Harnessing Nigeria's Biodiversity: A Computational Approach to Discovering Plant-Based Topoisomerase IIα Inhibitors

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Abstract
This study uses a molecular docking approach to explore the potential of selected Nigerian anti-tumour plants as inhibitors of human topoisomerase IIα. Given the longstanding use of plant materials in traditional cancer treatments, this research leverages computational methods to elucidate the mechanisms of action of phytochemicals. Plant isolates were clustered with known topoisomerase IIα inhibitors to identify promising candidates. Molecular docking simulations were performed using an enzyme complexed with DNA, revealing binding affinities of various compounds. The results indicated that most compounds with high similarity to known inhibitors originated from Olea europea and Cadaba farinosa. Notably, cadabacine diacetate exhibited the lowest binding energy, while 3(4-formylphenoxy)-4-methoxybenzaldehyde presented the highest. Compounds such as Apigenin-7-O-glucoside and suspensaside demonstrated higher affinity for topoisomerase IIα compared to etoposide, suggesting their potential as effective inhibitors. Additionally, rutin also showed significant affinity, while secologanoside presented the highest binding energy with topoisomerase IIb. The findings highlight the efficacy of molecular docking in identifying potential anti-cancer agents derived from indigenous plants. However, further studies on the structure-activity relationships (SAR) of these compounds are essential to ascertain their therapeutic potential. This research underscores the importance of combining traditional knowledge with modern computational techniques in the pursuit of novel cancer therapies.

Keywords: Docking, topoisomerase IIα, plant isolates

Introduction

The use of plant materials in treating malignant diseases has a long history, dating back centuries. Phytochemical evaluations of these plants, particularly those used in traditional medicine, have revealed various compounds that have progressed to modern cancer treatments (Dhanamani, 2011). Notable examples include Podophyllum, which was historically used in ancient Chinese medicine as an anti-tumour agent, ultimately leading to the development of the semi-synthetic derivatives etoposide and teniposide used in chemotherapy today (Chang *et al*., 1992). Other significant plant-derived drugs include vinca alkaloids from *Catharanthus roseus*, taxanes from *Taxus brevifolia*, and camptothecins from *Camptotheca acuminata*, which underscore the therapeutic potential of plant-based compounds in oncology (Sofowora, 2008). Despite the well-documented anti-tumour activities of many plants, their clinical applications are often impeded by a lack of understanding of their mechanisms of action. This knowledge gap presents a barrier to effectively utilising these natural products in cancer therapy. With insight into the chemical composition and pharmacological properties of these plants, researchers can explore their mechanisms through computational methods, such as molecular docking (Glushchenko *et al*., 2015).

Molecular docking allows for the modelling of interactions between small molecules and target proteins at an atomic level, which is vital for elucidating biochemical pathways. The process of molecular docking entails two fundamental steps: predicting the conformation and orientation of the ligand within the binding site of the target protein and assessing the binding affinity of the ligand (Meng *et al*., 2011). This technique serves to expedite the drug discovery process, reducing both time and costs compared to traditional high-performance biological screening methods (Sarfaraz and Feroz, 2014). By analysing the spatial structures of ligands and receptors, researchers can better understand their interactions at the molecular level, enabling the calculation of binding strengths and the identification of optimal ligand configurations (Kitchen *et al*., 2004). The potential of molecular docking extends to improving ligand-receptor interactions by identifying factors that enhance binding efficacy (Lu *et al*., 2010). The outcomes of docking simulations yield conformations where ligands engage with protein binding sites most effectively, paving the way for the identification of promising therapeutic candidates (Cerqueira *et al*., 2009). Consequently, these findings underscore the value of computational approaches in modern drug discovery, particularly concerning the development of anti-cancer agents from indigenous plant sources.

This study aims to conduct an in silico search for compounds that bind to topoisomerase IIα, derived from indigenous plants known for their anti-cancer properties. The objectives include identifying and downloading the phytochemical structures of these plants, using cheminformatics to cluster their three-dimensional structures with those of known topoisomerase inhibitors, determining the molecular binding poses of the clustered compounds, and evaluating their pharmacological profiles in terms of absorption, distribution, metabolism, excretion, and toxicity. The Nigerian plants included in this study have been utilised by traditional healers for cancer treatment. A previous study identified compounds with anti-tumour activity from these plants that clustered with the topoisomerase 1β enzymes, as well as analysed the physicochemical properties of all the chemical structures present in the selected plants using open Babel descriptors in ChemMine R (Afolayan *et al*., 2023).

This study specifically focuses on identifying topoisomerase IIα binding compounds from indigenous plants in Nigeria that have reported anti-cancer properties.

