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IN-SILICO STUDY OF *CASSIA TORA* LINN IN THE TREATMENT OF GAUCHER DISEASE: A SCIENTIFIC ETHNOMEDICAL STUDY

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The field of pharmacognosy and herbal medicine has been growing steadily over the years due to the increasing number of studies on the side effects of modern medicines and the development of new drug lines. Plants possess therapeutic properties. Gaucher disease is a rare disorder caused by a defective GBA1 gene, which encodes the acid-β-glucosidase enzyme. The molecular docking technique revealed good binding efficiency of the selected bioactive compounds from Cassia tora (C. tora) against the acid-β-glucosidase enzyme that causes GD. A computational approach was used to analyze the ADMET profiles of various phytocompounds using admetsar, protox-ii, and swissadme software. ADMET analysis revealed that Obtusifolin-2-glucoside and Cassiaside had good Health Impact Assessment (HIA) and showed no toxic effects. Preventive measures for GD result in side effects that are inaccessible and result in the emergence of phytocompounds with fewer toxic effects. The obtusifolin-2-glucoside and Cassiaside of C. tora exhibited good docking scores of -7.2 and -7 kcal/mol, respectively, and could be further analyzed using molecular dynamics and in vitro studies.

Keywords: *Obtusifolin-2-glucoside, Cassia tora Linn, Gaucher Disease, Acid-β-glucosidases, In-silico, ADMET*

INTRODUCTION

Plants and plant extracts are the main sources of health care for most of the world's population. According to WHO reports, approximately 40% of all plant species worldwide can be used as medicine. To modernize its use, it is essential to identify and predict the pharmacological basis of traditional plant compounds. Several clinical studies have used in silico models to develop drugs for the treatment of specific diseases.

The field of pharmacognosy focuses on the properties of drugs and their natural origins.

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According to Dridhbala and Charaka, the use of herbal medicines in India dates back to ancient times[1]. Approximately 60% of the world's population uses alternative medicines, which are commonly used in rural and developed countries[2]. Traditional medical practitioners in India also prepare formulations and deliver them to patients. The demand for this treatment has grown owing to the increasing number of people interest in traditional medicine. It is believed that herbal medicines can help prevent and treat illnesses and diseases more rationally.

The low molecular weight of the organic molecules produced by plants, microbes, and other organisms makes them ideal for the production of various pharmaceutical products. Of the more than 17,000 to 18,000 plant species in India, over 7,000 are used as medicinal plants[3]. These include antivirals, antimicrobials, neuroprotective agents, and therapeutic proteins.

Through gene packet analysis and in silico pharmacology, genetic researchers can identify substances that can be used to treat specific diseases. This field is one of the fastest-growing areas in the biotechnology industry. Using *in silico* pharmacology, researchers can analyze and integrate various biological and medicinal sources to make predictions and improve quality of life. The first step in the discovery of a drug is to identify its targets[4]. This process involves the identification of various biomolecules that can be used to target drugs. They include DNA, RNA, proteins, ion channels, and receptors. Once a compound has been identified as a potential drug, it can be tested in clinical trials [5].

Inactivated mutations in the GBA1 gene prevent the enzyme from breaking down the -glucosyl linkage of glucose-cerebroside to form ceramide and glucose [6]. Human GBA1 contains 11 introns and 12 exons. The 16kb downstream of the introns was homologous to the pseudogene located on chromosome 1q22 [7]. Mutations in this gene cause the protein to lose its amino acid stability, which reduces the catalytic activity of the enzyme. GD is a heterogeneous disorder that can be divided into three different phenotypes. Type 1 was the most common type of condition. Individuals with type 1 GD typically experience various conditions, such as thrombosis, avascular necrosis, bone crises, and hepatosplenomegaly. In addition, some people with type 2 GD have neuropsychiatric complications caused by the accumulation of abnormal enzymes in the brain. Symptoms in type 1 patients include various physical and mental conditions such as hypotonia, strabismus, dysphagia, and gastrointestinal problems. In contrast, in type 3 patients, the symptoms are more severe and include anemia, thrombocytopenia, and laryngeal spasm. Other conditions such as mental deterioration and myoclonic seizures can also occur.

Acid-β-glucosidases hydrolyze oligosaccharides, flavonoids, isoflavonoid glycosides, and glycosyl residues found in plants, bacteria, fungi, and eukaryotes. Different treatment options for GD include enzyme replacement therapy (ERT), substrate reduction therapy (SRT), and synthetic drugs[8], which are not only effective but also help prevent or minimize the effects of the disease.

