In silico analysis of druggability, pharmacokinetics, and target identification of key molecules from *Cassia angustifolia* and *Cassia acutifolia*

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ABSTRACT

This study explores the therapeutic potential of *Cassia angustifolia* and *Cassia acutifolia*, commonly known in the market as Senna. In-silico tools were employed for druggability assessment of ten major molecules, namely Sennoside A, Sennoside B, Sennoside C, Sennoside D, Chrysophanol, Rhein, 6-Hydroxymusizin, Kaempferol, Isorhamnetin, and Aloe-Emodin. Structure-based virtual screening was carried out using PharmMapper, and molecular docking using AutoDock. Analysis of permeability properties revealed adherence to Lipinski's rule of five for six molecules, with blood-brain barrier penetrability observed in all except Isorhamnetin. Although Sennosides A, B, C, and D affirmed their laxative effects, they were not considered drug-like. In silico target prediction and molecular docking identified potential targets, with binding energies ranging from -9.2 to -4.82 kcal/mol, including Human Liver Carboxylesterase 1 (-4.82 kcal/mol), Estrogen receptor β (-7.3 kcal/mol), Carbonic anhydrase II (-6.06 kcal/mol and -9.2 kcal/mol), and Stromelysin-1 (-7.1 kcal/mol and -7.53 kcal/mol). Notably, Aloe-Emodin and Chrysophanol emerged as promising candidates with potential anticancer and anti-arthritis activities. Our findings suggest their utility in developing innovative therapeutic interventions, contributing to pharmaceutical advancements.

KEYWORDS

biological activities; drug targets; in silico pharmacokinetics; molecular docking; Senna

Received 3 September 2023, revised 15 December 2023, accepted 8 March 2024

INTRODUCTION

Cassia, a significant genus within the Leguminosae family, comprises a diverse array of more than 580 species, including herbs, shrubs, and trees.[1] Among the medicinally valuable species within this genus, *Cassia angustifolia* and *Cassia acutifolia* stand out. These particular species are notably rich in phyto-constituents, with a particular abundance of phenolic compounds, such as flavonoids and anthraquinones.[1]

The leaves and pods of various *Cassia* species, commonly known in the market as Senna, exhibit laxative and purgative properties, alongside other effects on the gastrointestinal tract. Furthermore, these species have demonstrated a wide range of pharmacological activities, including antioxidant, analgesic, antipyretic, anti-inflammatory, hepatoprotective, antidepressant, muscle relaxant, immunosuppressant, anticancer, antimicrobial, antifungal, antimalarial, antiasthmatic, antiviral,[2] and have shown potential in the treatment of leprosy and syphilis.[1,3]

In the 19th century, chemists initiated investigations to isolate the active ingredients. The anthraquinone nature of these compounds was substantiated by Tschirch in 1900 and Tutin in 1913.[4] Additionally, their presence was documented in various pharmacopoeias, including the Chinese Pharmacopoeia of 2005, British Pharmacopoeia of 1973, European Pharmacopoeia of 1975, Japanese Pharmacopoeia of 1976, and the United States Pharmacopeia.[5,6] *Cassia* and *Senna* belong to a group called Cassia sensu lato. While this grouping has some taxonomic complexities, *Senna* is considered part of *Cassia* species. Recent DNA studies confirm that *Cassia* and *Senna* are related.[7] *Senna* contains active ingredients in the form of anthraquinone derivatives, such as Rhein, Aloe-Emodin, Chrysophanic, and Physcion. They are found in both free form and as glycosides. Sennosides A and B present in *Senna* are the dianthrone derivatives of Rhein with two glucose units.[8] When hydrolyzed yield aglycones sennidin A and B resepctively, Sennidin A is dextrorotatory and B is its mesoform.[9] Other Sennosides C and D, hetero-anthrone were found with their aglycones Rhein and Aloe-Emodin respectively. Two naphthalene glycosides have also been isolated from leaves and pods, used to distinguish between two species, 6-Hydroxymusicin for *Cassia acutifolia*, and Tinnevellin glucoside for *Cassia angustifolia*.[10] Prenyloxyanthraquinones were isolated from dried leaves and pods of *Senna*, namely 3-isopentenyloxyemodin and 3-geranyloxyemodine.[11] Flavonoids present in *Senna* are flavanol, Kaemferol and their respective glycosides Kaemferin and Isorhamnetin.[9] Later, three flavonoids were isolated and identified quercimeritrin, scutellarein and rutin.[12] Three triterpenoids saponins were isloated from *Senna* leaves: 3-O-{-D-glucuronopyranosyl-(1-4)-[-D-galactopyranosyl-(1-2)]-D-xylopyranosyl-(1-3)-D glucopyranosyl}-2,16α dihydroxy-4, 20-hydroxy methyl olean-12-ene-28-oic acid.[13]