Materials and Methods

Structure download and cleaning: The medicinal plants and their active compounds were identified through an extensive literature search. The structures of the isolated compounds were obtained from PubChem using their Chemical Identifiers (CIDs) and imported into the ChemMine Tools workbench. For compounds not available on PubChem, structures were drawn using ChemDraw 8.0 Pro (PerkinElmer Informatics, Waltham, MA, USA) and then imported into ChemMine Tools using their SMILES entries (Vaniya *et al*., 2016).

Screening based on clustering and physicochemical property analysis: The compounds from each plant were clustered with reference to topoisomerase inhibitors based on the Tanimoto coefficient. Additionally, the chemical structures were evaluated for favourable oral bioavailability by applying Lipinski's rule of five filters (Beg & Athar, 2020).

Conversion and optimisation: The compounds that passed the screening were converted from their SMILES format to Protein Data Bank (PDB) format using Open Babel GUI and optimised with PyMol software (Beg & Athar, 2020).

Preparation, analysis and validation of target protein structure: The protein structures of topoisomerase IIα complexed with various ligands were downloaded from rcsb.org (ID: 1TL8 and 4FM9) (Wendorff *et al*., 2012). The protein was then separated from the complex using Discovery Studio 4.5 Visualizer and ActiveX Control.

Protein-ligand docking: The protein structure and all ligands were converted to PDBQT format using autodock tools. Molecular docking studies were conducted to determine the active binding poses of inhibitors in the enzymes' active sites using AutoDock Vina.

ADMET prediction: The compound's ability to be absorbed into systemic circulation (absorption), efficiently reach its target (distribution), be stable enough to survive the journey (metabolism), be eliminated from the body within a reasonable timeframe (elimination), and have its LD50 measured in rats, fish, and protozoa (toxicity) was assessed using admetSAR, an online tool for predicting ADMET endpoints (Cheng *et al*., 2012).

Results and Discussion

This study focused on exploring the topoisomerase IIα - binding properties of natural compounds derived from African medicinal plants using various in silico applications. the development of computer-aided drug design targeted specifically at anticancer compounds that inhibit the topoisomerase IIα enzyme. The primary objective was to identify and evaluate plant-derived compounds from Nigeria that exhibit validated anti-tumour activity. While there are multiple mechanisms addressing cancer progression, the inhibition of topoisomerase IIα was selected for this research due to the notable number of plant-derived compounds that act through this pathway (Sarkar *et al*., 2021). In this study, six plants were screened. They were *Annona reticulata* (Annonaceae), *Annona senegalensis* Pers. (Annonaceae), *Cadaba farinosa* Forssk (Capparaceae), *Crinum ornatum* (Amaryllidaceae), *Kigelia africana* (Lam.) Benth (Bignoniaceae), and *Olea europaea* L. (Oleaceae). Table 1 contains a list of compounds with possible anti-tumour compounds present in these plants.

Table two presents an analysis of the lead compounds that clustered with topoisomerase IIα enzymes (Table 1). Notably, no compounds from *Crinum ornatum* or *Kigelia africana* grouped with the topoisomerase IIα inhibitors. However, compounds quercetin, isoquercetin, and isoorientin in *Cadaba farinosa* clustered with the topoisomerase IIα inhibitors. Compounds Secologanoside, apigenin-7-O-rutinoside, rutin, acetoside, apigenin-7-O-glucoside, luteolin, hellicoside, suspensaside, orobanchoside, and luteolin-7-O-glucoside in *Olea europea* clustered with the topoisomerase IIα inhibitors (Figures 1 & 2).

Table 1: Table 1: Selected plants and their predicted bioactive compounds.

