrene B	-	-	-	-	-	-	-	-	-
15	Germacrone	-	-	-	-	-	-	-	-	-
16	Humuladienone	-	-	-	-	-	-	-	-	-
17	Humulene	-	-	-	-	-	-	-	-	-
18	Mrycene	-	+	-	-	+	-	-	-	-
19	Myrtenol	-	-	-	-	-	-	-	-	-
20	O-Cymene	-	+	-	-	-	+	-	-	-
21	Sesquisabinene	-	+	-	-	-	-	+	-	-
22	Thymol	-	+	-	+	-	-	-	-	-
23	Turmeronol	+	-	-	-	-	-	-	-	-
24	Zingiberene	-	-	-	-	-	-	-	-	-

+ active; - inativve

Discussion

Molecular docking of ligands has recently aided drug discovery, reducing the time, cost, and number of animals used, which hitherto have hindered the release of new medicinal agents into clinical use [24]. A total of 24 phytochemicals, each from *Ocimum gratissimum* and *Curcuma longa,* and 3 controls (metformin, pioglitazone, and rosuvastatin) were docked with the target proteins: 5LX9, 1PKW, 1DQ9, and 6TSG using the AutoDock Vina plugin in PyRx with varied binding affinity scores ranging from -4.1 to -10.8 kcal/mol across all protein targets used in this study. The standard agents had binding affinities ranging between -6.2 and -9.4 kcal/mol across all protein targets.

Ocimum gratissimum

The docking scores suggest that the phytochemicals in OG exhibit stronger intermolecular interactions with the target sites of 5LX9, with binding affinity scores ranging from -5.9 to -9.4 kcal/mol, which may enhance their activities in managing NAFLD. Another ligand (PubChem CID 5280443) showed an equivalent binding affinity to Pioglitazone (-9.4 kcal/mol). These findings suggest that the selected phytochemicals may exhibit stronger interactions with 1PKW, indicating their potential as therapeutic alternatives to Pioglitazone in NAFLD treatment. This suggests that these compounds may exert stronger inhibitory activities on 1DQ9 than Rosuvastatin, potentially contributing to the regulation of lipid metabolism in NAFLD. These results suggest that these phytochemicals exhibit stronger binding interactions with 6TSG, potentially making them more effective than Pioglitazone in modulating 6TSG activity in NAFLD management.

Curcuma longa

As shown in Table 3a, the phytochemicals from *Curcuma longa* exhibited binding affinities ranging from -5.0 kcal/mol to -10.1 kcal/mol with 5LX9. Most of these phytochemicals demonstrated stronger interactions than metformin (-6.2 kcal/mol), except for three ligands with PubChem CIDs 10976, 3314, and 31253. The docking scores indicate favorable intermolecular interactions of these phytochemicals within the protein-ligand complex, suggesting that they may have stronger excitatory activities with 5LX9 than metformin, thereby offering potential benefits in managing NAFLD.

According to Table 3b, the phytochemicals demonstrated binding affinities ranging from -4.5 kcal/mol to -9.3 kcal/mol with 1PKW. Two ligands, identified by their PubChem CIDs 1550890 and 5469424, exhibited high binding affinities of -9.0 kcal/mol and -9.3 kcal/mol, which are close to that of Pioglitazone (-9.4 kcal/mol). These results suggest that these phytochemicals may have strong interactions with the active sites of 1PKW, potentially enhancing its stimulating activities in managing NAFLD. The docking results presented in Table 3c indicate that the phytochemicals interacted with 1DQ9, showing binding affinities ranging from -4.1 kcal/mol to -6.7 kcal/mol. None of the ligands achieved a binding affinity higher than rosuvastatin (-7.4 kcal/mol). However, four ligands (PubChem CIDs 1550890, 5469424, 6436348, and 11117927) displayed binding affinities of -6.6, -6.7, -6.6, and -6.7 kcal/mol, respectively.

While these values are slightly lower than those of rosuvastatin, they suggest that these phytochemicals may exhibit moderate inhibitory interactions with 1DQ9, indicating a potential for further investigation in NAFLD treatment. In Table 3d, the phytochemicals demonstrated binding affinities ranging from -4.3 kcal/mol to -8.4 kcal/mol with 6TSG. Two ligands (PubChem CIDs 5469424 and 101297706) exhibited binding affinities of -8.4 kcal/mol and -7.8 kcal/mol, respectively, which are higher than Pioglitazone (-7.7 kcal/mol). These results suggest that these phytochemicals form stronger intermolecular interactions with 6TSG and may have greater stimulatory activities, making them promising candidates for NAFLD management. Representative chemical structures of some potent ligands from OC and CL are shown in Figures 2 and 3, respectively. These structures were extracted from the literature, identified using the PubChem database, and drawn using ChemDraw software.

