

A Computational Antidiabetic Analysis of the Therapeutic Potentials of Phytochemicals in *Garcinia Kola* Extract

*A. A. Fowotade^{1,4}, S. O. Ibrahim², Y. S. Akinbo³, F. O. Akinbo⁴

¹Department of Morbid Anatomy, University of Ilorin Teaching Hospital, Ilorin, Nigeria

²Department of Industrial Chemistry, University of Ilorin, Ilorin, Nigeria

³Department of Molecular Diagnostics, Northwestern Memorial Hospital, Chicago, USA

⁴Department of Medical Laboratory Science, University of Benin, Benin City, Nigeria

*Correspondence Author

DOI: <https://doi.org/10.51584/IJRIAS.2026.11090008>

Received: 16 September 2026; Accepted: 21 September 2026; Published: 29 September 2026

ABSTRACT

Background: Herbal medications have an extensive history of use in treating various diseases, attributed to their perceived efficacy and safety. *G. kola* is a medicinal plant commonly utilized in traditional West African countries for diabetes therapy. While numerous reports have validated its biological potency, studies on the drug-likeness and antidiabetic properties of its compounds are limited. **Aim:** The research aims to identify drug-like phytochemicals from *Garcinia kola* extract and evaluate their antidiabetic potential through in silico screening. **Materials and methods:** The *in silico* pharmacological, and toxicological profile of aqueous/methanolic phytochemicals from previously reported work was analyzed using Swiss ADME and Protox II online server. The docking process was performed using PyRx-0.8, coupled with AutoDock Vina. Phytochemicals that aligned with Lipinski's rules for drugs were then subjected to a virtual docking simulation. **Results:** This simulation replicated the inhibitory effects of *Garcinia kola* phytochemicals on sodium-glucose co-transporters (SGLT2) and α -amylase, similar to Metformin, an FDA-approved antidiabetic medicine utilized as a control. **Conclusion:** Phytochemicals such as Rutin (-11.34kcal/mol), Morelloflavone (-9.38kcal/mol), Amentoflavone (-8.54kcal/mol), Garcinianin (-8.40kcal/mol) and Volkensiflavone (-8.39kcal/mol) exhibited stronger binding than Metformin, suggesting *G. kola* as a promising antidiabetic source.

Keywords: *Garcinia kola*, Phytochemicals, Docking simulation, Sodium-glucose co-transporters (SGLT2), α -amylase, Metformin

INTRODUCTION

Medicinal plants are a rich source of anti-diabetic compounds and have gained global interest as affordable and accessible treatments for chronic diseases, particularly diabetes mellitus [1]. Despite the availability of numerous standard drugs like insulin and oral hypoglycemic agents, issues like adverse effects, high cost, limited accessibility in low-resource settings, and the emergence of drug resistance highlight the urgent need for alternative remedies [2]. Many traditional medicinal plants have demonstrated promising antidiabetic properties, including antioxidant, hypoglycemic, and insulin-sensitizing effects, and continue to be investigated for their bioactive phytochemicals and mechanisms of action [3]. Consequently, integrating ethnomedicinal knowledge with modern scientific validation offers a sustainable pathway for developing safer, cost-effective treatments to manage and prevent diabetes and its complications [4].

Garcinia kola commonly called bitter kola, is traditionally used for diabetes management in West and Central Africa. Its biflavonoid extract, kolaviron, has exhibited antioxidant, anti-inflammatory, and hypoglycemic properties in various in vivo and in vitro studies [5]. Phytochemicals, derived from these medicinal plants are

been used for various therapeutic purposes. During the extraction of these phytochemicals, it is essential to consider their physicochemical properties. This study aims to identify drug-like phytochemicals from *G. kola* extract and evaluate their antidiabetic potential through *in silico* screening.

MATERIALS AND METHODS

Plant Collection and Identification

Garcinia kola seeds were purchased from a market in the city of Ilorin, Nigeria, were authenticated at the Plant Biology Herbarium, University of Ilorin by Bolu Ajayi (voucher no: UILH/001/1217/2024).

Plant Extraction Preparation

Fresh *Garcinia kola* seeds were dried, pulverized, and about 100g of the powder was defatted using petroleum ether. The ethanolic extraction was carried out at room temperature (18⁰-22⁰C) as described by [6] using a Soxhlet apparatus (Infitek, SE-6P, China).

Phytochemical Identification

Phytochemicals present in the extract of *Garcinia kola* seeds were identified using the preliminary phytochemical screening techniques. Various tests for alkaloids, tannins, phenols, flavonoids, saponins, and carbohydrate were subsequently conducted.

Molisch's test for Carbohydrates

Three drops of Molisch's reagent were added to 2ml of the extract dissolved in distilled water, this was followed by addition of 1ml of conc. H₂SO₄ by the side of the test tube. The mixture was then allowed to stand for 2 min and then diluted with 5ml of distilled water. Formation of a red or dull violet colour at the interphase of the two layers was a positive test as previously described [7].

Test for Tannins

Test extract (0.5 g) was stirred with about 10ml of distilled water and then filtered. Two drops of 1% ferric chloride solution were added to 2ml of the filtrate. The occurrence of a blue-black, green or blue-green precipitate indicates the presence of tannins as previously described [8].

Test for Terpenoids

About 0.5 g of the test extract was dissolved in 5ml of ethanol. A 1ml volume of Acetic anhydride was added followed by the addition of 1ml of conc. H₂SO₄. A change in colour from pink to violet showed the presence of terpenoids as previously described [8].

Test for Saponins

Garcinia kola seeds' extract (1 g) was boiled with 5ml of distilled water and filtered. To the filtrate, 3ml of distilled water was further added and shaken vigorously for 5 mins. Frothing which persisted on warming was taken as evidence for the presence of saponins as previously described [9].

Ferric chloride Test for Flavonoids:

Test extract (0.5 g) was boiled with 10ml of distilled water and then filtered. A 2ml volume of the filtrate was kept aside and three drops of 10% Ferric chloride solution was then added to it. A green-blue or violet colouration indicated the presence of a phenolic hydroxyl group as previously described [8].