S/N	Name	Active compounds present
1	*Annona reticulata*	Annonaretin A, Kaurenoic acid, Taraxerol, β-sitosterol, 16α-hydro-19-al-ent-kauran-17-oic acid, 6β-hydroxystigmast-4-en- 3-one, 16α-hydro-ent-kauran-17, 19-dioic acid,2S)-di-O-methylquiritigenin, Annoreticuin, Annoreticuin-9-one, Cis bullatacinone, Trans-bullatacinone, Bullatacin, Squamosine, Rolliniastatin, Molvizarin, Kaurane, Liriodenine
2	*Annona senegalensis* Pers.	α-thujene, α-pinene, β-pinene, Myrcene, Cymene, Benzyl alcohol, 1, 8-cineole, Cis-ocimene, γ-terpinene, Iso-Artemisia, Linalool, Pinine-2-ol, Allo ocimene, Citronellal, Borneol, Terpinen-4-ol, α-terpineol, Citronellol, Neral, Linalyl acetate, Geranial, Borneol acetate, Thymol, Carvacrol, β-elemene, α-copaene, β-caryophyllene, Ethyl cinnamate, Germacrene D, Bicyclogermacrene, β-bisabolene, Acetyleugenol, Elemicin, Viridiflorol, Torreyol, Benzyl benzoate.
3	*Cadaba farinosa* Forssk	Lupeol, β-sitosterol, Ursolic acid, 12-aminododecanoic, Stachydrine, Cadabacine, Cadabacine methylester, Cadacine di acetate, Cadabicilone, Vanillic acid, Isoorientin, Thiazolidine compound, Syringic acid, L-strychidine, 3-hydroxy stachydrine, Methyl cinnamate, methyl ferulate ester, 3(4-formyl phenoxy) 4-methoxy benzaldehyde, Isoquercetin, Quercetin, 3-hydroxybenzoic acid, A,β- dihydroferulic acid, 2-hydroxy-4-methoxy benzoic acid, Ether of p-cinnamic acid-m-ferulic acid.
4	*Crinum ornatum*	2,4-dimethylhexane, Methyl benzene, Nonacosane, Cis-1,3-dimethylcyclohexane, Cis-decahydronaphthalene, Undecanoic acid, ethylester, Caryophyllene, Dodecanoic acid, 1 4-Methylpentanedecanoic acid methylester, 2,6,10,15-Tetramethylheptanedecane, n-hexanedecanoic acid, Eicosane, Heneicosane, 9,12-Octadecadienoic acid, Eicosanoic acid, ethylester, Tetratriacontane, Tetratetracontane, Trans-decahydronaphthalene
5	*Kigelia africana* (Lam.) Benth	Hentriaoontane, 3,4 dihydro-8-phytene, Trans-phytol, (9Z,12Z)methyloctadeca-9,12-dienoate, 1,3,3,5,6,6-hexmethylcyclo hexa-1,4-diene, Beta-tocopherol
6	*Olea europaea* L.	Oleuropein, Secologanoside, Hydroxytyrosol-elenolate, Elenolic acid methyl ester, Ligstroside, β-amyrin, β-sitosterol, Oleanolic acid, Erythrodiol, Betulinic acid, Uvaol, Ursolic acid, Maslinic acid, Rutin, Diosmetin, Apigenin-7-O-rutinoside, Luteolin-7-O-glucoside, Apigenin-7-O-glucoside, Hydroxyl tyrosol, Suspensaside, Hellicoside, Orobanchoside, Acetoside, Wedelosine, Oleuropein aglycone, Ligstroside aglycone, Elenolic acid, P-coumaric acid, Vanillin, Homovanillyl alchohol, Apigenin, Luteolin

Reference: Afolayan *et al*., 2023

Table 2: Clustering data

Plant	Compounds which formed a cluster with Topoisomerase IIα inhibitors
Annona reticulata	-
Cadaba farinosa,	Quercetin, Isoquercetin and Isoorientin
Olea europea	Secologanoside, Apigenin-7-o-rutinoside, Rutin, Acetoside, Apigenin -7 -o-glucoside, Luteolin, Hellicoside, Suspensaside, Orobanchoside, Luteolin-7-o-glucoside

The inhibition of topoisomerase IIα plays a crucial role in cancer treatment due to its impact on DNA replication and repair. Recent studies underscore the potential of plant-derived compounds targeting this enzyme. Notably, flavonoids like quercetin have shown efficacy in inhibiting topoisomerase IIα, leading to increased cytotoxicity in cancer cells (Bisol *et al*., 2020). Alkaloids, particularly camptothecin from Camptotheca acuminata, have demonstrated significant inhibitory effects. Research by Wang *et al*. (2023) indicates that certain camptothecin derivatives improve potency against topoisomerase IIα. Additionally, terpenoids like resveratrol from grapes not only inhibit this enzyme but also enhance the effectiveness of other topoisomerase-targeted therapies, as highlighted by Ravi *et al*. (2023).