Other constituents were described in leaves and pods of *Senna*: β-sitosterol, salicylic acid, oxalate, resin, and a list of 44 compounds were isolated.[9,14] Senna is administered in the form of an infusion.[8] Senna has a slow onset time of action 6-8 hours and it may lead to a reduction in whole-gut transit-time.[15]

This article focuses on an in silico study of the major phytochemicals of *Senna* to identify the molecules responsible for its pharmacological effects and to explore possible future drug candidates. The findings of this study could offer new perspectives on the use of *Senna* and its molecules for various therapeutic purposes.

EXPERIMENTAL

Molecule files were obtained from PubChem. Various free web servers and software tools, including Molinspiration, ADMET SAR, PharmMapper, and AutoDock, were utilized to investigate ten common molecules (Sennoside A, Sennoside B, Sennoside C, Sennoside D, Chrysophanol, Rhein, 6-Hydroxymusizin, Kaempferol, Isorhamnetin, and Aloe-Emodin) present in both pods and leaves of *C. angustifolia* and *C. acutifolia*, known for their significant pharmaceutical value. The aim was to analyze their activity, druggability, ADMET profiles, and molecular docking.

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ISSN 1996-840X Online / South African Chemical Institute / http://saci.co.za/journal

https://doi.org/10.17159/0379-4350/2024/v78a13

Finding molecular properties and drug likeness

In this investigation, the selected compounds underwent a comprehensive analysis using the Molinspiration tool. This webserver was utilized to calculate various molecular properties, including Log P, total polar surface area (TPSA), the count of hydrogen bond donors and acceptors, molecular weight, atom count, and the number of rotatable bonds. Additionally, the tool was employed to predict bioactivity scores associated with diverse drug targets such as GPCR ligands, kinase inhibitors, ion channel modulators, enzymes, and nuclear receptors. Evaluating these properties and bioactivity scores is crucial in the identification of promising drug candidates.

Predicting ADMET profile

The focus of this study is on identifying potential drug candidates through an assessment of their pharmacokinetic aspects, absorption, and distribution. The ADMET SAR program was employed to predict the ADMET profiles of compounds found in *C. angustifolia* and *C. acutifolia*. The program's key features encompass absorption, distribution, metabolism, excretion, and toxicity. Various factors, including human intestinal absorption, blood-brain barrier penetration, plasma protein binding, cytochrome P450 substrate, and inhibition, were taken into consideration for predicting the ADMET of these compounds.

Estimating metabolites

SMILES notations of the selected compounds were submitted in MetaPrint2D in order to predict the probable metabolic transformations.

Evaluating biological potential

To predict the potential pharmacological activities and toxicities for each compound Pass online tool (Way2Drug) was used, each molecule was submitted in an SDF format. Pass online allows the following measures:

- PASS (Prediction of Activity Spectra for Substances);
- Pa (probability "to be active");
- Pi (probability "to be inactive").

Identifying potential targets

Each molecule was submitted in SDF format using PharmMapper. In this study, human targets were identified, and all other parameters were maintained at their default settings. The targets provided by PharmMapper were subsequently downloaded from the Protein Data Bank online server in a 3D structure, formatted as PDB.

In silico molecular docking

The ligand files for all compounds were retrieved from the PubChem database in SDF format. Subsequently, these files were converted to PDB format using Open Babel. Before the docking process, AUTODOCK 4.2 was employed to automatically categorize each atom and identify the ligand's rigid portion. The number of rotatable bonds was determined using the torsions option within the software. Finally, the ligand was saved in PDBQT format.

The target's PDB file was acquired from the Protein Data Bank (PDB). Prior to docking, all water molecules and extraneous chemical entities on the macromolecule's surface were removed. Hydrogen atoms were added, followed by the assignment of Gastiger partial charges. The resulting target file was then saved in PDBQT format.