Test for Alkaloids

About 1 g of the test extract was stirred with 5ml of 1% aqueous Hydrochloric acid (HCl) on water bath and then filtered. About 1ml of the filtrate was dispensed into 2 test tubes. To the first 1ml, three drops of Dragendorff's reagent was added; occurrence of orange-red precipitate was taken as positive. To the second 1ml, an equal volume of potassium mercuric iodide solution (Mayer's reagent) was added and appearance of buffy coloured precipitate was an indication for the presence of alkaloids as previously described [8].

Liquid Chromatography – Mass Spectroscopy (LC-MS) Characterization of Extract

The ethanol extract of the *Garcinia kola* seeds was subjected to LC-MS analysis using Shimadzu QP2050SE-433 (Japan) equipped with column of 30m long (0.25 μ m x 250 μ m). 1 μ L of the sample was injected by an auto sampler, over the oven temperature programme; from 40⁰ to 300⁰C and a total run-time of 95 min. The relative percentage constituents were evaluated based on an estimate of the depicted peak area in the total ion chromatogram. Identification of the compounds was done by comparing the mass spectra fragmentation pattern with National Institute of Standards and Technology database (<https://icsd.nist.gov>).

Computational Study

Data Mining of *Garcinia kola* Phytochemicals

Information about the bioactive phytochemicals present in *Garcinia kola* (*G. kola*) was obtained from a literature review previously conducted by Tauchen et al. [10]. This review identified twenty-eight phytochemicals reported in *G. kola* extract (including the seed, leaves, stem and root) while fourteen phytochemicals alone were reportedly found in the seed extract. This dataset of five putatively bioactive compounds formed the basis for the current study.

Prediction of Absorption, Distribution, Metabolism, Elimination (ADME) and Toxicity

The SwissADME was employed to predict the physicochemical properties, ADME parameters, and drug-likeness of the identified small phytochemicals. SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. This online platform facilitates the study of these properties, aiding in the drug discovery process. Canonical SMILES strings generated using ChemDraw were uploaded into SwissADME to obtain predictions for physicochemical properties (e.g., lipophilicity, water solubility), pharmacokinetics, drug-likeness, and medicinal chemistry friendliness.

Retrieval, Preparation, and Identification of Protein Active sites

To predict the potential antidiabetic properties of the identified druggable phytochemicals from *Garcinia kola*, *in silico* molecular docking simulations was employed. Metformin and Acarbose (established antidiabetic drugs), were used as references to understand their mechanisms of action. Information regarding their mechanisms was retrieved from the ChEMBL database (<https://www.ebi.ac.uk/chembl/>). Metformin is known to inhibit α -amylase; an enzyme responsible for carbohydrate digestion while Acarbose inhibit sodium glucose co-transporter 2 (SGLT2) [11].

The crystal structures of human SGLT2 (PDB ID 8HDH) and α -amylase (PDB ID 4GQR) were obtained from the Protein Data Bank (<https://www.rcsb.org/>). These protein structures were then optimized for docking simulations. The binding site coordinates for each enzyme were identified by analyzing the co-crystallized inhibitors within the respective protein structures, utilizing the Maestro 12.8 [14]. Docking simulations were performed for each phytochemical against SGLT2 and α -amylase. The docking scores and the most favourable binding poses for each complex were documented [12].

Ligand Preparation and Molecular docking

To gain insights into the potential mechanism of action of identified phytochemicals, *in silico* docking simulations were performed. The known mechanism of the standard drugs Metformin (SGLT2 inhibitor) and

Acarbose (α -amylase inhibitor) were retrieved from ChEMBL database. Crystal structures of these standard drugs, along with all phytochemicals identified through Gas Chromatography-Mass Spectroscopy (GC-MS) analysis were downloaded in SDF format from PubChem. Open Babel was employed to prepare and optimize the downloaded structures for docking simulations. The PyRx platform coupled with AutoDock Vina was then utilized for docking simulations. Briefly, the phytoconstituents isolated from the methanolic and aqueous extracts of *Garcinia kola* were docked into the active sites of Human α -amylase and SGLT2. The protein structures used for docking were retrieved from the Protein Data bank, focusing on crystallized forms to incorporate the bound ligand information. The specific amino acid residues constituting the active sites were selected based on the downloaded PDB structures [13].

Statistical Analysis

Following the docking simulations, the ligand-protein complex with the most favorable binding affinity (ΔG ; kcal/mol) and pose was selected. This complex was then saved in the PDB file format for further analysis. The Discovery Studio Visualizer was employed to visualize and analyze the intermolecular interactions formed between the ligands and the target protein [14].

RESULTS/DISCUSSION

Phytochemical screening conducted confirmed presence of alkaloids, flavonoids, saponins, tannins, and phenols while terpenoids were absent. Alkaloids, flavonoids, saponins, tannins and phenol are often linked to antioxidant, anti-inflammatory, antimicrobial, and other pharmacological activities [5] (Table 1).

All the tested compounds such as Rutin (-11.34 kcal/mol), Morelloflavone (-9.38), Amentoflavone (-8.54), Garcinianin (-8.40), and Volkensiflavone (-8.39) exhibited greater binding affinities than Metformin (-2.2 kcal/mol). Acarbose had the strongest (-12.726 kcal/mol) (Table 2).

The higher the negative value of MMGBSA, the stronger the Hydrogen bond between the ligand and protein. Acarbose had the highest MMGBSA negative value while Rutin, Morelloflavone, Amentoflavone, Garcinianin and Volkensiflavone stood out with docking scores ranging from -11.337 to -8.389 kcal/mol, and favorable MMGBSA binding energies (Table 2).

Furthermore, analysis of interaction of phytochemicals against standard drugs used as control shows that they interacted with similar amino acids residue of the Human pancreatic *amylase* enzyme (PDB ID – 4W83). Crucially, GLU-233 which may imply they share similar mechanism of action, and support that *G. kola* phytochemicals are viable drug-like molecules with potential antidiabetic efficacy (Figure 1a–1h).