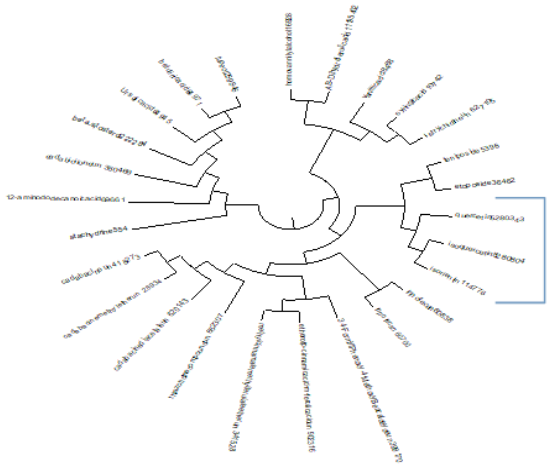

Fig. 1: Clustered compounds from *Cadaba farinosa* Forssk

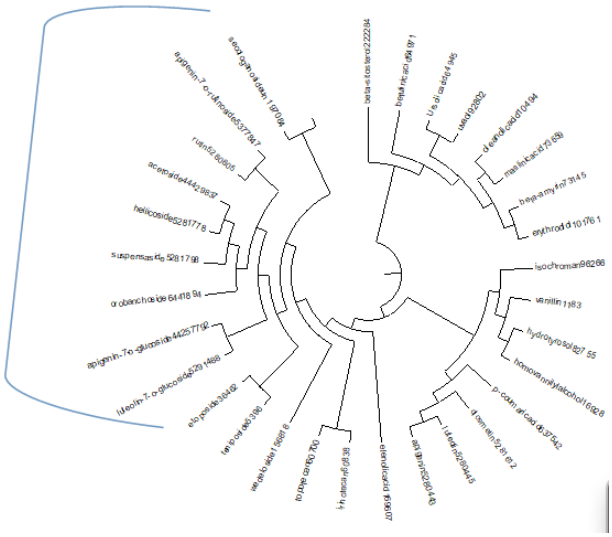

Fig. 2: Clustered compounds from *Olea europea*

Protein-Ligand Docking

The diagrams (Figures 3-11) show the best docked conformation of the topoisomerase IIα enzyme with the compounds. The topoisomerase enzyme is shown in white; the DNA is in yellow, blue, orange and red while the compound is in purple. The plant extracts were analysed and compared with established topoisomerase IIα inhibitors based on Tanimoto coefficients.

This analytical approach facilitates the grouping of compounds that share similarities and offers insights into potential off-target effects (Sliwoski *et al*., 2014). The Tanimoto coefficient computes the similarity between two sets by comparing their intersecting and union values. Notably, the compounds clustered with topoisomerase IIα predominantly included those from *Cadaba farinosa* and *Olea europea*. To establish a comparative standard, known topoisomerase IIα inhibitors, such as etoposide, were docked onto the topoisomerase IIα enzyme to identify the ligand binding site and evaluate the binding affinities of the plant-derived compounds. Each compound was subjected to docking simulations, resulting in the generation of ten conformational models, with the binding energy indicating their affinity—the more negative the binding energy, the stronger the affinity.

The Root Mean Square Deviation (RMSD) was also considered, as it quantifies the variance between atoms of the superimposed protein structures and the predicted conformations (Sliwoski *et al*., 2014). Etoposide exhibited a binding energy of -10.2 kcal/mol when docked to the topoisomerase IIα enzyme. Among the compounds that clustered with etoposide, apigenin-7-O-glucoside and suspensaside demonstrated the best binding interactions, each with a binding energy of -11.7 kcal/mol, indicating higher affinity than etoposide. Rutin also displayed a stronger affinity than etoposide with a binding energy of -10.7 kcal/mol. Compounds such as quercetin and isoorientin had similar binding energies to etoposide at -10.0 kcal/mol, while secologanoside presented the least favourable interaction with a binding energy of -8.2 kcal/mol.

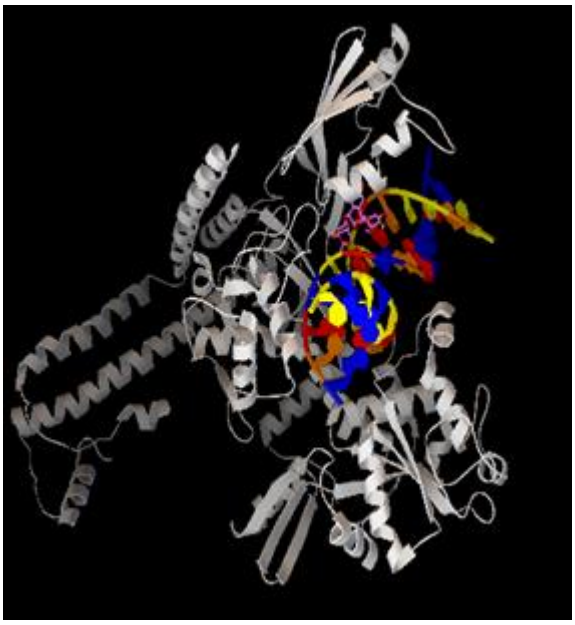

Fig. 3: Best docked conformation of etoposide on topoisomerase IIα and DNA with binding energy of -10.2kcal/mol.