As shown in Tables 1a-1d, the ligands from OC and CL interacted with different amino acids in the binding pockets of the proteins. In particular, the ligands of OC interacted with the amino acids of the 5LX9 protein at TYR321 and LEU320 through conventional hydrogen bonds,

and with ALA395 and LEU224 through pi-alkyl bonds. Other interactions involve BAL355, ALA325, GLY324 (van der Waals interactions), and TYR321 through pi-pi stacking interactions. The 2D and 3D interaction images of the ligands of OC and CL, as well as the standards, with the amino acids of 5LX9, 1PKW, 1DQ9, and 6TSG are presented in Figures 4(A-H) and 5(A-F and G-H).

ADMET properties of ligands

The absorption, distribution, metabolism, excretion, and toxicity (ADMET) properties of the phytochemicals of *Ocimum gratissimum* and *Curcuma longa,* which show their pharmacokinetics and pharmacodynamics parameters, are presented in Tables 4a, 4b, 4c, 5a, 5b and 5c, respectively. From the result of the pharmacokinetic parameters in Table 4b, ligands of *Ocimum gratissimum* with PubChem CIDs 1203, 17100, 5280443, 5281607, 2758, 3314, 370, 5280863, 6549, 5280445, and 5280343 have high gastrointestinal absorption hence making them a promising drug candidate for oral administration, ligand 1203 and 5280805 are substrate for P-glycoprotein meaning that they can easily be bound to and transport across cell membranes. Lipinski's rule of five, which is determined by a complex balance of various molecular properties and structural features such as lipophilicity, electronic distribution, hydrogen bonding characteristics, molecule size, and flexibility, as well as the presence of multiple pharmacophores that influence the behavior of a molecule in a living organism, were used to predict the drug likeliness of the compounds.

A good drug candidate should not violate more than one of the rules [25]. The molecular weights of the ligands of *Ocimum gratissimum* compounds were <500, except for ligands 5381675, 107878, and 5280805, which violated more than one rule. The hydrogen bond donor (≤ 2 hydrogens) and hydrogen bond acceptor (< 5 hydrogens) of the compounds were in line with the rule. These observations show that these ligands can serve as promising drug candidates. From the result of the pharmacokinetic parameters analysis, all the ligands of *Curcuma longa* have high gastrointestinal absorption except ligands with PubChem CIDs 14014430, 10104370, 7461, 5281519, 5281520, 31253, 10703, 25202482, and 92776, hence making them a promising drug candidate for oral administration, ligand 5315469 is a substrate for P-glycoprotein meaning that it can easily be bound to and transport across cell membranes (Table 5b).

Lipinski's rule of five was also used to predict the drug-likeliness of the phytochemicals of *Curcuma longa.* The molecular weights of the ligands of *Curcuma longa* compounds were <500, and the hydrogen bond donor (≤ 2 hydrogens) and hydrogen bond acceptor (not more than 5 hydrogens) of the compounds were in line with the rule (Table 5a). These observations show that these ligands can serve as promising drug candidates. The drug-likeness properties of these ligands are shown in Table 5c. The table shows the lipophilicity characteristics and drug-likeness potentials of compounds of CL. From these data, the ligands of CL have drug-like properties and, hence, can easily be developed into a pharmaceutical product.

Toxicity profiling of the ligands

The toxicity profiling of ligands from *Ocimum gratissimum* and *Curcuma longa* was conducted to assess their potential adverse effects on living organisms, including humans. As presented in Table 6, the results indicate significant variation in the toxicity profiles of the phytochemicals from *Ocimum gratissimum*, with activity observed against different organs. Among the tested ligands, only two compounds (PubChem CIDs: 10494 and 64945) exhibited hepatotoxicity, suggesting potential liver-related toxic effects. Several ligands (6654, 637518, 5281553, 222284, 3314, and 31253) demonstrated neurotoxic activity, indicating possible effects on the nervous system.