Table 1: Qualitative Phytochemical Detection of *G. kola* Constituents

Phytochemicals	Presence
Alkaloids	++*
Flavonoids	++**
Saponin	++*
Tannins	++*
Phenol	++*
Terpenoids	Nil

** ++ (Presence): Indicates significant concentration of the phytochemical in the *Garcinia kola* extract, as detected during the screening process.

Nil (Absent): Indicates that the phytochemical was not detected in the extract.

Table 2: Docking Metrics for Top Compounds Compared to Standard Drugs.

Phytochemicals	Docking score (kcal/mol)	Interacted Amino acids residue	MMGBSA (ΔG_{bind}) (kcal/mol)
Acarbose	-12.726	THR-163, HIE-201, GLU-233, HIP-305	-35.569
Rutin	-11.337	ARG-195, LYS-200, HIE-201, GLU-233, GLU-240, ASP – 300	-33.1383
Morelloflavone	-9.381	TRP-59, GLN – 63, ASP-197, HIP-305, ASP-356	-55.8476
Amentoflavone	-8.535	GLN-63, TRP-59, ASP-197, ASP – 300, ASP-356	-37.382
Garcinianin	-8.404	GLN-63, TPP-62, ARG-195, ASP-197, HIP305	-40.1841
Volkensiflavone	-8.389	GLN-63, ARG-195, ASP-197, HIP-305, ASP-356	-55.4146
Ranirestat	-6.159	TRP-59, ARG-195, GLU-233, HIP-305	-48.6705
Metformin	-2.178	ASP-197, GLU-233	5.639992

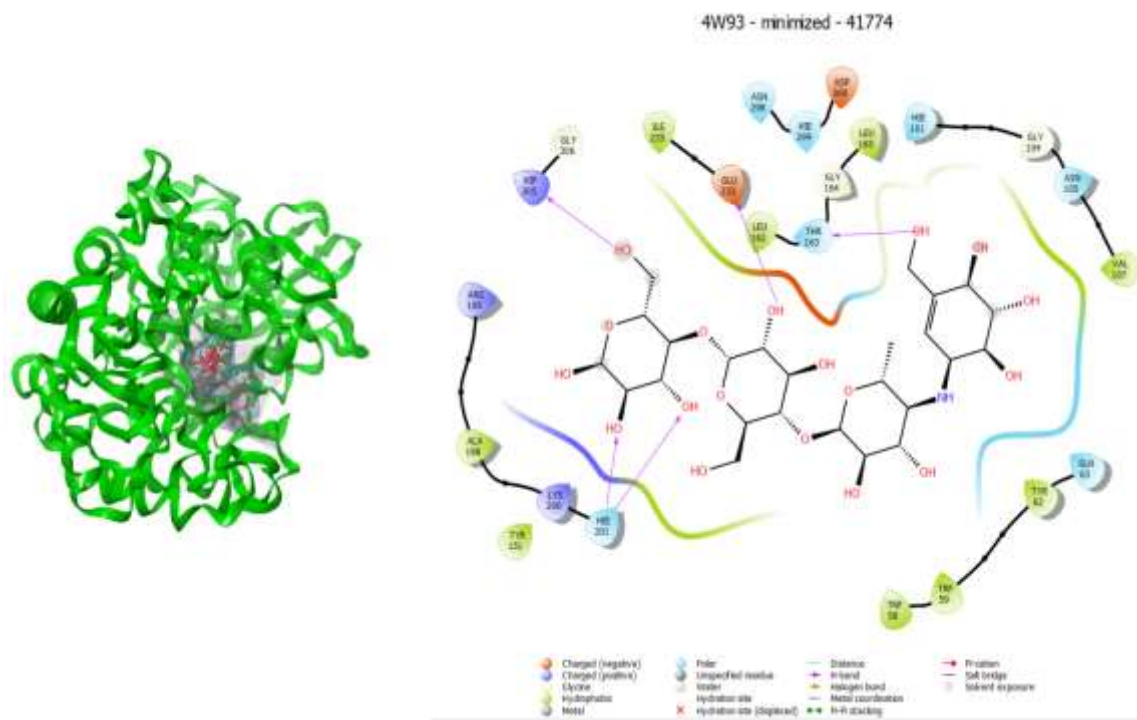


Figure 1a: 2D and 3D Binding poses of interaction of Acarbose (PUBCHEM ID – 41774) with amino acid residues of Human pancreatic *amylase* enzyme (PDB ID – 4W83)

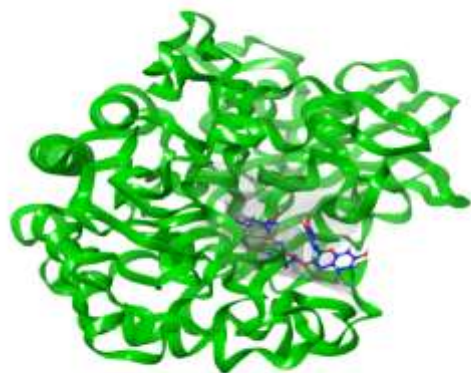


Figure 1b: 2D and 3D Binding poses of interaction of Rutin (PUBCHEM ID – 5280805) with amino acid residues of Human pancreatic *amylase* enzyme (PDB ID – 4W83)

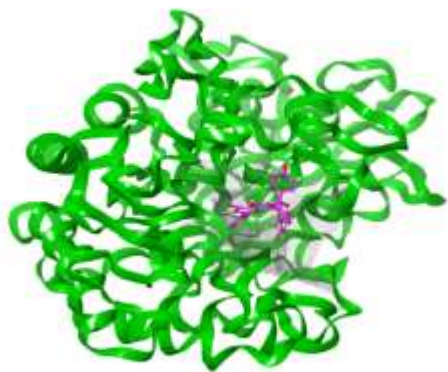


Figure 1c: 2D and 3D Binding poses of interaction of Morelloflavone (PUBCHEM ID – 5464454) with amino acid residues of Human pancreatic *amylase* enzyme (PDB ID – 4W83)