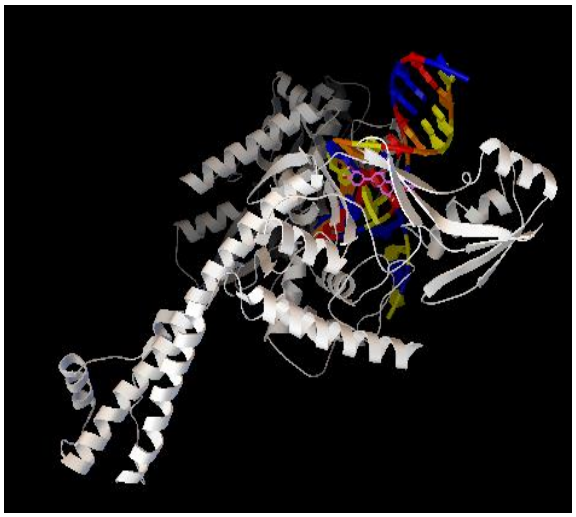

Fig. 4: Best docked conformation of isoorientin on topoisomerase IIα and DNA with binding energy of -10kcal/mol.

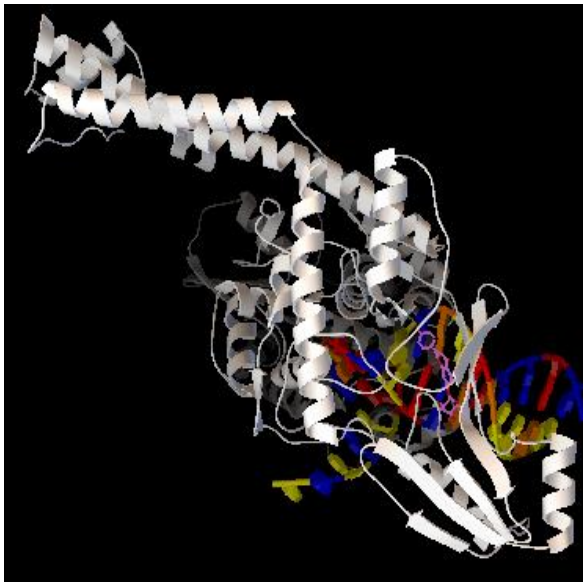

Fig. 5: Best docked conformation of apigenin-7-O-glucoside on topoisomerase IIα and DNA with binding energy of -9.6kcal/mol

Fig. 6: Best docked conformation apigenin-7-O-rutinoside on topoisomerase IIα and DNA with binding energy of -11.7kcal/mol

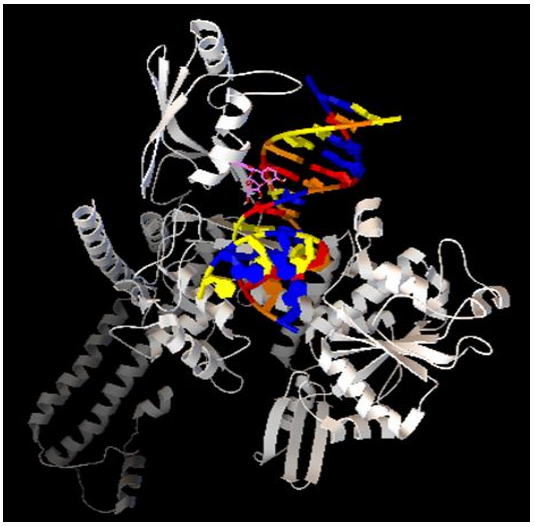

Fig. 7: Best docked conformation of isoquercetin on topoisomerase IIα and DNA with binding energy of -9.6kcal/mol.

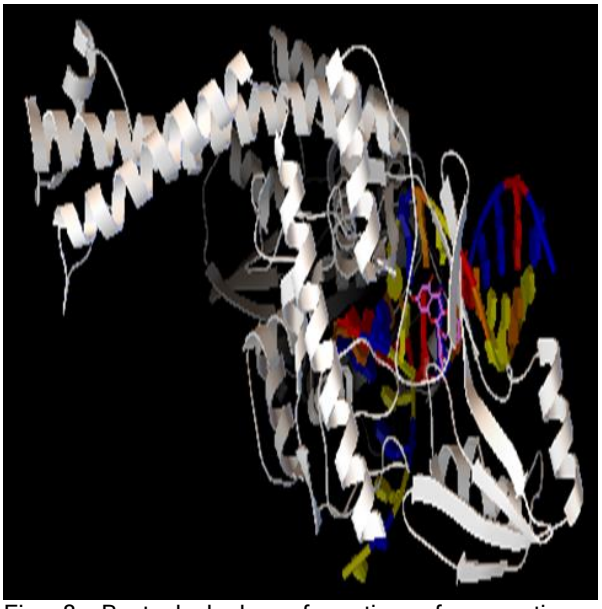

Fig. 8: Best docked conformation of quercetin on topoisomerase IIα and DNA with binding energy of -10.0 kcal/mol.