The Autogrid file was created with predefined dimensions. The grid size was adjusted based on flexible residues, and the grid spacing was modified according to the size of each macromolecule. The grid file was positioned strategically on the receptor surface to facilitate the desired ligand-receptor interaction. Ultimately, the prepared grid file was saved in gpf format.

Following the meticulous preparation of input files for both ligands and proteins, affinity maps were calculated. Docking runs were executed using AUTODOCK 4.2, employing the Lamarckian Genetic Algorithm for docking. The resulting structure files generated by AUTODOCK 4.2 were utilized in these runs.[16] Docking can be performed through various methods, but the Lamarckian genetic algorithm has proven to be the most effective. Multiple AUTODOCK runs were conducted to produce diverse docked conformations, which were subsequently used to evaluate the predicted docking energy. The selection of binding sites for these molecules was based on the ligand-binding pocket of the templates.[17]

RESULTS AND DISCUSSION

Finding molecular proprieties and drug-likeness

This study assesses the oral bioavailability of six drug compounds based on Lipinski's rule of five, encompassing cLog P, molecular weight, hydrogen bond donors, and hydrogen bond acceptors. The six compounds demonstrated favorable bioavailability attributed to their lipophilicity, TPSA values, and molecular weight. However, Sennoside A and B violated Lipinski's rule, indicating poor absorption or permeability. These glycosidic Sennosides, being hydrophilic, do not readily pass through gastrointestinal tract membranes. Results from Molinspiration, including drug-likeness and bioactivity scores, are summarized in Table 1.

Table 1. Physicochemical parameters predicted by Molinspiration for each lead and their interpretation.

Ligand	miLogP	TPSA	MW	natoms	nON	nOHNH	Nviol	Nrtotb	Volume	Interpretation
Sennoside A/B	0.86	347.96	862.75	62	20	12	3	9	698.52	Not drug like
Sennoside C/D	0.29	330.88	848.76	61	19	12	3	9	696.34	Not drug like
Chrysophanol	3.54	74.60	254.24	19	4	2	0	0	215.17	Drug like
Rhein	3.00	111.90	284.22	21	6	3	0	1	225.61	Drug like
6-Hydroxymusicin	2.31	77.75	232.24	17	4	3	0	1	204.19	Drug like
Kaempferol	2.17	111.12	286.24	21	6	4	0	1	232.07	Drug like
Isorhamnetin	1.99	120.36	316.26	23	7	4	0	2	257.61	Drug like
Aloe-Emodin	2.42	94.83	270.24	20	5	3	0	1	270.24	Drug like

In green: Obedience of Lipinski's rule of 5
In red: Violation of the rule of 5

Predicting drug-likeness

Bioactivity scores for the selected compounds were computed using Molinspiration. Values greater than 0.00 indicate considerable biological activity, scores between -0.50 to 0.00 indicate moderate activity, and scores less than -0.50 indicate inactivity. Among the lead compounds, Sennoside A, B, C, and D were found to be inactive. In contrast, Chrysophanol, Rhein, 6-Hydroxymusicin, Kaempferol, Isorhamnetin, and Aloe-Emodin exhibited varying levels of biological activity as enzyme inhibitors, nuclear receptor ligands, kinase inhibitors, ion channel modulators, GPCR ligands, and protease inhibitors. A summary of all bioactivity results is provided in Table 2.

The study identified Kaempferol, Isorhamnetin, Aloe-Emodin, Rhein, and Chrysophanol as potential ligands for nuclear receptors and modulators of ion channels with promising therapeutic alternatives. All lead compounds were predicted to have human intestinal absorption, and all except Kaempferol and Sennosides penetrate Caco-2 monolayers. Except for Rhein and Aloe-Emodin, all molecules were potential substrates for P-gp, and all compounds were non-inhibitors for the P-gp inhibitor. Sennosides A, B, C, and D, Chrysophanol, and Rhein were found to have low CYP inhibitory promiscuity. All compounds were non-substrates for CYP450 isoforms. The study revealed that none of the ten compounds were inhibitors of hERG, indicating no risk of cardiotoxicity. However, Sennosides A, B, C, D, Chrysophanol, and Aloe-Emodin were found to be AMES toxic, which could lead to mutations in DNA, while Rhein and 6-Hydroxymuzicin were found to be non-toxic or non-carcinogenic. The full results of ADMET profiles of each lead compound are available in Table 3.