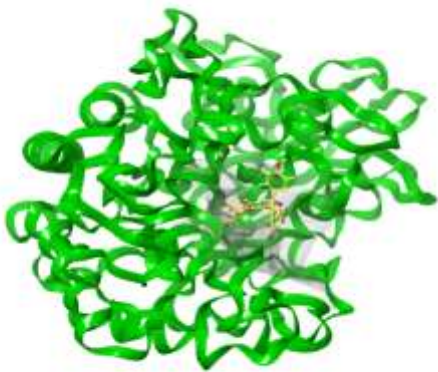


Figure 1d: 2D and 3D Binding poses of interaction of Amentoflavone (PUBCHEM ID – 5281600) with amino acid residues of Human pancreatic *amylase* enzyme (PDB ID – 4W83)

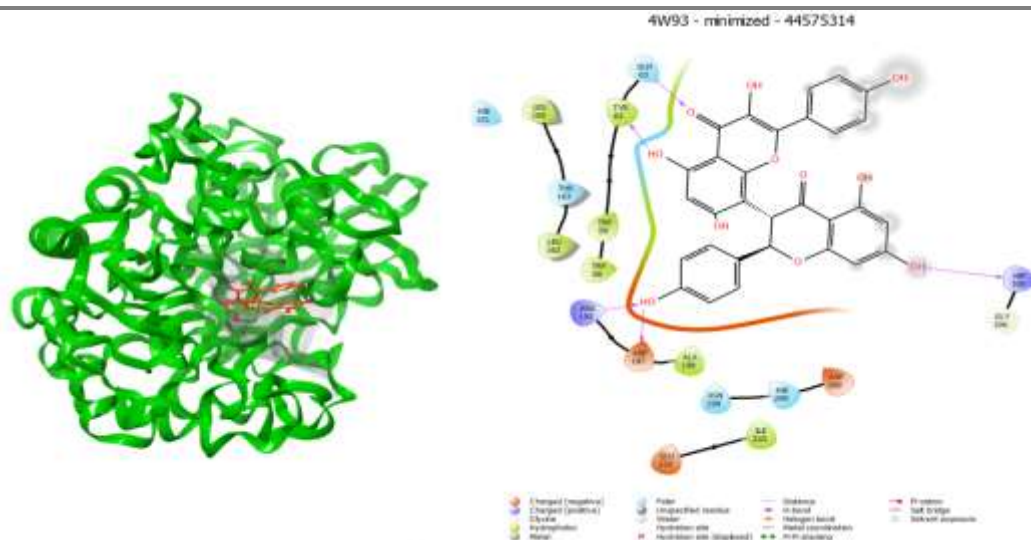


Figure 1e: 2D and 3D Binding poses of interaction of Garcinianin (PUBCHEM ID – 44575314) with amino acid residues of Human pancreatic *amylase* enzyme (PDB ID – 4W83)

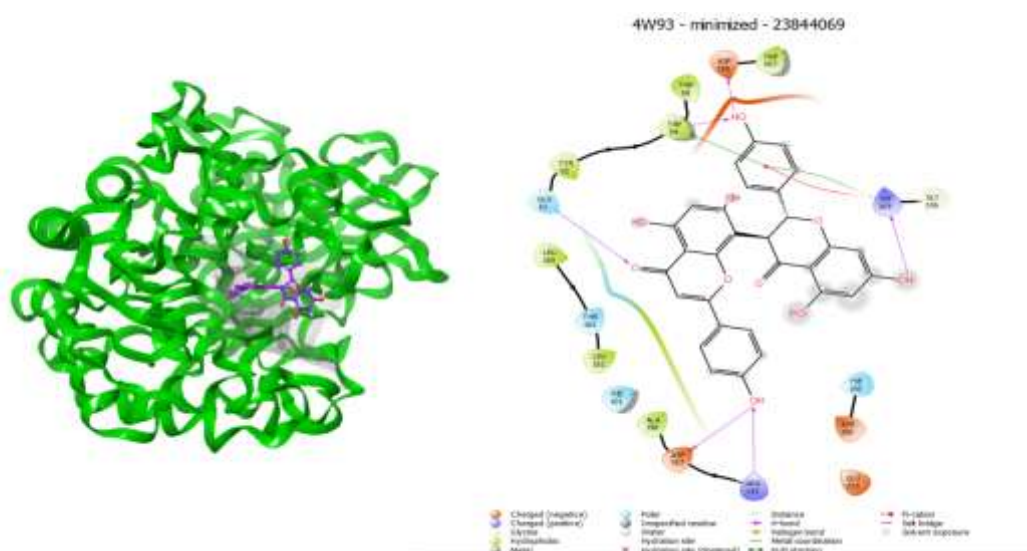


Figure 1f: 2D and 3D Binding poses of interaction of Volkensiflavone (PUBCHEM ID – 23844069) with amino acid residues of Human pancreatic *amylase* enzyme (PDB ID – 4W83)

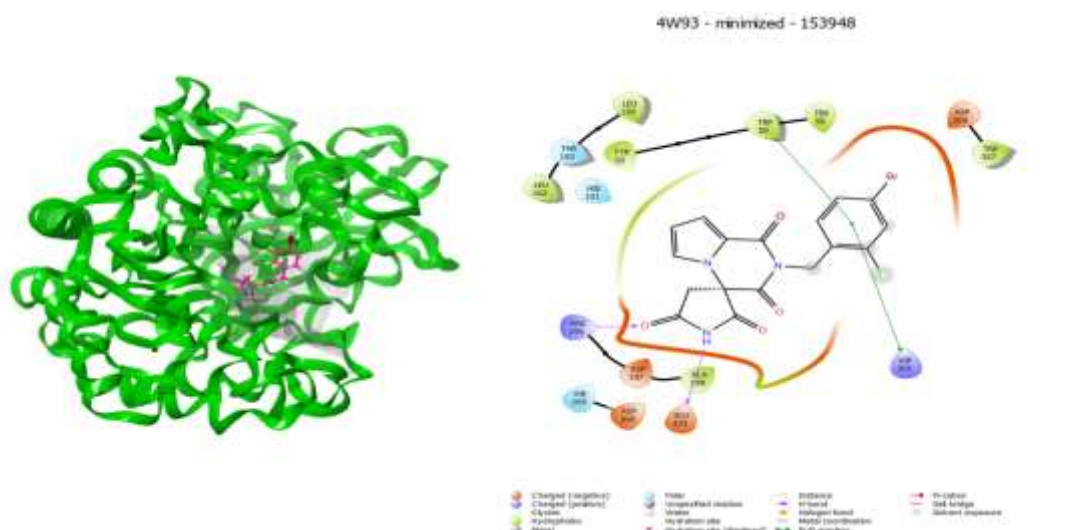


Figure 1g: 2D and 3D Binding poses of interaction of Ranirestat (PUBCHEM ID – 153948) with amino acid residues of Human pancreatic *amylase* enzyme (PDB ID – 4W83)