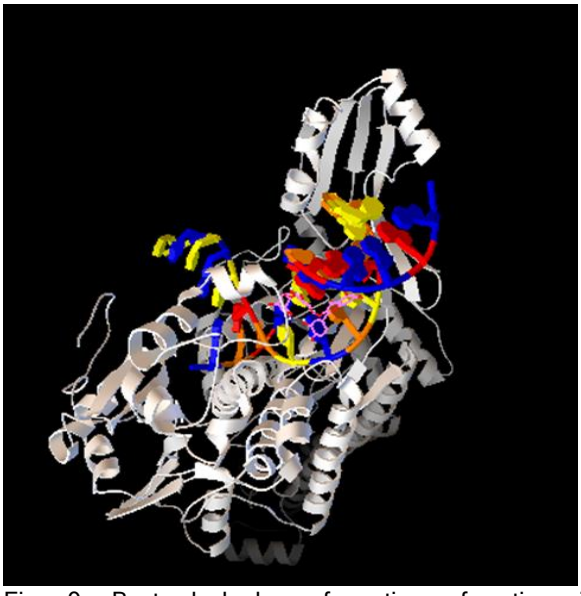

Fig. 9: Best docked conformation of rutin with topoisomerase IIα and DNA with binding energy of -10.7 kcal/mol.

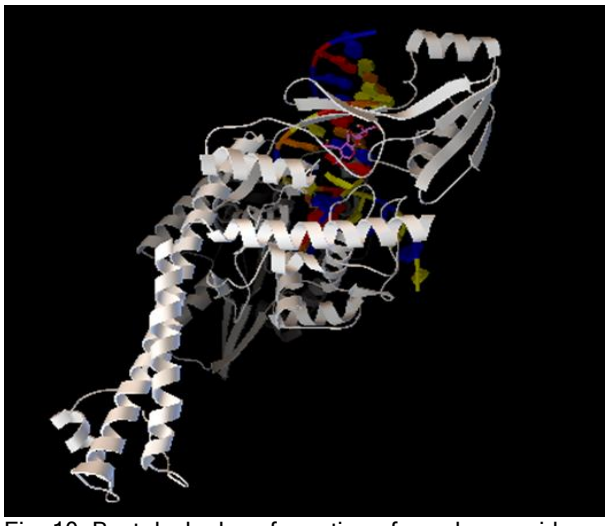

Fig. 10: Best docked conformation of secologanoside on topoisomerase IIα and DNA with binding energy of -8.2 kcal/mol.

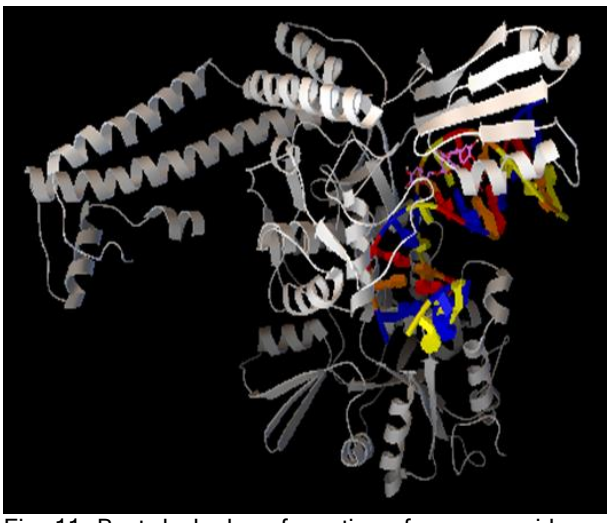

Fig. 11: Best docked conformation of suspensaside on topoisomerase IIα and DNA with binding energy of -11.2 kcal/mol

Table 3a: Summary of the Absorption, Distribution, Metabolism, Excretion and Toxicity (ADMET) parameters predicted in silico for predicted active compounds versus Topoisomerase IIα binders