Estimating metabolites

MetaPrint2D, a reliable predictor for metabolic transformations, provides high NOR values indicating frequently reported sites of metabolism. Sennosides exhibit multiple sites with high NOR values (6 sites) for metabolic transformations, including dealkylation at the 7th and 31st atom, resulting in aglyka and glycosidic parts, and at the 23rd and 24th atom, leading to Rhein, Chrysophanol, or Aloe-Emodin (Figure 4). These findings align with prior studies indicating that Sennosides undergo metabolism into aglycones Senndins and glucose, subsequently cleaved to the active metabolite anthrone by gut bacteria and acid hydrolysis. Notably, Sennidin A is dextratory, and Sennidin B is his mesoform, exhibiting no rotation.[9]

Evaluating biological potential

The PASS online server was employed to assess the potential biological activity of the selected bioactive constituents, based on Pa and Pi values. As presented in Table 5, Sennosides exhibit strong laxative properties, and all compounds demonstrate enzyme inhibitor potential. Kaempherol, Rhein, 6-Hydroxymusicin, and Isorhamnetin display promise as inhibitors of chlordecone reductase, while Rhein and Chrysophanol emerge as potent inhibitors of alkane 1-monooxygenase. Additionally, 6-Hydroxymusicine shows potential as a histidine kinase inhibitor, a target investigated in cancer treatment. Aloe-Emodin and Isorhamnetin are identified as substrates of CYP2C12, an enzyme involved in the physiological pathway for excreting corticosterone metabolite in females.[18-22]

Identifying potential targets

The PharmMapper server was employed to predict the optimal targets for several compounds. Notably, 6-Hydroxymusicin and Kaempferol exhibited potential influence on Carbonic Anhydrase 2 (PDB ID: 2OSF), while Rhein's target was identified as Human Liver Carboxylesterase 1 (PDB ID: 1YA8). Aloe-Emodin and Chrysophanol were predicted as ligands for Stromelysin-1 (PDB ID: 1BM6), and Isorhamnetin demonstrated activity on the Estrogen Receptor (PDB ID: 2POG).

In silico molecular docking

The docking results are shown in Table 6.

Docking of Rhein with Human Liver Carboxylesterase 1

Carboxylesterases (hCE1) are enzymes distributed across various tissues, playing a role in drug metabolism and the activation of prodrugs. In the study, Rhein was identified to dock with 1YA8, displaying a comparable value to Mevastatin. Notably, Rhein formed hydrogen bonds with TRP357 and LYS414, illustrated in Figure 1, akin to Mevastatin's hydrogen bond interaction with hCE1 and Van Der Waals contact with TRP357. The findings suggest that Rhein could potentially act as a weak inhibitor of hCE1.[23-25]

Docking of Isorhamnetin with Estrogen receptor β

The Estrogen receptor β (ER β) is a member of the steroid nuclear hormone receptor family, expressed in various tissues of males and females. It functions as a ligand-activated gene transcription factor and is involved in important physiological processes.[26] Isorhamnetin was found to bind to LEU346 of 2POG via a hydrogen bond exhibiting a binding energy of -7.3 Kcal/mol, as shown in Figure 2. Selective estrogen receptor β agonists were also found to bind with LEU 343 or ARG 346, possibly due to protein mutation which requires further in vitro study.

Table 2. Bioactivity scores for lead compounds using Molinspiration.

Ligand	GPCR ligand	Ion channel modulator	Kinase inhibitor	Nuclear receptor ligand	Protease inhibitor	Enzyme inhibitory
Senoside A B	-2.75	-3.52	-3.33	-3.25	-2.17	-2.93
Senoside C D	-2.53	-3.40	-3.17	-3.09	-1.92	-2.75
Chrysophanol	-0.23	-0.17	-0.06	0.02	-0.26	0.16
Rhein	-0.08	-0.10	0.01	0.29	-0.06	0.28
6-Hydroxymusicin	-0.30	-0.17	-0.41	-0.02	0.48	0.21
Kaempferol	-0.10	-0.21	0.21	0.32	-0.27	0.26
Isorhamnetin	-0.10	-0.26	0.25	0.28	-0.30	0.22
Aloe-Emodin	-0.02	0.02	0.12	0.24	0.04	0.38

In green: Considerable activity (>0)
In orange: Moderate activity (>-0.5 / <0)
In red: No activity (<0.5)

Table 3. ADMET predictions using ADMET SAR.