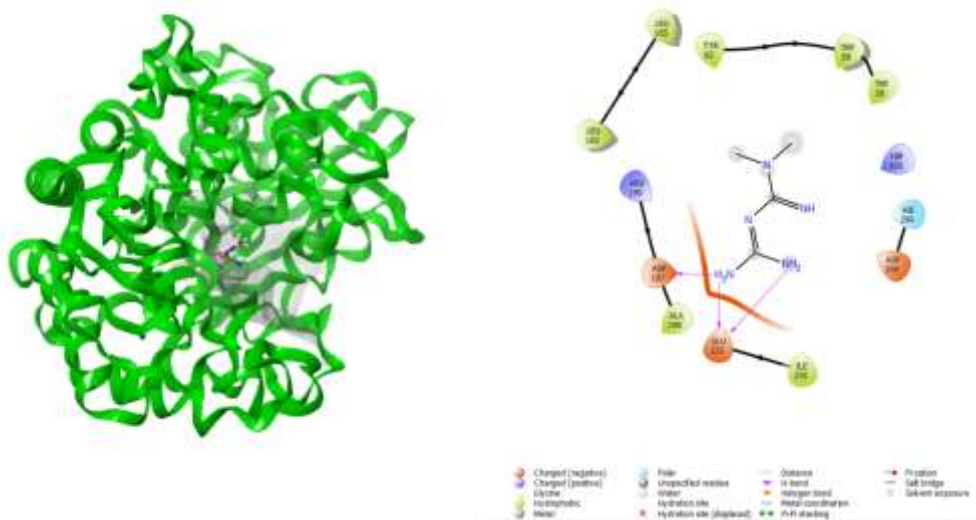


Figure 1h: 2D and 3D Binding poses of interaction of Metformin (PUBCHEM ID – 4091) with amino acid residues of Human pancreatic *amylase* enzyme (PDB ID – 4W83)

The physicochemical properties of substances serve as markers of their potential efficacy as therapeutic candidates. Compounds characterized by high molecular weight and lipophilicity are considered to exhibit limited drug-like potential [15].

The Lipinski Rule of Five provides criteria for oral bioavailability, stipulating that a chemical must possess no more than 5 hydrogen bond donors, 10 hydrogen bond acceptors, a molecular weight of less than 500 g/mol, and a log P of less than 5 [16]. Acarbose and all the phytochemical compounds in *G. kola* extract have high molecular weight that is >500g/mol with more than 5 Hydrogen donors and more than 10 Hydrogen acceptors except for Amentoflavone and Volkensiflavone which has 10 Hydrogen acceptors each while Ranirestat and Metformin (Control) have low molecular weight that is <500g/mol with <5 Hydrogen donors and <10 Hydrogen acceptors. Additionally, each phytochemical compound in *G. kola* including Acarbose has high TPSA values when compared with the TPSA values of the standard drugs (Table 3).

The solubility qualities of phytochemicals in water are essential, as they ensure a minimum concentration in the circulatory system, hence facilitating enhanced absorption in the body. These attributes affect its application in medication formulation and management throughout drug development to facilitate absorption, particularly through oral administration [17]. The various models for assessing water solubility, including ESOL-Ali and SILICOS-IT, are typically predicted using SWISSADME. The initial two differ in the fundamental general solubility equation as they omit melting point parameters; all exhibit a robust linear correlation between predicted and observed values [17].

As anticipated, Acarbose was very soluble in all the three class models used but only Rutin was soluble especially moderately soluble in the Ali Class model among all the phytochemicals found in *G. kola* extract while the already established drugs (Ranirestat and Metformin) remain substantially soluble in all the three solubility class models used. Only Rutin showed maximum absorption potential among the phytochemicals in *G. kola* extract while others remain poorly soluble (Table 4).

Table 3: Physicochemical Properties of the Phytochemicals in *Garcinia kola* Extract

Molecule	MW	Heavy atoms	Aromatic heavy atoms	Rotatable bonds	H-bond acceptors	H-bond donors	TPSA
Acarbose	645.6	44	0	9	19	14	321.17
Rutin	610.52	43	16	6	16	10	269.43
Morelloflavone	556.47	41	28	3	11	7	198.12
Amentoflavone	538.46	40	32	3	10	6	181.8
Garcinianin	556.47	41	28	3	11	7	198.12
Volkensiflavone	540.47	40	28	3	10	6	177.89
Ranirestat	420.19	26	11	2	5	1	88.48
Metformin	129.16	9	0	2	2	3	91.49

MW- Molecular weight, TPSA - Topological Polar Surface Area, H-bond - Hydrogen bond

Table 4: Water Solubility Characteristics of Phytochemicals in *Garcinia Kola* Extract

Phytochemicals	ESOL Class	Ali Class	Silicos-IT Class
Acarbose	Highly soluble	Highly soluble	Soluble
Rutin	Soluble	Moderately soluble	Soluble
Morelloflavone	Poorly soluble	Poorly soluble	Poorly soluble
Amentoflavone	Poorly soluble	Poorly soluble	Poorly soluble
Garcinianin	Poorly soluble	Poorly soluble	Poorly soluble
Volkensiflavone	Poorly soluble	Poorly soluble	Poorly soluble
Ranirestat	Soluble	Soluble	Moderately soluble
Metformin	Highly soluble	Very soluble	Soluble

The GI absorption of compounds, particularly those delivered orally, may be influenced by factors such as age, genetics, health status, and ethnicity, thereby impacting drug pharmacokinetics [18]. The low glycemic index absorption may be ascribed to the compound's non-polar characteristics, resulting in diminished solubility within the intestinal lumen and consequently lower bioavailability [19]. The Gastrointestinal (GI) absorption of Acarbose and all the phytochemical compounds found in *G. kola* extract was low indicating low solubility in the intestinal lumen in comparison with the high GI absorption patterns exhibited by Ranirestat and Metformin as demonstrated during this study using SwissADME predictions (Table 5).