Cassia tora Linn. (Caesalpiniaceae) is generally distributed throughout India, Sri Lanka, western China, and the tropics. It is known as Charota (Hindi), Foetid Cassia (English), and Jui Ming Zi (Chinese). The plant is an annual herbaceous fetid herb, almost an under-shrub, up to 30-90 cm in high, with pinnate leaves. The leaflets were in three pairs: opposite, obovate, oblong with an oblique base, and up to 10 cm long. The flowers were paired in the axils of the leaves with five petals and were pale yellow in color. Under Indian conditions, flowering time is favorable after monsoon rain. The pods are somewhat flattened or four angled, 10-15 cm long, and sickle-shaped; hence, the common name is sicklepod. The seeds are 30-50 in a rhombohedral pod, collected in autumn, and dried in the sun[9&10]. Leaves and seeds are also useful in the treatment of leprosy, ringworm, flatulence, bronchitis, cough, dyspepsia, and cardiac disorders, and are the most popular ingredients in the Ayurvedic formulation Chakramadha Tailam[11]. The plant is reported to possess hypolipidemic, anticancer, hepatoprotective, antifungal, antioxidant,

antibacterial, anthelmintic, antinociceptive, and antihypertensive[12]. This plant contains mainly anthraquinone glycosides and flavonoids. Chrysaphanol is a marker of *C. tora*. Three naphthopyrone glucosides, cassiaside, rubrofusarin-6-O-β-D-gentiobioside, and toralactone-9-O-β-D-gentiobioside[12].

In this study, we aimed to establish relationships between various biological targets and medicinal plants. Through deep virtual screening, we identified the most effective bioactive compounds from plants as potential drug candidates. Therefore, we can discover an alternative solution for GD by elucidating the basic biology of the natural compounds found in medicinal plants and predicting their potential pharmacological activities. In this study, we aimed to identify the potential of the natural compounds of *C. tora* for the treatment of GD.

MATERIALS AND METHODS

Preparation of Ligands

A list of active phytochemicals was obtained from previous studies[13&14]. Nineteen active compounds from *Cassia tora*, that is, 3,5,8,3 ‘, 4’, 5’-Hexahydroxyflavone, 6-Hydroxymusizin[15], Aloe-emodin[16], Cassiaside, Cassitoroside[17], Chrysarobin, Chryso-obtusin[18], Chrysoobtusin[19], Chrysophanol, Emodin, Kaempferol, Nor-rubrofusarin, Obtusifolin[20], Obtusin, Physcion, Rhein, Rubrofusarin, Torachrysone[21], and Toralactone[22] were retrieved from the PubChem database **(Fig. 1).** These bioactive chemicals were extracted in SDF format from the PubChem database. Open Babel was used to convert the SDF structures to PDB. The PDB format was opened using the AutoDock tools. For docking, the file was saved in pdbqt format[23&24].