	Lead						
ADMET	Sennoside A, B, C and D	Chrysophanol	Rhein	6-Hydroxy-musizin	Kaempferol	Isorhamnetin	Aloe-Emodin
Absorption							
Blood-Brain Barrier	BBB-	BBB+	BBB+	BBB+	BBB+	BBB-	BBB+
Human Intestinal Absorption	HIA+	HIA+	HIA+	HIA+	HIA+	HIA+	HIA+
Caco2 permeability	Caco2 -	Caco2 +	Caco2 +	Caco2 +	Caco2 -	Caco2 +	Caco2 +
P-glycoprotein Substrate	Substrate	Substrate	Non-substrate	Substrate	Substrate	Substrate	Non-substrate
P-glycoprotein inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor
Renal Organic Cation Transporter	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor
Distribution							
Subcellular localization	Mitochondria	Mitochondria	Mitochondria	Mitochondria	Mitochondria	Mitochondria	Mitochondria
Metabolism							
CYP450 substrate							
CYP450 2C9	Non-	Non	Non	Non	Non-	Non	Non
CYP450 2D6	Non	Non	Non	Non	Non	Non	Non
CYP450 3A4	Non	Non	Non	Non	Non	Non	Non
CYP450 inhibitor							
CYP450 1A2	Non	Inhibitor	Non	inhibitor	inhibitor	inhibitor	Inhibitor
CYP450 2C9	Non	Inhibitor	Inhibitor	inhibitor	inhibitor	inhibitor	Inhibitor
CYP450 2D6	Non	Non	Non	Non	Non	Non	Non
CYP450 3A4	Non	Non	Non	Non	inhibitor	inhibitor	Non
CYP450 2C19	Non	Non	Non	Non	inhibitor	inhibitor	Non
CYP IP (Inhibitory promiscuity)	Low	Low	Low	High	High	High	Low
Toxicity							
Human Ether-a-go-go-Related Gene Inhibition	Weak inhibitor Non-inhibitor	Weak inhibitor Non-inhibitor	Weak inhibitor Non-inhibitor	Weak inhibitor Non-inhibitor	Weak inhibitor Non-inhibitor	Weak inhibitor Non-inhibitor	Weak inhibitor Non-inhibitor
AMES Toxicity	AMES toxic	AMES toxic	Non AMES toxic	Non AMES toxic	Non AMES toxic	Non AMES toxic	AMES toxic
Carcinogens	Non-carcinogens	Non-carcinogens	Non-carcinogens	Non-carcinogens	Non-carcinogens	Non-carcinogens	Non-carcinogens
Fish Toxicity	High FHMT	High FHMT	High FHMT	High FHMT	High FHMT	High FHMT	High FHMT
Tetrahymena Pyriformis Toxicity	High TPT	High TPT	High TPT	High TPT	High TPT	High TPT	High TPT
Honey Bee Toxicity	High HBT	High HBT	High HBT	High HBT	High HBT	High HBT	High HBT
Biodegradation	Not ready biodegradable	Not ready biodegradable	Not ready biodegradable	Not ready biodegradable	Not ready biodegradable	Not ready biodegradable	Not ready biodegradable
Acute Oral Toxicity	IV	II	II	III	II	III	II
Carcinogenicity (Three-class)	Non-required	Non-required	Non-required	Non-required	Non-required	Non-required	Non-required
Rat Acute Toxicity, LD50 (mol/kg)	2.1271	2.9132	2.7118	2.2993	3.0825	2.7192	2.9280

Docking of Aloe-Emodin and Chrysophanol with Stromelysin-1

The study investigated the interactions between two leads, Chrysophanol and Aloe-Emodin, with stromelysin-1 as shown in Figures 3 and 4, a member of the matrix metalloproteinase family implicated in various human diseases. Molecular docking studies showed that both leads had a strong interaction with stromelysin-1, with Aloe-Emodin binding to the key residues ALA165, TYR223, and LEU164 via three hydrogen bonds, while Chrysophanol interacted with LEU164, ALA165, and ASN162 via three hydrogen bonds. Stromelysin-1 is a pro-enzyme that may be activated via the "cysteine switch" mechanism to produce a 19 kDa stromelysin catalytic domain (SCD). The results of this study suggest that the inhibition of stromelysin-1 may be a promising strategy for cancer and arthritis treatment.[27-29]