The permeability glycoprotein (P-gp) substrate is a transporter predominantly expressed in the intestine that serves to safeguard the central nervous system from foreign chemicals by expelling them into the intestinal lumen, thereby limiting their absorption. The overexpression of the P-glycoprotein substrate leads to multidrug-resistant cancer [17]. Fortunately, all of the phytoconstituents are not substrates of P-glycoprotein, indicating their potential bioavailability. Furthermore, Permeability glycoprotein (Pgp) substrate was expressed mainly by Acarbose and Rutin while other phytochemicals in *G. kola* including Ranirestat and Metformin found in already standardized drugs are not Pgp substrate indicating bioavailability (Table 5).

However, CYP1A2, CYP2C19, CYP2D6 and CYP3A4 presents no inhibitory activity compared to CYP2C9 hence most of the phytochemical compounds are not likely to affect Cytochrome P450 (CYP) isoenzymes reaction in drug metabolism. The fewer the inhibition, the better the metabolism of drugs into polar excretable form. In addition, most compounds were predicted to be non-Blood brain barrier (BBB) permeant as observed in the Control drugs, Acarbose and all phytochemicals in *Garcinia kola* extract (Table 5).

Table 5: Pharmacokinetics Properties of Phytochemicals in *Garcinia Kola*

Phytochemicals	Pgp substrate	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor	GI absorption	BBB Permeant
Acarbose	Yes	No	No	No	No	No	Low	No
Rutin	Yes	No	No	No	No	No	Low	No
Morelloflavone	No	No	No	Yes	No	No	Low	No
Amentoflavone	No	No	No	No	No	No	Low	No
Garcinianin	No	No	No	Yes	No	No	Low	No
Volkensiflavone	No	No	No	Yes	No	No	Low	No
Ranirestat	No	No	No	No	No	No	High	No
Metformin	No	No	No	No	No	No	High	No

An evaluation of the bioavailability score and drug-likeness of compounds was conducted using the SwissADME database, which employs five rule-based filters (Lipinski's rule of five, Ghose, Veber, Egan, and Muegge), each possessing distinct criteria that determine a molecule's qualification as a drug-like compound [20]. Analysis based on Lipinski's rule indicated that only Metformin and Ranirestat complied fully while Volkensiflavone, Garcinianin, More than 2 violations is generally agreed as implying non-drug likeness properties [21]. Amentoflavone and Volkensiflavone, two flavonoids found in *Garcinia kola*, show the best drug like properties amongst the phytochemicals and have potential to serve as precursor to druggable compounds (Table 6).

Furthermore, Acarbose, Rutin, Morelloflavone, Amentoflavone, Garcinianin, Volkensiflavone and Metformin did not adhere fully with Ghose's and Egan's rules violating more than two of their respective criteria while Ranirestat adhered strictly to these rules. This shows that these compounds may have limited oral bioavailability potential (Table 6).

Control drugs (Metformin and Ranirestat) exhibited significant Bioavailability scores (0.55) with lower Synthetic accessibility scores that is less than 4.0. However, Acarbose, Rutin, Morelloflavone, Amentoflavone, Garcinianin and Volkensiflavone exhibited low Bioavailability scores (0.17) but high Synthetic accessibility scores of more than 4.0. Lower synthetic accessibility scores generally indicate greater ease of synthesis.

Additionally, Rutin and Morelloflavone have one PAINS warning while others, including Acarbose, Amentoflavone, Garcinianin, Volkensiflavone, Ranirestat and Metformin have none. All phytochemicals with the exception of Garcinianin and Volkensiflavone did not comply with the Brenk's criteria. Metformin, Ranirestat and Rutin are more lead-like compounds while the remaining compounds are less lead-like (Table 7).

Table 6: Drug-likeness of Phytochemicals in *Garcinia kola* Extract

Phytochemicals	log Kp (cm/s)	Lipinski violations	Ghose violations	Veber violations	Egan violations	Muegge violations
Acarbose	-16.29	3	4	1	1	5
Rutin	-10.26	3	4	1	1	4
Morelloflavone	-6.52	3	2	1	1	3
Amentoflavone	-6.01	2	2	1	1	3
Garcinianin	-6.37	3	2	1	1	3
Volkensiflavone	-6.17	2	2	1	1	2
Ranirestat	-7.95	0	0	0	0	0
Metformin	-7.99	0	3	0	0	2

Table 7: Medicinal Chemistry Properties of Phytochemicals in *Garcinia Kola* Extract

Phytochemicals	Bioavailability Score	PAINS #alerts	Brenk #alerts	Leadlikeness #violations	Synthetic Accessibility
Acarbose	0.17	0	1	2	7.34
Rutin	0.17	1	1	1	6.52
Morelloflavone	0.17	1	1	2	5.03
Amentoflavone	0.17	0	0	2	4.27
Garcinianin	0.17	0	0	2	5.09
Volkensiflavone	0.17	0	0	2	4.98
Ranirestat	0.55	0	2	1	3.56
Metformin	0.55	0	2	1	3.02

The toxicological profile of a molecule in medication development is critically significant due to its impacts on human health. Mutagenicity refers to the toxicity associated with alterations in an organism's DNA sequence,

which may occur spontaneously or be induced, and can potentially be transmitted to progeny [22]. A medication candidate that fails a mutagenicity test is likely to induce chromosomal abnormalities, frame shift mutations, or point mutations.