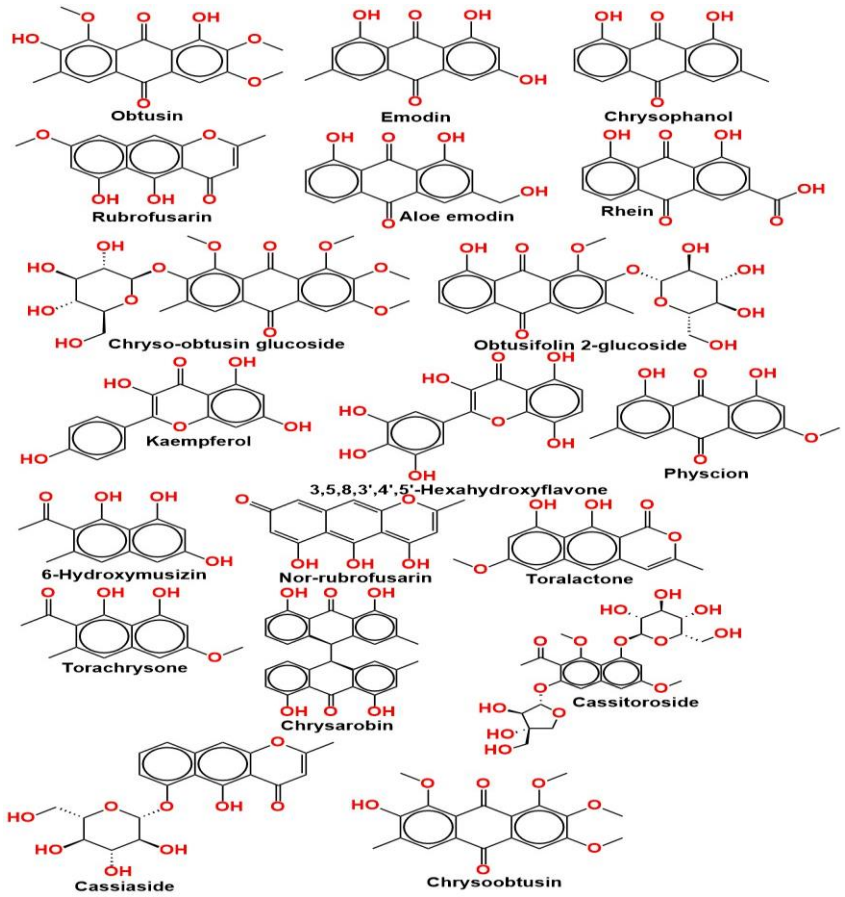

Fig. 1: The structure and identifiers of the ligands produced by *Cassia tora* were used for the molecular docking of acid-β-glucosidase (ABG) (PDB ID:2NT1).

Protein Preparation

The three-dimensional structure of Homo sapiens acid-β-glucosidase (ABG) (PDB ID:2NT1) was extracted from the Protein Data Bank. These were then saved in the PDB format. They were opened using the BioVIA Discovery Studio 2020 Visualizer. After the files were opened, water molecules and other related structures were removed. AutoDock Tools were used to add polar hydrogen atoms to the receptors. Subsequently, the files were saved as pdbqt files.[25].

Active site prediction

The use of computational tools is one of the most important steps in determining the location of the active sites in a target area. This process was performed at the Super Computing Facility for Bioinformatics and Computational Biology, IIT Delhi (scfBio-iitd. res.in). Data collected from the main structure files were visualized using Biovia Discovery Studio Visualizer **(Fig. 2).**[26].

Drug-likeliness and ADMET analysis

Based on PubChem, the reported phytochemical compounds were converted to the SDF format, and the likelihood of the drug was predicted using DruLiTo [27, 28]. The pharmacokinetic properties of these compounds were studied to determine their roles and effects on the body. ProTox-II, admetSAR, and Swiss ADME web servers were used to analyze the ADMET profiles of various ligands[29&30].

Compound screening using the PyRx program

AutoDock Vina (AV) was used for the loading analysis. We copied the pdbqt files of the ligands and targets into the Vina folder. Next, Vina is run by typing the configuration file into a notepad and saving it as "conf.txt." A command prompt was used to run the Vina[31].

Analysis and visualization

The docking results were displayed in the Notepad format in the output. The ligand docking conformation with the lowest Gibbs free energy of binding had the highest affinity. The BIOVIA Discovery Studio Visualizer 2020 was used to merge, analyze, and visualize the three-dimensional conformations of the docking results.[32&33]

Fig.2: Active site of acid-β-glucosidase (ABG) (PDB ID:2NT1).

RESULTS AND DISCUSSION

Results

Drug Likeliness Properties

Drug Likeliness plays a critical role in screening drug candidates during drug discovery and development. It is used to assess the relationship between the physicochemical properties and biopharmaceutical properties of a substance, particularly the impact of these properties on oral bioavailability[34].

The DruLito program was used to study the physicochemical characteristics of selected active chemicals. Most of the compounds used in this study did not violate the Ro5. However, Chryso-obtusin glucoside and Cassitoroside do not meet Ro5 (Table 1)[35&36]. As with the drug-likeness rule, this rule determines whether a chemical compound has chemical and physical properties that would make it suitable for use as a drug that can be consumed orally by humans [37]. Moreover, it can be used to predict the probability of a compound developing into a drug with a particular pharmacological or biological activity that succeeds or fails. Furthermore, this rule suggests that if a compound fails to meet two of these requirements, it will have a low solubility or permeability[38].

Table 1: Physicochemical properties of active compounds and in accordance with the drug-likeliness rule.

