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In silico molecular docking and prediction of drug-likeness, medicinal chemistry and toxicity properties of antidiabetic compounds present in leaves of the medicinal plant of *trigonella foenum-graecum*

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ABSTRACT

The current research aims to find anti-diabetic compounds in Trigonella foenum-graecum leaves using gas chromatography-mass spectrometry assessment, in silico molecular docking ,drug-likeness, medicinal chemistry and toxicity screening. The extracts were subjected to gas chromatography-mass spectrometry and molecular docking. The gas chromatography-mass spectrometry analysis discovered the existence of six compounds in Trigonella foenum-graecum ethyl acetae leaf extracts. The outcomes of the in silico molecular docking studies proved that all six compounds have antidiabetic potential, and even though 26-hydroxy-cholesterol from Anand demonstrated the best effectiveness in antidiabetic action. All six compounds have promising drug-likeness properties. In predicted medical chemistry four compounds have not show any PAIN alert but for BRENK alert some compounds predicted this alert. In predicted toxicity out of six compounds, five compounds are nontoxic compounds. As a result Trigonella foenum-graecum leaves can be a valuable pharmaceutical agent in the treatment and management of diabetes complications.

***Key words**:* Leaves, gas chromatography-mass spectrometry, molecular docking*, trigonella foenum-graecum*, drug-likeness, medicinal chemistry, toxicity

INTRODUCTION

Diabetes is a metabolic form that ascends when the pancreas doesn't generate sufficient insulin or the physique does not use the insulin which is produced successfully. Insulin controls blood sugar levels. Elevated sugarlevel, is a complication of uncontrolled diabetes, and it can cause significant harm to many organ functions, particularly the nervous system and blood flow, over time. Diabetes mellitus is a illness resulting from a variety of etiological factors that is characterised by high blood sugar as well as malfunctions through starch, fat, as well as carbohydrate metabolism due to diminished insulin sensitivity, insulin production, or even both (Gupta and Mamidi, 2020). According to the CentralBureau of Health Intelligence's National Health Credentials from 2015, Gujarat has the strongest diabetes prevalence in the nation. According to the healthprofile report, there are 1,61,578 diabetics in Gujarat, accounting for 20.5% of the overall 7,87,435 community checked. Diabetes covers approximately 4 crore peopleinIndia according to the InternationalDiabetes Federation. Gujarat has 8 to 10% of the suspicious cases of diabetes. Well, almost 10% of scenarios are form one or juvenile diabetes, with the rest 90% being type two diabetes (Koria *et al.,* 2013)**.** Herbal plants are common in routine in our day-to-day life. Either as a nutrient or as a basis of food these herbs are getting used by the patient and a healthy person has easy access to raw consumption. It has minimum side effects and a low price. Diabetes and herbs have gotten a protracted relationship in the past. Therefore, plants are a potential provider of anti-diabetic medication**.** *Trigonella foenum-graecum* medicinal plants have many therapeutic applications **(**Branch, 2013).

Drug discovery has long been a difficult as well as time-consuming procedure. It's indeed time-consuming as well as monetarily draining, with affiliated methodological hurdles as well as constraints. The introduction of laptop drug development methods has recently accelerated the concept of pharmaceutical research, layout, as well as improvement. Molecular docking is indeed a technique in use in structure-based pharmaceutical research that analyses the conjugation as well as alignment of compounds in such a complex molecular recipient's binding pocket. Docking was mainly invented to aid in the understanding of specific molecular processes among large molecules and

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molecules; even so, applications of docking in pharmaceutical research have grown dramatically.It encourages researchers to discover new treatment substances previous to and in vitro or vivo assay methods, estimate ligand-target interconnections just at the atomic level, as well as demarcate structure-activity connections without recognising the chemical composition of many other intended signaling pathways (Ononamadu and Ibrahim, 2021). The main objective of the present study is to carry out molecular docking analysis and screening drug-likeness,medicinal properites,toxicity properites of identified of active compounds found through gas chromatography-mass spectrometry from *Trigonella foenum-graecum* medicinal plants.