Mutagenicity is intrinsically linked to carcinogenicity, as many mutagenic agents may also exhibit carcinogenic and genotoxic properties. Immunotoxicity, conversely, refers to chemicals that are detrimental to organisms. Severe toxicities can lead to severe pathological conditions, including inflammation, neurological disorders, aging, diabetes, cardiovascular diseases, organ abnormalities, and several types of cancer [23].

The ProTox-II is a complimentary web server that predicts the hazardous endpoints (acute or targeted) of compounds for drug development as binary outcomes (active or inert), the lethal dose for 50% of a population (LD₅₀), and the toxicity classifications [24].

All compounds except Metformin a standard antidiabetic drug; exhibited relatively high LD₅₀ values indicating low acute toxicity. Metformin displayed a predicted LD₅₀ of 680mg/kg, placing it within Toxicity Class 4. In addition, *in silico* analysis also predicted potential carcinogenicity for Morelloflavone (prediction probability: 0.58) within the aqueous extract with LD₅₀ of 5000mg/kg. Majority of identified compounds showed predicted tendencies to induce immunotoxicity (prediction probability ≥ 0.50) with the exception of Metformin which pose minimal acute toxicity concerns (Table 8).

Table 8: *In silico* Toxicological Profile of Phytochemicals in *Garcinia Kola*

Compound Name	LD ₅₀ value and Tox Class	Prediction Accuracy (%)	Immunotoxicity	Carcinogenicity	Mutagenicity	Cytotoxicity
Acarbose	24,000mg/Kg 6	100	Active (0.99)	Inactive	Inactive	Inactive
Rutin	5,000mg/Kg 5	100	Active (0.98)	Inactive	Inactive	Inactive
Morelloflavone	5000mg/Kg 5	67.38	Active (0.86)	Active (0.58)	Inactive	Inactive
Amentoflavone	3919mg/Kg 5	68.07	Active (0.51)	Inactive	Inactive	Inactive
Garcinianin	5000mg/Kg 5	67.38	Active (0.78)	Inactive	Inactive	Inactive
Volkensiflavone	2000mg/Kg 4	67.38	Active (0.59)	Inactive	Inactive	Inactive
Ranirestat	2,000/Kg 4	54.26	Active (0.90)	Inactive	Inactive	Inactive
Metformin	680mg/Kg 4	54.26	Inactive	Inactive	Inactive	Inactive

CONCLUSION

In silico assessment of *Garcinia kola* compounds revealed promising drug-like properties and broad applicability in pharmaceutical development. The identified compounds exhibited a range of hydrophobicities, suggesting their potential for various administration routes beyond oral delivery. This is further supported by the favorable bioavailability scores, placing them within the acceptable range for druggable candidates. Additionally, the *in silico* inhibition profiles against diabetic targets suggest a potential role for these compounds in diabetes management. However, further investigations are warranted to validate these findings. *In vitro* and *in vivo* studies are recommended to confirm the antidiabetic activity and establish the binding stability of the compounds with the identified diabetic targets.

ACKNOWLEDGMENT

The authors gratefully acknowledge Siwe et al [27]. for their significant contributions to this research.

Authors' Contribution

Conceptualization: Adekunle A. Fowotade, Fredrick O. Akinbo

Daturation: Adekunle A. Fowotade, Sulyman O. Ibrahim

Formal analysis: Adekunle A. Fowotade, Sulyman O. Ibrahim

Funding acquisition: Adekunle A. Fowotade, Fredrick O. Akinbo

Investigation: Adekunle A. Fowotade, Sulyman O. Ibrahim

Methodology: Adekunle A. Fowotade, Sophie Y. Akinbo

Project administration: Adekunle A. Fowotade, Fredrick O. Akinbo

Supervision: Adekunle A. Fowotade, Fredrick O. Akinbo

Visualization: Adekunle A. Fowotade, Sulyman O. Ibrahim

Writing, review & editing: Adekunle A. Fowotade, Sophie Y. Akinbo

Data Availability

None

Conflict Of Interest

The authors declare no conflicts of interest.

REFERENCES

1. Yedjou, C. G., Grigsby, J., Mbemi, A., Daryllynn, N., Mildort, B., Latinwo, L., and Tchounwou, P. B. (2023). The Management of Diabetes Mellitus Using Medicinal Plants and Vitamins. *International Journal of Molecular Sciences*; 24(10), 9085.
2. Sugandh, F. N. U., Chandio, M., Raveena, F. N. U., Lakshya, K., Karishma, F. N. U., Khuwaja, S., Unaib, A. M., Karoona, B., Maham, K., Giustino, V., Mahima, K., and Satesh, K. (2023). Advances in the Management of Diabetes Mellitus: A Focus on Personalized Medicine. *Cureus*; 15(8): e43697. doi: 10.7759/cureus.43697.
3. Sharanjeet, K., and Singh, S. (2025). The commercial availability of plant-based phytochemical components used in GLP-1 inhibition for the treatment of type-2 diabetes. *Phytomedicine Plus*; 5(3), 100825.
4. American Diabetes Association. (2020). Standards of Medical Care in Diabetes. *Diabetes Care*, 43(Supplement 1), S1–S212.
5. Tauchen, J., Adela, F., Anna, M., Irena, V., Bohdan, L., and Olga, L. (2023). *Garcinia kola*: A Critical Review on Chemistry and Pharmacology of an Important West African Medicinal Plant. *Phytochemistry Review*. Nature Publishing Group. Page 1-47.
6. Airaodion, A. I., Elenjoku, J. A., Ngwogu, A. C., and Ngwogu, K. O. (2020). Ethanolic Extract of *Garcinia kola* (Heckel) Seed Possesses Antiplasmodial Properties against *Plasmodium berghei*. *Asian Journal of Medical Principles and Clinical Practice*; 3(1), 33-39.
7. Junaid, R. S., and Patil, M. K. (2020). Qualitative Tests for Preliminary Phytochemical Screening: An Overview. *International Journal of Chemical Studies*, 8(2), 603-608.
8. Ujah, I. I., Ugochukwu, J. I., and Alozieuwa, U. B. (2021). An evaluation of phytochemical and biopesticidal composition of scent leaf. *GSC Biological and Pharmaceutical Sciences*; 17(01), 117–123.