Sr. No.	Title	MW	logp	Alogp	HBA	HBD	TPSA	AMR	nRB	nAtom	nAcidicGroup	RC	nRigidB	nAromRing	nHB	Meet RO5 Criteria
1	Obtusin	328	1.107	-0.68	7	0	61.8	95.15	3	25	0	3	24	2	7	Yes
2	Emodin	260	0.517	0.254	5	0	34.1	76.82	0	20	0	3	22	2	5	Yes
3	Chrysophanol	244	0.598	0.817	4	0	34.1	75.22	0	19	0	3	21	2	4	Yes
4	Rubrofusarin	260	1.328	-0.38	5	0	35.5	79.38	1	20	0	3	21	2	5	Yes
5	Aloe emodin	260	-0.65	-0.27	5	0	34.1	76.99	1	20	0	3	21	2	5	Yes
6	Chryso-obtusin glucoside	497	0.122	-2.71	12	0	89.5	132.9	7	42	0	4	33	2	12	No
7	Obtusifolin 2-glucoside	429	-0.68	-1.77	10	0	61.8	114.6	4	37	0	4	31	2	10	Yes
8	Rhein	276	-0.26	-0.07	6	0	51.2	76.93	1	21	0	3	22	2	6	Yes
9	Kaempferol	276	1.486	-0.68	6	0	26.3	81.83	1	21	0	3	22	2	6	Yes
10	3,5,8,3',4',5'-Hexahydroxyflavone	308	2.182	-1.81	8	0	26.3	85.04	1	23	0	3	24	2	8	Yes
11	Physcion	272	0.838	0.318	5	0	43.4	81.86	1	21	0	3	22	2	5	Yes
12	6-Hydroxymusizin	220	1.698	0.255	4	0	17.1	67.8	1	17	0	2	17	2	4	Yes
13	Nor-rubrofusarin	248	1.007	-0.56	5	0	26.3	74.27	0	19	0	3	21	1	5	Yes
14	Toralactone	260	1.539	0.301	5	0	35.5	78.24	1	20	0	3	21	2	5	Yes
15	Torachrysone	232	2.019	0.32	4	0	26.3	72.84	2	18	0	2	17	2	4	Yes
16	Chrysarobin	456	2.384	2.159	6	0	34.1	147.2	1	36	0	6	40	4	6	Yes
17	Cassitoroside	523.9	-1.19	-4.47	14	0	72.5	134.9	9	39	0	4	33	2	14	No
18	Cassiaside	389	-0.01	-1.98	9	0	44.8	105.4	3	34	0	4	29	2	9	Yes
19	Chrysoobtusin	340	1.428	-0.61	7	0	71.1	100.2	4	26	0	3	24	2	7	Yes

MW = Molecular Weight; HBA: Hydrogen bond acceptor; HBD: Hydrogen bond donor; TPSA: topological polar surface area; AMR = molar refractivity; nRB: No. of rotatable bonds; RC = Rotatable bond Count; nHB: No. of hydrogen bonds.

ADMET Analysis

The ADMET attributes of the ligands were studied using Swiss ADME (http://www.swissadme.ch/), admetSAR (http://lmmd.ecust.edu.cn/admetsar2/), and Protox-II (https://tox-new.charite.de/protox_II/) web servers. Tables 2 and 3 list the predicted ADMET properties for the selected phytocompounds.

During the early stages of drug discovery and design, the ADMET profile of a molecule must be evaluated to avoid drug withdrawal from the market [39]. Using these descriptors, it is possible to determine whether a compound is absorbed, distributed, metabolized, and excreted as well as whether it is toxic. Although there are different in vitro methods to establish ADMET profiles, in silico determination is a faster, cheaper, and life-saving method for determining ADMET profiles [40].

In addition to being non-toxic, ideal drug candidates should exhibit acceptable ADME characteristics. Based on SwissADME, ProTox-ii, and admetSAR, we examined the ADME profiles of the identified molecules, including drug similarity, partition coefficients, solubility, HIA, BBB, and cytochrome P450 inhibition (Table 2)[34].

Table 2: ADMET analysis of phytoconstituents from *Cassia tora*.