Additionally, multiple ligands (1203, 5280443, 5281607, 370, 5280863, 5280445, 5281675, 107876, 5280343, 5280805, and 5280441) were found to exhibit both nephrotoxicity (kidney toxicity) and respiratory toxicity. Furthermore, three ligands (31252, 10494, and 64945) showed cardiotoxicity, implying potential adverse effects on heart function. Carcinogenicity was observed in five ligands (370, 5280445, 10494, 5280343, and 64945), suggesting a possible risk of cancer development. Seven ligands (222284, 5281515, 10494, 5281675, 5281792, 5280805, and 5280441) exhibited immunotoxicity, indicating potential suppression or adverse modulation of the immune system. Moreover, mutagenicity was detected in four ligands (5281675, 5281675, 5280343, and 5280441), suggesting possible genetic alterations.

Notably, none of the ligands exhibited cytotoxicity, indicating that they do not directly induce cell death. Table 7 presents the toxicity profile of selected phytochemicals from *Curcuma longa*. The analysis revealed that only two ligands exhibited hepatotoxicity, identified by their PubChem CIDs 3314 and 11117927. Several ligands displayed neurotoxic effects, including 10364, 3081930, 7461, 31253, 10703, 25202482, and 689. Nephrotoxicity was observed in only one ligand (PubChem CID: 5469424). Additionally, ligands 10364 and 6989 exhibited respiratory toxicity, while ligands 5469424 and 31253 were found to be cardiotoxic. Furthermore, carcinogenicity was detected in ligands 150890, 3081930, 10248, and 10703. Immunotoxic effects were noted in ligands 10104370, 5469424, and 25202482. Ligands 1550890 and 10248 exhibited mutagenicity, suggesting a potential for genetic alterations. Notably, none of the evaluated ligands demonstrated cytotoxicity.

However, given the observed toxicity profiles, these ligands require further screening and structural modifications to develop safer derivatives with optimized toxicity and improved therapeutic potential.

Conclusion

The results revealed that phytochemicals from *Ocimum gratissimum* and *Curcuma longa* have potential against key target proteins involved in NAFLD management. Furthermore, several phytochemicals exhibited higher binding affinities than standard drugs, indicating their potential as therapeutic alternatives. Notably, ligands from *Ocimum gratissimum* demonstrated strong interactions with 1PKW and 1DQ9, while those from *Curcuma longa* showed promising binding with 5LX9 and 6TSG. The best-performing phytochemicals from *Ocimum gratissimum* were *β*-Sitosterol, apigenin, chrysin, luteolin, oleanolic acid, procyanidins, rosmarinic acid, and rutin, with strong interactions with 1PKW, 1DQ9, and 6TSG, suggesting their potential for the treatment and management of NAFLD.

Similarly, compounds from *Curcuma longa*, Cinnamyl cinnamate, Demethoxycurcumin, Germacrone, Turmeronol, and Humuladienone showed high binding affinities with 5LX9, 1PKW, and 6TSG, indicating their suitability for further investigation. The ADMET analysis further supported the drug-likeness of these phytochemicals, with many exhibiting high gastrointestinal absorption and favorable pharmacokinetic properties. However, toxicity profiling revealed potential risks, including hepatotoxicity, neurotoxicity, nephrotoxicity, and carcinogenicity in some ligands. These findings suggest that further optimization and structural modifications are needed to enhance safety while maintaining therapeutic efficacy. Overall, this study highlights the potential of *Ocimum gratissimum* and *Curcuma longa* phytochemicals as promising candidates for the treatment of NAFLD. Future research should focus on *in vitro* and *in vivo* validation, structural refinement, and formulation development to ensure the safe and effective clinical application of these compounds.

Abbreviations

3D: Three-dimensional, **ADME:** Absorption, Distribution, Metabolism and Excretion, **ADMET:** Absorption, Distribution, Metabolism, Excretion and Toxicity, ASN: Asparagine, ASP: Aspartic acid, **LD50:** Lethal Dose, 50%, **PDB:** Protein Data Bank, **PHE**: Phenylalanine, **RCSB:** Research Collaboratory for Structural Bioinformatics, RNA: Ribonucleic 53 Acid, **SDF:** Structure Data File, **SER:** Serine, **THR:** Threonine, **TYR:** Tyrosine, **VAL**: Valine, PyRx: Python Prescription – Virtual Screening Tool, ChemDraw: Chemical Structures Drawing tool, AutoDock Vina: Automated docking tool

Conflict of interest

No conflict of interest is associated with this work.

Contribution of authors

We declare that this work was done by the author(s) named in this article, and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. UI conceived, designed, and supervised the study. UI and VIO collected and analysed the data and prepared the manuscript. All the authors read and approved the final draft submitted.

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