S/N	Compound	Absorption and Distribution							
		BBB	Water sol/ubility (LogS)	$CaCO_2$ permeability (LogPapp, cm/s)	Intestinal absorption (human)	P-glycoprotein substrate	P-glycoprotein I inhibitor	P-glycoprotein II inhibitor	Renal Organic Cation Transporter
1	Apigenin-7-O-glucoside	- (0.688)	-2.332	-0.923	HIA+ (0.825)	S (0.573)	NI (0.878)	NI (0.775)///	NI (0.886)
2	Apigenin-7-O-rutinosde	-	-2.678	-0.720	HIA+ (0.841)	S (0.670)	Non-Inhibitor (0.872)	Non-inhibitor (0.841)	NI (0.892)
3	Isoorientin	- (0.647)	-2.398	0.278	HIA+ (0.944)	S (0.584)	NI (0.921)	NI (0.878)	NI (0.891)
4	Isoquercetin	- (0.697)	-2.449	0.858	HIA+ (0.786)	NS (0.591)	NI (0.878)	NI (0.797)	NI (0.892)
5	Luteolin-7-O-glucoside	+ (0.698)	-2.449	0.940	HIA+ (0.786)	S (0.591)	NI (0.879)	NI (0.796)	NI (0.891)
6	Quercetin	+ (0.571)	-2.999	0.225	HIA+ (0.965)	S (0.563)	NI (0.930)	NI (0.838)	NI (0.931)
7	Rutin	+ (0.854)	-2.772	-0.651	HIA+ (0.804)	S (0.690)	NI (0.876)	NI (0.855)	NI (0.898)
8	Secologanoside	+ (0.954)	-2.937	0.940	HIA+ (0.918)	S (0.873)	I (0.580)	I (0.583)	I (0.602)
9	Suspensaside	- (0.730)	-1.632	-0.399	HIA- (0.653)	S (0.752)	NI (0.764)	NI (0.870)	NI (0.875)

Table 3 shows the ADMET prediction for the selected compounds. Compounds from *Olea europea* and *Cadaba farinosa* showed significant similarity to known inhibitors. Cadabacine diacetate exhibited the lowest binding energy, indicating a strong affinity for the enzyme. Other promising compounds included Apigenin-7-O-glucoside and suspensaside, which displayed higher affinities compared to the chemotherapeutic drug etoposide. Rutin also demonstrated significant binding potential, while secologanoside showed the highest binding energy with topoisomerase IIα.

It is important to emphasise that while the compound with the strongest binding interaction may appear to be the most effective drug candidate, successful drug design encompasses additional pharmacokinetic considerations.

These include the drug's capacity for absorption into systemic circulation, efficient distribution to the tumour site, metabolic stability, and timely elimination from the body. Consequently, the physicochemical properties of the identified compounds were assessed, and their ADMET (Absorption, Distribution, Metabolism, Excretion, and Toxicity) profiles were predicted. According to the Lipinski rule, compounds must adhere to certain criteria for optimal bioavailability: no more than ten hydrogen bond acceptors, no more than five hydrogen bond donors, a logP value no greater than five, and a molecular weight under 500 daltons (Lipinski *et al.*, 1997). In this investigation, compounds such as apigenin-7-O-glucoside, rutin, and quercetin met these bioavailability criteria.

To enhance pharmacokinetics, various strategies can be employed, such as masking polar functional groups

Table 3b4: Summary of the Metabolism, Excretion and Toxicity (ADMET) parameters predicted in silico for predicted active compounds versus Topoisomerase IIα binders

S/N	Compound	Metabolism								
		CYP450 2C9 Substrate	CYP450 2D6 Substrate	CYP450 3A4 Substrate	CYP450 1A2 Inhibitor	CYP450 2C9 Inhibitor	CYP450 2D6 Inhibitor	CYP450 2C19 Inhibitor	CYP450 3A4 Inhibitor	CYP Inhibitory Promiscuity
1	Apigenin-7-O-glucoside	NS (0.824)	NS (0.892)	NS (0.594)	NI (0.920)	NI (0.945)	NI (0.950)	NI (0.943)	NI (0.919)	Low (0.783)
2	Apigenin-7-O-rutinosde	NS (0.778)	NS (0.897)	NS (0.527)	NI (0.902)	NI (0.9288)	NI (0.953)	NI (0.934)	NI (0.928)	Low (0.670)
3	Isoorientin	NS (0.804)	NS (0.877)	NS (0.603)	NI (0.836)	NI (0.907)	NI (0.948)	NI (0.924)	NI (0.831)	Low (0.781)
4	Isoquercetin	NS (0.812)	NS (0.892)	NS (0.604)	NI (0.908)	NI (0.930)	NI (0.951)	NI (0.930)	NI (0.919)	Low (0.773)
5	Luteolin-7-O-glucoside	NS (0.812)	NS (0.891)	NS (0.603)	NI (0.909)	NI (0.931)	NI (0.950)	NI (0.929)	NI (0.918)	Low (0.774)
6	Quercetin	NS (0.790)	NS (0.912)	NS (0.653)	I (0.911)	NI (0.582)	NI (0.929)	NI (0.903)	I (0.695)	High (0.582)
7	Rutin	NS (0.764)	NS (0.896)	NS (0.537)	NI (0.867)	NI (0.907)	NI (0.955)	NI (0.903)	NI (0.925)	Low (0.679)
8	Secologanoside	NS (0.778)	S (0.514)	S (0.773)	I (0.813)	NI (0.903)	I (0.884)	NI (0.880)	NI (0.895)	Low (0.875)
9	Suspensaside	NS (0.714)	NS (0.892)	NS (0.577)	NI (0.901)	NI (0.896)	NI (0.873)	NI (0.915)	NI (0.878)	Low (0.677)