Phytocompounds	Swiss ADME								ADMETSAR						
	log P o/w	Water Solubility	GI Absorption	Lipinski Rule	Veber's Rule	PAINS Alert	TPSA	Lead Likeliness	HIA	CaCO2	BBB	CYP1A2	CYP2C19	CYP2C9	CYP2D6
3,5,8,3',4',5'-Hexahydroxyflavone	1.02	Soluble	Low	Yes	No	1	151.6	Yes	0.965	0.8957	0.571	Inhibitor	Non-Inhibitor	Non-Inhibitor	Non-Inhibitor
6-Hydroxymusizin	2.02	Soluble	High	Yes	Yes	0	77.76	No	0.993	0.9011	0.508	Inhibitor	Inhibitor	Inhibitor	Non-Inhibitor
Aloe-emodin	1.5	Soluble	High	Yes	Yes	1	94.83	Yes	0.982	0.5847	0.739	Inhibitor	Non-Inhibitor	Inhibitor	Non-Inhibitor
Cassiaside	0.57	Soluble	Low	Yes	Yes	0	149.8	No	0.709	0.8778	0.572	Non-Inhibitor	Non-Inhibitor	Non-Inhibitor	Non-Inhibitor
Cassitoroside	-1.15	Soluble	Low	No	No	0	214.1	No	0.5	0.8171	0.874	Non-Inhibitor	Non-Inhibitor	Non-Inhibitor	Non-Inhibitor
Chrysarobin	4.69	Poorly soluble	Low	Yes	Yes	0	115.6	No	1	0.7531	0.553	Inhibitor	Non-Inhibitor	Inhibitor	Non-Inhibitor
Chryso-obtusin glucoside	0.76	Soluble	Low	No	No	1	170.4	No	0.706	0.8117	0.906	Non-Inhibitor	Non-Inhibitor	Non-Inhibitor	Non-Inhibitor
Chrysoobtusin	2.4	Soluble	High	Yes	Yes	1	91.29	No	0.988	0.8426	0.752	Inhibitor	Non-Inhibitor	Non-Inhibitor	Non-Inhibitor
Chrysophanol	2.38	Moderately soluble	High	Yes	Yes	1	74.6	No	0.994	0.7477	0.655	Inhibitor	Non-Inhibitor	Inhibitor	Non-Inhibitor
Emodin	1.87	Soluble	High	Yes	Yes	1	94.83	Yes	0.988	0.7801	0.566	Inhibitor	Non-Inhibitor	Inhibitor	Non-Inhibitor
Kaempferol	1.58	Soluble	High	Yes	Yes	0	111.1	Yes	0.986	0.7447	0.629	Inhibitor	Inhibitor	Inhibitor	Non-Inhibitor
Nor-rubrofusarin	1.41	Soluble	High	Yes	Yes	0	90.9	Yes	0.979	0.9249	0.59	Inhibitor	Non-Inhibitor	Inhibitor	Non-Inhibitor
Obtusifolin 2-glucoside	0.38	Soluble	Low	Yes	No	1	163	No	0.687	0.8237	0.501	Non-Inhibitor	Non-Inhibitor	Non-Inhibitor	Non-Inhibitor
Obtusin	2.21	Moderately soluble	High	Yes	Yes	1	102.3	Yes	0.979	0.8289	0.514	Inhibitor	Non-Inhibitor	Non-Inhibitor	Non-Inhibitor
Physcion	2.27	Soluble	High	Yes	Yes	1	83.83	Yes	0.981	0.8187	0.578	Inhibitor	Non-Inhibitor	Non-Inhibitor	Non-Inhibitor
Rhein	1.47	Soluble	High	Yes	Yes	1	111.9	Yes	0.969	0.6092	0.762	Non-Inhibitor	Non-Inhibitor	Inhibitor	Non-Inhibitor
Rubrofusarin	2.41	Soluble	High	Yes	Yes	0	79.9	Yes	0.93	0.9472	0.555	Inhibitor	Inhibitor	Inhibitor	Non-Inhibitor
Toralactone	2.63	Moderately soluble	High	Yes	Yes	0	79.9	Yes	0.808	0.9237	0.609	Inhibitor	Non-Inhibitor	Non-Inhibitor	Non-Inhibitor
Torachrysone	2.41	Soluble	High	Yes	Yes	0	66.76	No	0.98	0.92	0.577	Inhibitor	Inhibitor	Non-Inhibitor	Non-Inhibitor

TPSA: topological polar surface area; HIA: human intestinal absorption; CaCO2: human colon epithelial cancer cells; BBB: Blood-brain barrier; LD_{50} = Lethal dose, 50%.

Table 3: Toxicity profiles of *cassia tora* by Protox-II server.

Phytocompounds	PROTOX- II				
	LD50 (mg/kg)	Hepatotoxicity	Carcinogenicity	Immunotoxicity	Cytotoxicity
3,5,8,3',4',5'-Hexahydroxyflavone	5000 (Class5)	Inactive	Inactive	Active	Inactive
6-Hydroxymusizin	2830 (Class5)	Inactive	Inactive	Inactive	Inactive
Aloe-emodin	5000 (Class5)	Inactive	Inactive	Active	Inactive
Cassiaside	5000 (Class5)	Inactive	Inactive	Inactive	Inactive
Cassitoroside	5000 (Class5)	Inactive	Inactive	Active	Inactive
Chrysarobin	2000 (Class4)	Inactive	Inactive	Active	Inactive
Chryso-obtusin glucoside	3000 (Class5)	Inactive	Inactive	Active	Inactive
Chrysoobtusin	5000 (Class5)	Inactive	Inactive	Active	Inactive
Chrysophanol	5000 (Class5)	Inactive	Inactive	Active	Inactive
Emodin	5000 (Class5)	Inactive	Inactive	Inactive	Inactive
Kaempferol	3919 (Class5)	Inactive	Inactive	Inactive	Inactive
Nor-rubrofusarin	1000 (Class4)	Inactive	Inactive	Inactive	Inactive
Obtusifolin 2-glucoside	5000 (Class5)	Inactive	Inactive	Inactive	Inactive
Obtusin	5000 (Class5)	Inactive	Inactive	Active	Inactive
Physcion	5000 (Class5)	Inactive	Inactive	Active	Inactive
Rhein	5000 (Class5)	Inactive	Inactive	Inactive	Inactive
Rubrofusarin	100 (Class3)	Inactive	Inactive	Inactive	Inactive
Toralactone	1000 (Class4)	Inactive	Inactive	Inactive	Inactive
Torachrysone	2830 (Class5)	Inactive	Inactive	Active	Inactive