Docking of 6-Hydroxymusicin and Kaempferol with Carbonic anhydrase II

The enzyme Carbonic anhydrase II (HCAII) is a zinc-dependent enzyme that catalyzes the conversion of carbon dioxide and bicarbonate. It is a single polypeptide chain consisting of 259 amino acids and a zinc ion. HCAII deficiency is associated with osteopetrosis with renal tubular acidosis and cerebral calcification.[30,31] Two potential ligands for HCAII, 6-Hydroxymusicin and Kaempferol, were identified through molecular docking studies with PDB ID 1IF4 and 2OSF respectively. 6-Hydroxymusicin was found to bind with three hydrogen bonds to ASP19, LYS18 and ASN11, while Kaempferol formed five hydrogen bonds with THR37, GLN248, THR3, ASP32 and ASP34.

Table 4. Predicted Metabolism sites using Metaprint2D.

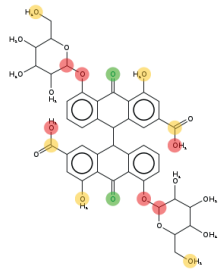
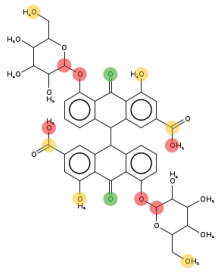
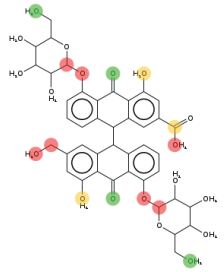
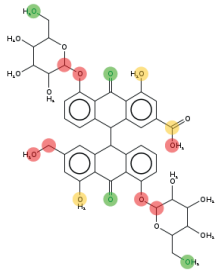
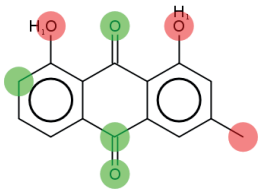
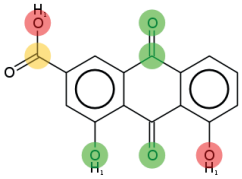
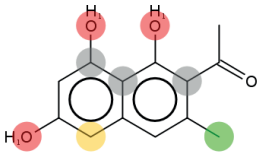
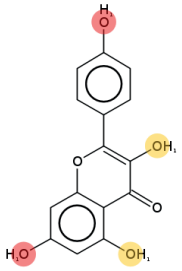
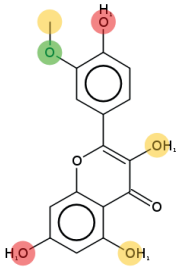
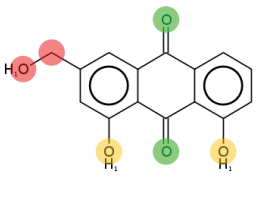
Metabolism sites
 
 
 
 
 

Table 5. Estimated activity retrieved from PASSONLINE Way2Drug (Top 3 Pa Values).

Compound	Pa	Pi	Activity
Senoside A and B	0,979	0,000	Laxative
	0,953	0,002	Alkenylglycerophosphocholine hydrolase inhibitor
	0,940	0,003	Antiinfective
Senoside C and D	0,983	0,000	Laxative
	0,940	0,003	Alkenylglycerophosphocholine hydrolase inhibitor
	0,923	0,003	Sugar-phosphatase inhibitor
Kaempferol	0,983	0,001	Chlordecone reductase inhibitor
	0,974	0,002	Membrane integrity agonist
	0,969	0,002	HIF1A expression inhibitor
Rhein	0,949	0,001	Alkane 1-monooxygenase inhibitor
	0,935	0,003	Chlordecone reductase inhibitor
	0,927	0,003	Antiseptic
Isorhamnetin	0,986	0,001	Chlordecone reductase inhibitor
	0,969	0,001	CYP1A1 inhibitor
	0,965	0,003	Membrane integrity agonist
Chrysophanol	0,938	0,005	CYP2C12 substrate
	0,920	0,002	Alkane 1-monooxygenase inhibitor
	0,884	0,005	Antiseborrheic
6-Hydroxy-musicin	0,970	0,001	Histidine kinase inhibitor
	0,905	0,010	Membrane integrity agonist
	0,871	0,008	Chlordecone reductase inhibitor
Aloe-Emodin	0,906	0,011	CdYP2C12 substrate
	0,881	0,004	NAD(P)+-arginine ADP-ribosyl-transferase inhibitor
	0,874	0,003	Antimutagenic

Table 6. Docking results (Hydrogen bonds, binding energy and involved amino acids).