S/N	Compound	Toxicity									
		HERG Inhibition	AMES Toxicity	Carcinogens	Fish Toxicity (pLC_{50}, mg/L)	Rat Acute Toxicity (LD_{50}, mg/L)	*T. Pyriformis* Toxicity ($pIGC_{50}$, ug/L)	Honey Bee Toxicity	Biodegradation	Acute Oral Toxicity	Carcinogenicity (Three-class)
1	Apigenin-7-O-glucoside	WI (0.975)	Non-toxic (0.738)	Non-carcinogen (0.956)	1.101 High (0.911)	2.276	0.211 High (0.934)	High (0.682)	No (0.712)	III (0.625)	Non-required (0.669)
2	Apigenin-7-O-rutinosde	WI (0.975)	Toxic (0.624)	Non-carcinogen (0.957)	0.880 High (0.938)	2.437	0.409 High (0.993)	High (0.677)	No (0.884)	III (0.652)	Non-required (0.619)
3	Isoorientin	WI (0.973)	Toxic (0.723)	Non-carcinogen (0.955)	0.977 High (0.828)	2.366	0.224 High (0.964)	High (0.592)	No (0.782)	IV (0.375)	Non-required (0.725)
4	Isoquercetin	WI (0.981)	Toxic (0.578)	Non-carcinogen (0.959)	1. 016 High (0.884)	2. 387	0. 328 High (0.954)	High (0.640)	No (0.626)	III (0.405)	Non-required (0.714)
5	Luteolin-7-O-glucoside	WI (0.980)	Toxic (0.579)	Non-carcinogen (0.959)	1.016 High (0.883)	2.386	0.328 High (0.953)	High (0.641)	No (0.626)	III (0.406)	Non-required (0.713)
6	Quercetin	WI (0.978)	Non-Toxic (0.722)	Non-carcinogen (0.945)	0.479 High (0.956)	3.020	0.685 High (0.996)	High (0.633)	No (0.867)	II (0.735)	Non-required (0.675)
7	Rutin	WI (0.981)	Non-Toxic (0.512)	Non-carcinogen (0.961)	0.807 High (0.918)	2.499	0.541 High (0.995)	High (0.633)	No (0.834)	III (0.597)	Non-required (0.674)
8	Secologanoside	WI (0.713)	Non-Toxic (0.722)	Non-carcinogen (0.959)	1.167 High (0.836)	2.691	0.748 High (0.883)	Low (0.597)	No (0.974)	III (0.735)	Non-required (0.717)
9	Suspensaside	WI (0.952)	Non-Toxic (0.882)	Non-carcinogen (0.949)	0.812 High (0.927)	2.315	0.786 High (0.999)	High (0.584)	No (0.783)	III (0.815)	Non-required (0.649)

*Recommended values: QPlogS: predicted aqueous solubility should be between -6.5 and 0.5 mol dm^{-3}; Caco-2 cell permeability: <25 nm/s poor and >500 nm/s great; Binding to human serum albumin: QPlogKhsa should be between -1.5 and 1.5; Human oral absorption: <25% poor and >80% great; Rat oral LD_{50}: <50mg/kg is fatal if swallowed; Blockage of hERG K^+ channels: concern if predicted QPlogHERG is < -5.

that facilitate metabolic processing, thus reducing toxicity. Given the aim of this research to discover anticancer agents that selectively inhibit topoisomerase IIα, parameters such as logP are particularly significant as they influence a compound's ability to traverse biological barriers, including the blood-brain barrier (BBB) and the testicular barrier (Kujawski *et al*., 2012; Yakkala *et al*., 2023). Modulating compound polarity could enable targeted delivery to tumour cells using specific transport systems. Linking the active drug to essential building blocks, like certain amino acids or nucleobases such as uracil mustard, may improve uptake by rapidly dividing cancer cells.

Conclusion

This study has uncovered promising potential topoisomerase IIα inhibitors derived from plant sources, particularly from Cadaba farinosa and Olea europaea. To enhance their applicability as anti-cancer therapies, it is essential to further investigate the structure-activity relationship of these compounds. This understanding will pave the way for optimising their effectiveness in cancer treatment.

Declaration of interest

The authors have no relevant financial or non-financial interests to disclose.

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