One of the most important properties of ADMET is its ability to absorb drugs in the human gut [HIA]. HIA plays a pivotal role in transporting drugs to their targets, HIA plays a pivotal role [41]. Higher HIA resulted in improved intestinal absorption of the compound. In addition to Cassiaside, Cassitoroside, Chryso-obtusin glucoside, obtusifolin 2-glucoside, and toralactone, all compounds showed HIA values greater than 0.9, indicating good membrane permeation. Different features of the CNS vasculature are predicted by the blood-brain barrier [BBB]. The lack of pores on the cell surface of vessels in the central nervous system makes it extremely difficult to transport various types of cells and molecules. This makes the delivery of compounds to the central nervous system extremely difficult. Chryso-obtusin glucoside and obtusifolin 2-glucoside showed better BBB penetration with values greater than 0.9. Aloe-emodin, Cassitoroside, Chryso-obtusin glucoside, Chrysoobtusin, and Rhein predicted a strong ability to cross the blood-brain barrier, which can be combined with CNS toxicity, and

the rest of the compounds displayed a low BBB penetration ability.

A Pan-Assay Interference Structural (PAINS) alert was used to determine the toxicity of compounds with desirable physicochemical properties. The assay is also known as a toxicophore test because of the presence of group elements that affect biological processes by interfering with DNA or proteins, which can cause fatal conditions such as cancer and hepatotoxicity[42]. PAINS analysis provides information on the potential toxicity of a molecule. However, the majority of phytocompounds had 0 PAINS structural alerts, indicating their nontoxic nature (Tables 2 and 3).

Many human microsomal p_{450} aromatases catalyze the metabolism of a wide variety of compounds including xenobiotics and drugs[43]. Thus, inhibition of cytochrome P450 isoforms might cause drug-drug interactions, in which co-administered drugs do not metabolize and accumulate to toxic levels[44]. In particular, some cytochrome p_{450} isoforms were inhibited by one or more of the tested compounds. As shown in Table 3, most compounds were inhibitors of CYP1A2, CYP2C19, CYP2C9 and CYP3A4, except cassiaside, cassitoroside, chryso-obtusin glucoside, and obtusifolin 2-glucoside. Therefore, these four phytoconstituents may not have side effects (such as liver dysfunction)[45].

These compounds were evaluated for their hepatotoxic, carcinogenic, and mutational potentiality[46]. The ProTox II results revealed that, except for septicine and tylorebrine, they were all non-carcinogenic. They can also be used as drugs to treat various diseases. Because these compounds cannot accumulate in the body, they are less likely to cause cancer if treated for a long time. 6-Hydroxymusizin, Cassiaside, Emodin, Kaempferol, Nor-rubrofusarin, Rhein, Rubrofusarin, and Toralactone exhibited no immunotoxicity, and the remaining compounds exhibited immunotoxicity. No Hepatotoxicity or cytotoxicity was observed for any of the tested compounds. In ADMET studies, these properties are often used to analyze drug behavior.

Molecular Docking

This study aimed to analyze the optimized structure of the ligand–receptor complex based on the lowest binding energy. This method has been used to develop rational drug designs by studying interactions between different biomolecular components. The resulting adduct structures were ranked according to their scoring function. This study aimed to determine the interactions between acid-β-glucosidase (2NT1) and various plant phytocompounds in *C. tora*. The results of this study are shown in Table 4, where the docking scores of the phytocompounds against the target are mentioned.

Table 4: Molecular docking of selected compounds with acid-β-glucosidase (2NT1) target proteins.