MATERIAL AND METHODS

Trigonella foenum-graecum tissue culture leaves were collected in Anand, Gujarat, India. and were fresh and healthy. The collected sample was washed well to eliminate dirt and leaves were separated. The separated leaves were shadedried and created into a powder employing a mixer grinder. The powder is placed inside a flask by the solvent over time. Periodically enthused the content. Through filtration, a micelle is parted from the marc at end of extraction. Powder of *Trigonella foenum-graecum* leaf was extracted through ethyl acetate respectively (Abubakar and Haque, 2020). Analysis of gas chromatography-mass spectrometry was performed on a Clarus 500 Perkin-Elmer gas chromatograph equipped with as well as combined to a detector of mass Turbomas 5.2 spectra were recorded with just an Elite-1, 300 m x 0.25 mm x 1 m df glass capillary. The device was set to an initial temperature of 110°C and kept there for two min. At the end of the time, the oven temperature was increased to 280°C at a rate of 5°C/min and managed to maintain for minutes. The injection port-temperature was adjusted to 250°C, and the helium air velocity was set to 1 ml/min. The output of ionisation was 70 eV. The samples were administered in a 10:1 split mode.The spectral data search range had been set to 45-450. (MHz). Gaschromatography mass spectroscopy was used to recognize the chemical components. By using National Instituteof Standards andTechnology Mass Spectral dataset, the scattering forms of spectral data were evaluated by comparing to all of those stored in the spectrometer dataset (NIST-MS). Component Recognition The mass spectrum of gaschromatography mass spectroscopy was interpreted using NationalInstitute ofStandards andTechnology (NIST) database, which contains over 3 million patterns. The recognised component's frequency band was especially in comparison to the spectral range of known components stored in the library of NIST (Padma *et al*. 2019).

For the study of docking, targets of anti-diabetic protein were chosen. From www.rcsb.org, target receptors in protein data bank format were obtained and utilised for docking studies. The three-dimensional structures of target proteins alpha-amylase, alpha-glucosidase, Interleukin 6, tumor necrosis factor-, beta-glucosidase, and pancreatic lipase were obtained from the Protein Data bank of the Research Collaboratory for Structural Bioinformatics (RCSB) (Ferreira and Ricardo, 2015). From the outcomes of gas chromatography-mass spectrometry analysis of leaf extract of *Trigonella foenum-graecum* the active compounds exhibited antidiabetic properties and were chosen for the study of docking. All the ligands were downloaded from Pub Chem in structure data format (SDF). Openbabel software was used to convert this ligand structures.pdb format.

Drug-likeness candidature was implemented by Lipinski (2001), and Veber (2002) rules screening (Veber *et al*. 2002) (Lipinski *et al*. 2001). In medicinal chemistry PAINS, Brenk and Synthetic Accessibility were evaluated (Bakchi *et al*. 2022). In the toxicity of compounds Cytotoxicity, Mutagenicity, Immunotoxicity and Hepatotoxicity were predicted (Drwal *et al*. 2014).

Pymol software was used to for visualise and reconfigure receptor-ligand formations pymol was used.The CB-dock2 software was employed to assess the binding affinity of pharmacological treatments between both the receptor protein and ligand molecules initially. Also, Patchdock and CB-Dock2 is a stand-alone tool suite used mostly for receptor-ligand complex docking and virtual screening. Both receptor and ligand compounds have interactive interfaces in the software. The *in silico* drug-likeness and medicinal chemistry screening were performed

using the free web tool Swiss ADME .ProTox-II, a webserver for the prediction of toxicity of chemicals was used.

RESULTS AND DISCUSSION

Trigonella foenum-graecum plants are frequently found in our daily lifestyles. Healthy and patient humans are using these herbal remedies as a nutrient or as a basis for food. Flavour enhancer preparations are the supreme ruler of any treatment options because of their ease of availability, uncooked consumption, no adverse effects, and inexpensive. Diabetes and *trigonella foenum-graecum* have such a longstanding experience next to each other. Once compared with synthetic substances, plant-based substances have achieved better performance reactions and no side effects. The existence of the most widely known phytochemicals could explain their therapeutic benefits. The occurrence of several of the significant components identified by gas chromatography-mass spectrometry analysis is reported here, and *in silico* docking was used to verify their anti-diabetic qualities