Molecule (ligand) + Enzyme ID	Binding Energy (Kcal/mol)	Nbre of HB	Distance Å	Involved amino acids
6-Hydroxymu-sicin+1IF4	-6.06	3	1.875 1.872 1.739	ASP19 LYS18 ASN11
Rhein+1YA8	-4.82	2	1.927 1.714	SER21 SER22
Aloe-Emodin+IBM6	-7.53	3	2.07 1.968 1.885	ALA165 TYR223 LEU164
Chrysophanol+IBM6	-7.1	3	1.78 2.003 2.054	LEU164 ALA165 ASN162
Isorhamnetin+2POG	-7.3	1	1.93	LEU346
Kaempferol+2OSF	-9.2	5	2.005 2.061 2.234 1.933 1.942	THR37 GLN248 THR37 ASP34 ASP32

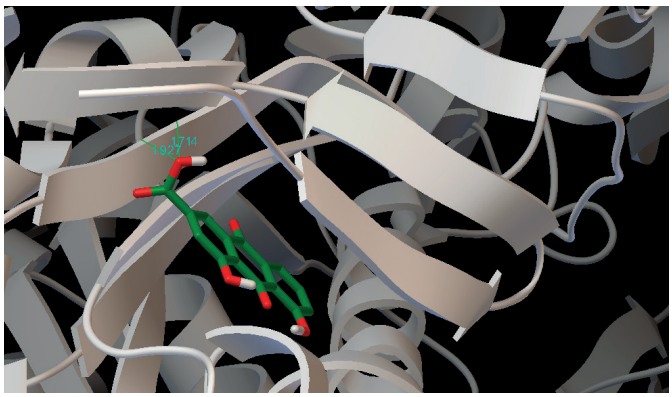


Figure 1. Rhein with Human Liver Carboxylesterase 1 complex with clear bond distances

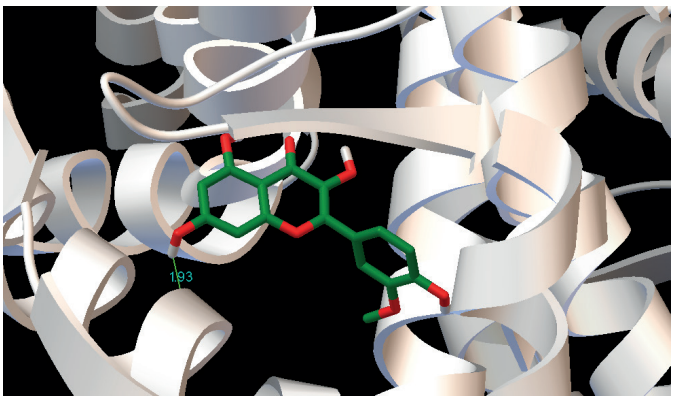


Figure 4. Aloe-Emodin with Stromelysin-1 with clear bonds distances

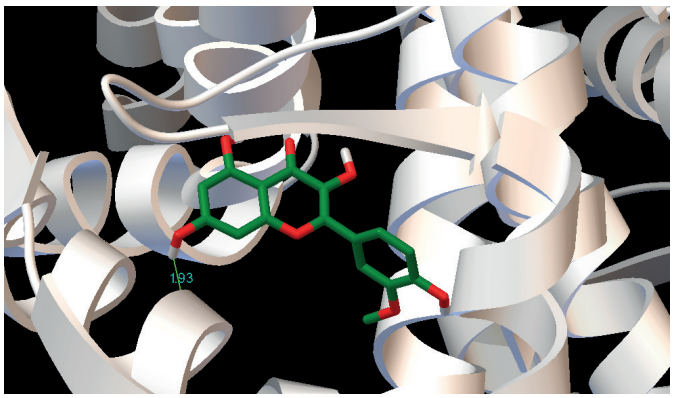


Figure 2. Isorhamnetin with Estrogen receptor β complex with clear bond distances