Phytocompounds	Binding Energy (kcal/mol)
	2NT1
3,5,8,3',4',5'-Hexahydroxyflavone	-4.5
6-Hydroxymusizin	-4.3
Aloe-emodin	-4.4
Cassiaside	-7
Cassitoroside	-4.3
Chrysarobin	-4.3
Chrysoobtusin glucoside	-3.5
Chrysoobtusin	-4.6
Chrysophanol	-4.5
Emodin	-4.5
Kaempferol	-4.5
Nor-rubrofusarin	-5.8
Obtusifolin-2-glucoside	-7.2
Obtusin	-4.5
Physcion	-4.2
Rhein	-5.6
Rubrofusarin	-4.5
Torachrysone	-4.3
Toralactone	-4.5

Obtusifolin-2-glucoside

Among the 19 ligands, *C. tora* had the lowest docking score of -7.2 kcal/mol (Table 5). It interacts with amino acids at the active site of β-glucosidase, that is, HIS A:306, VAL A:276, VAL A:305, and ARG A:279. Two hydrogen bonds were formed between the proteins and the residues HIS A:306 and VAL A:276 **(Fig. 2)**. This compound also formed a hydrophobic bond with VAL A:305, with a bond length of 6.12 **(Table 5 and Fig. 3a).**

Cassiaside

With a docking score of -7 kcal/mol, the Cassiaside ligand received a second docking score. Only four hydrogen bonds are formed between this compound and its interacting residues. ARG A: 277 (5.44, 5.80), HIS A: 274 (6.13), and TYR A: 304 (6.04) **(Table 5 and Fig. 3b).**

Table 5: Interactions between acid-β-glucosidase (2NT1) active site residues and the phytoconstituents of *C. tora*.

Ligands	Binding Affinity, ΔG (kcal/mol)	Amino acids involved and Distance (Å)		
		Hydrogen-Bond Interactions	Hydrophobic Interactions	Electrostatic Interactions
Obtusifolin-2-glucoside	-7.2	HIS A:306 (4.34), VAL A:276 (5.79)	VAL A:305 (6.12)	ARG A:277 (6.45, 6.73)
Cassiaside	-7	ARG A: 277 (5.44, 5.80), HIS A: 274 (6.13), TYR A:304 (6.04)	HIS A:306 (4.60, 5.74)	-
Nor-rubrofusarin	-5.8	VAL A:305 (4.84), HIS A:306 (3.80), ASN A:333 (5.04)	-	ARG A:277 (7.24)
Rhein	-5.6	ARG A:277 (5.36)	-	-