9. Dogara, A. M., Saber, W. H., Hama, H. A., Sarwan, W. B., Soran, K., Suwsan, S. A., and Lema, A. A. (2022). Biological Evaluation of *Garcinia kola* Heckel. *Advances in Pharmacological and Pharmaceutical Sciences*; <https://doi.org/10.1155/2022/3837965>.
10. Tauchen, J., Adela, F., Anna, M., Irena, V., Bohdan, L., and Olga, L. (2023). *Garcinia kola*: A Critical Review on Chemistry and Pharmacology of an Important West African Medicinal Plant. *Phytochemistry Review*. Nature Publishing Group. Page 1-47.
11. Brendon, L. N., Clare, A., Vlado, P., Genma, F., Greg, F., Min, J., Sophia, Z., Carol, P., Keneth, W. M., and Hiddo, J. L. (2021). Sodium-glucose co-transporter-2 inhibitors with and without Metformin. A Meta-analysis of Cardiovascular, Kidney and Mortality Outcomes. *Diabetes, Obesity and Metabolism*, 23(2), 382-390.
12. Fasooto, T. T., Oluwakemi, R. O., Abiola, F. A., David, B. O., Ezekiel, A. O., Oluwaseun, F., and Afolabi, C. A. (2024). In-silico and in-vivo Comparative Evaluation of the Cardioprotective Potential of Yellow turmeric and White turmeric in Manganese-induced Cardiac Oxidative Stress. *Pharmacological Research – Modern Chinese Medicine*, 10, 399-400.
13. Stephen, K. B., Helen, M. B., Jose, M. D., Zukang, F., Justin, W. F., Brian, P. H., Robert, L., Ezra, P., Dennis, W. P., Yana, R.⁴, Andrej, S., Monica, S., Chenghua, S., Brinda, V., Maria, V., John, D. W., Jasmine, Y. Y., and Christine, Z. (2022). Protein Data Bank: A Comprehensive Review of 3D Structure Holdings and Worldwide Utilization by Researchers, Educators, and Students. *Biomolecules*; 12(10),1425.
14. Agu, P. C., Afiukwa, C. A., Orji, O. U., Ezech, E. M., Ofoke, I. H., Ogbu, C. O., Ogwuja, E. I., and Aja, P. M. (2023). Molecular docking as a tool for the discovery of molecular targets of nutraceuticals in diseases management. *Scientific Reports*; 13, 13398.
15. Robert, J. Y., Sabine, L. F., Michael, G., Paul, D. L., Ronald, J. Q., Nicholas, J. T., Waldmann, H. (2022). The Time and Place for Nature in Drug Discovery. *Journal of American Chemical Society*, 2(11), 12-14.
16. Samukelisiwe, N., Musawenkosi, H. L., Brendeline, L. N., Thabile, D., Arnesh, T., Inderasan, M., Andre, V., and Uche, A. K. (2024). Druggability of Pharmaceutical Compounds Using Lipinski Rules with Machine Learning. *Sciences of Pharmacy*; 3(4), 177-192.
17. Natalia, V., Elisavet, S., Chrysoula, V., Zacharias, T., Georgios, R., Christina, T., and Eugenia, B. (2022). Interactions between Medical Plant-Derived Bioactive Compounds: Focus on Antimicrobial Combination Effects. *Antibiotics (Basel)*, 11(8), 1014-1015.
18. Stillhart, C., Katarina, V., Patrick, A., Abdul, W. B., Hannah, B., Talia, R. F., Ina, G., Rick, G., Daniel, K., Mikko, K., Christine, M. M., Christophe, M., Goran, M., Miriam, G. M., Neil, P., and Anna-Lena, U. (2020). Impact of gastrointestinal physiology on drug absorption in special populations--An UNGAP review. *European Journal of Pharmaceutical Sciences*, 147,105280.
19. Milan, K. L., Brajesh, S., Srigopal, S. and Madan, P. S. (2021). Glycemic index of starchy crops and factors affecting its digestibility: A review. *Trends in Food Science and Technology*, 10, 1016-1017.
20. Mahmud, S., Paul, G. K., Biswas, S., Kazi, T., Mahbub, S., Mita, M. A., and Salah, M. A. (2022). *Phytochemb*: A platform for Vital Screening and Computer-Aided Drug Designing. *Database*, 1. 1-14.
21. Ibrahim, S. O., Lukman, H. Y., Israel, E. E., Babamale, H. F., Abdulkadir, F. R., Hamid, A. A., Zubair, M. F., Atolani, O. (2024). Chemoinformatic-Aided Antidiabetic Analysis of the Therapeutic Potentials of Phytoconstituents in *Eremomastax speciosa* Extract. *Borneo Journal of Pharmacy*, 7(2), 172-186.
22. Fasiku, V., Kyagaba, D., Atlehang, H., Adegoke, A., Erukainure, E. L., and Mamello, S. (2025). A perspective review on factors that influence mutagenicity in medicinal plants and their health implications. *Toxicological Sciences*; 204(2),121–142.
23. Kumari, S., Sudhanshu, S., Advani, D., Akanksha, K., Pravir, K., and Ambasta, R. A. (2025). Unboxing the molecular modalities of mutagens in cancer. *Environmental Science and Pollution Research International*;29(41), 62111–62159.
24. Tian, B., Wu, N., Pan, X., Yan, C., Sharma, V. K., and Qu, R. (2022). Ferrate (VI) Oxidation of Bisphenol E-Kinetics removal Performance and Dehydroxilation mechanism. *Water Resource*, 210, 118025.
25. Siwe, G. T., Ernestine, N. Z., Amang, A. Mezui, C., Choughary, I., Tan, P. (2017). Comparative GC-MS Analysis of Two Crude extracts from *Eremomastax speciosa* (Acanthaceae) leaves. *Journal of Medical Plant Studies*, 7(2), 25-29.