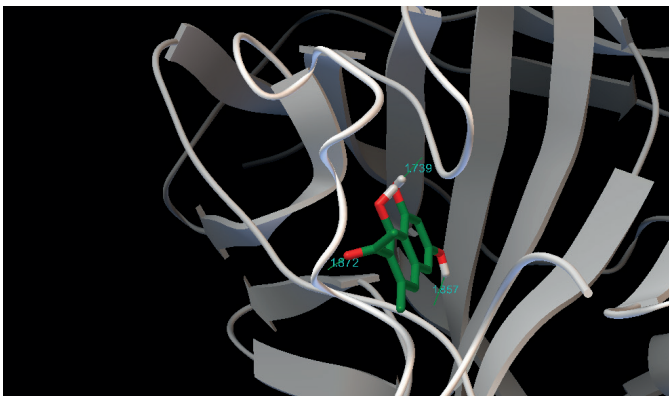


Figure 5. 6-Hydroxymusicin with Carbonic anhydrase II with clear bonds distances

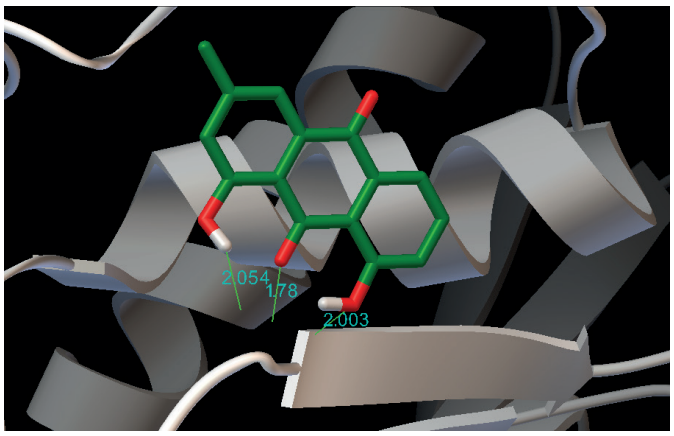


Figure 3. Chrysophanol with Stromelysin-1 with clear bonds distances

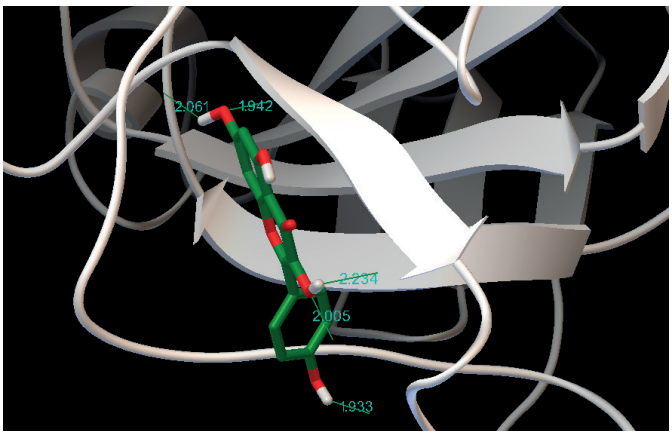


Figure 6. Kaempferol with Carbonic anhydrase II with clear bonds distances

CONCLUSION

The study focused on the *C. angustifolia* and *C. acutifolia* plants, commonly known as *Senna*, which contain numerous active compounds. The information found in literature and the phytochemicals studied showed similarities in activity, toxicity, and bioactivity. The study used in silico techniques to recognize drug targets and analyze pharmacokinetics and chemical properties. Results categorized molecules into two groups: the first, comprising active molecules like Kaempferol, Aloe-Emodin, Chrysophanol, 6-Hydroxymuzicin, Rhein, and Isorhamnetin, exhibited activity on human enzymes with strong binding energies. The second group, including Sennosides A, B, C, and D, was excluded from the molecular docking study for violating Lipinski's rule of 5. However, they proved effective as laxatives. The study affirmed the ethno-medical use of these plants and unveiled additional potential uses of other molecules for various ailments.

ACKNOWLEDGEMENT

The authors would like to express their gratitude for the training on molecular docking provided by Professor Ayman Waddad from the Department of Pharmaceutics, University of Gezira, Sudan.

SUPPLEMENTARY MATERIAL

The supplementary document provides the two-dimensional diagrams of the complexes in addition to the XYZ Cartesian coordinates.

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