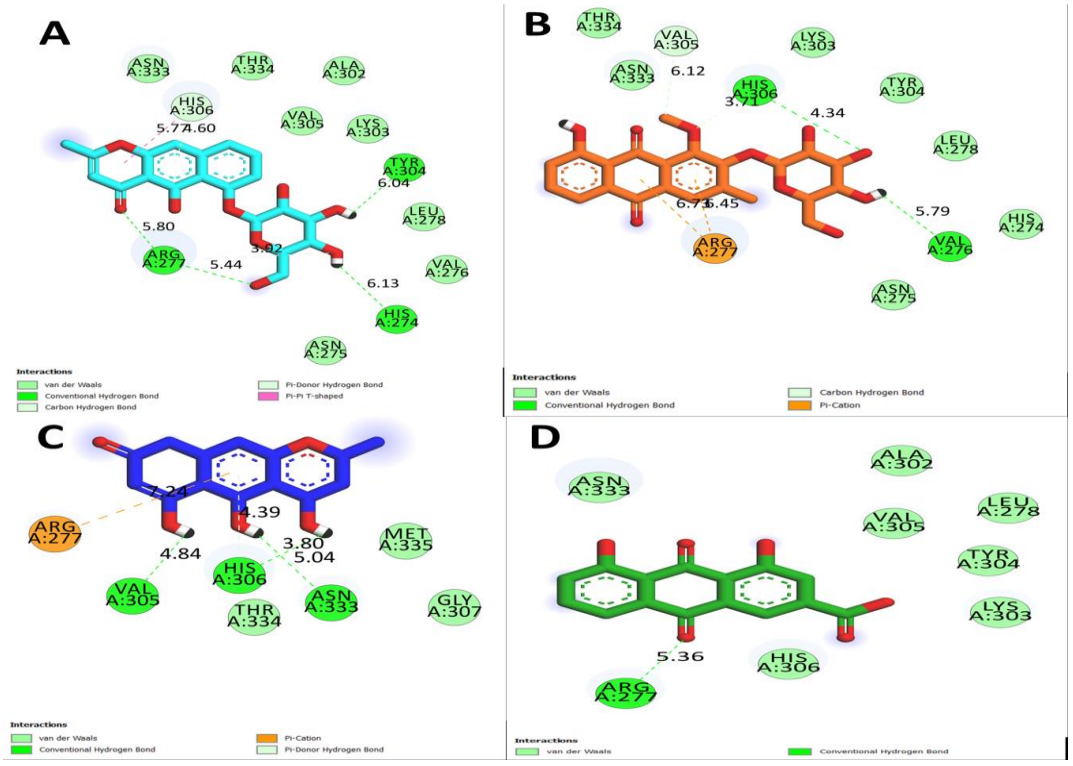

Fig. 3: 2D interactions of phytoligands of *C. tora* with the target protein, acid-β-glucosidase. (A) Obtusifolin-2-glucoside, (B) cassiaside, (C) nor-rubrofusarin, and (D) rhein.

Nor-rubrofusarin

There was a -5.8 kcal/mol docking score for Nor-rubrofusarin, which was the next leading docking score. There was an interaction between VAL A:305, HIS A:306, and ASN A:333. As shown in **Fig. 5**, the protein formed three hydrogen bonds with residues VAL A:305, HIS A:306, and ASN A:333 **(Fig. 5).** A hydrophobic interaction was formed with the remaining residue, ARG A:277 (7.24 Aº) **(Table 5 and Fig. 3c).**

Rhein

Rhein had the lowest docking score among the selected phytoligands. This compound had a docking score of -5.6 kcal/mol. There is a hydrogen bond between ARG A:277 and the protein, which has a length of 5.36 Ao **(Table 5 and Fig. 3d).**

These residues interact with plant compounds as part of a random protein-residue interaction. HIS A:306, VAL A:305, ARG A:277, HIS A:274, TYR A:304 and ASN A:333. Two random residue sites, HIS A:306 and ARG A:277, appeared to interact with most of the phytocompounds, including Obtusifolin-2-glucoside, Cassiaside, Nor-rubrofusarin, and Rhein. In addition to the findings of this study, future research on this disease will be based on the findings of this study. However, currently, few medications are available to treat this disease; therefore, relying on natural products will provide a better alternative to improve human health.

Conclusion

Most people suffering from serious illnesses rely on medicinal plants for their treatment. Many natural products can be used to treat acid–glucosidase deficiencies. In this study, we investigated the various mechanisms by which plants can be used to treat gaucher. This *in silico* study will help scientists to understand the active ingredients of *C. tora* and their potential to improve treatment. Among the phytocompounds, Obtusifolin-2-glucoside and Cassiaside had the highest bonding scores. These compounds exhibited the best ADME properties and drug-likeness, suggesting that they could be promising candidates for treating Gaucher's disease. Further *in vitro* and *in vivo* studies are needed to understand the mechanism of action of these compounds as therapeutic agents for Gaucher disease.

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نشرة العلوم الصيدليـــــة
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دراسة في السيليكو لكاسيا تورا لين في علاج مرض غوشيه: دراسة علمية إثنوطبية

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ينمو مجال العقاقير والأدوية العشبية بشكل مطرد على مر السنين بسبب العدد المتزايد من الدراسات حول الآثار الجانبية للأدوية الحديثة وتطوير خطوط أدوية جديدة. تمتلك النباتات خصائص علاجية. مرض غوشيه هو اضطراب نادر يسببه جين GBA1 المعيب ، الذي يشفر إنزيم الجلوكوزيداز βالحمضية. كشفت تقنية الالتحام الجزيئي عن كفاءة ربط جيدة للمركبات النشطة بيولوجيا المختارة من كاسيا تورا (C. tora) ضد إنزيم الجلوكوزيداز β الحمضي الذي يسبب مرض غوشيه. تم استخدام نهج حسابي لتحليل ملامح ADMET لمختلف المركبات النباتية باستخدام برامج admetsar و protox-ii و swissadme. كشف تحليل ADMET أن أوبتيسيفولين −٢−جلوكوزيد وكاسيسايد كان لهما تقييم جيد للأثر الصحي (HIA) ولم يظهرا أي آثار سامة. تؤدي التدابير الوقائية ل مرض جوشيه إلى آثار جانبية يتعذر الوصول إليها وتؤدي إلى ظهور مركبات نباتية ذات تأثيرات سامة أقل. أظهر أوبتيسيفولين −٢− جلوكوزيد وكاسيسايد من كاسيا تورا درجات جيدة في الالتحام تبلغ −٧,٢ و −٧ كيلو كالوري / مول ، على التوالي ، ويمكن تحليلهما بشكل أكبر باستخدام الديناميات الجزيئية والدراسات المختبرية.