Gas Chromatography-Mass spectrometry (GC-MS) analysis

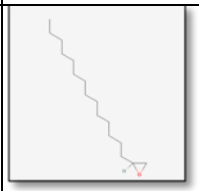
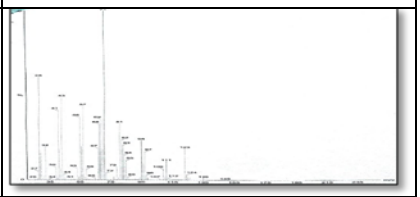
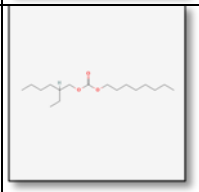
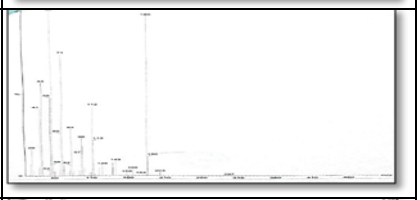
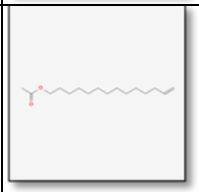
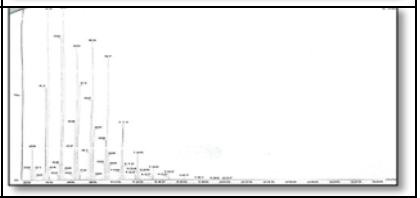
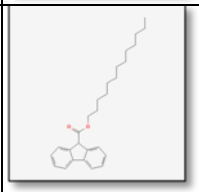
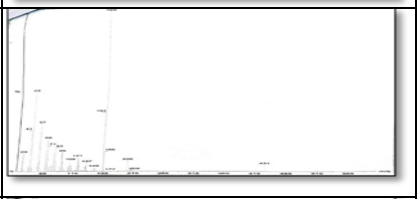
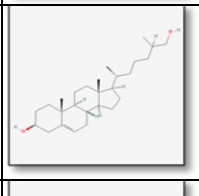
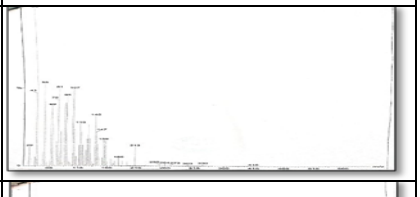
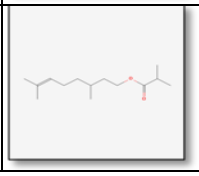
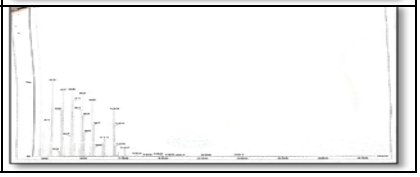
Active components found in ethyl acetate extract of *Trigonella foenum-graecum plant* leave by report. The gas chromatography-mass spectrometry investigation discovered the occurrence of six compounds from the leaf extract of *Trigonella foenum-graecum* (Table 1).

In silico Molecular docking studies

Six protein targets were preferred for in-silico molecular docking based on the diversity of binding site qualities.Crystal structures of alpha-amylase (PDB code: 4GQR), alpha-glucosidase (PDB code: 5NN5), interleukin 6 (PDB code: 1ALU), TNF-α (PDB code: 1 TNF), beta-glucosidase (PDB code:2ZOX)and pancreatic lipase(PDB code: 2OXE) were retrieved from the proteindata bank. From the outcomes of gaschromatography-mass spectrometry analysis of leaf extract 1,2-Epoxyhexadecane , Carbonic acid, 2-ethylhexyl octyl ester , 13-Tetradecen-1-ol acetate , 9H-Fluorene-9-carboxylic acid, tridecyl ester , 26-hydroxy-cholesterol and Citronellyl isobutyrate ligands found from *Trigonella foenum-graecum* of anand city. All six ligands are docked from each of the receptors to find the best anti-diabetic compounds.

The alpha-amylases are calcium essential micronutrients that cannot perform without calcium. One of the most essential digestive enzymes in human people is pancreatic alpha-amylase, which also acts as a catalytic reaction involving the hydroxylation of the alpha-1, 4 glycosidic bonds of carbohydrates, amylose, amylopectin, glycogen, as well as various maltose and therefore is willing to take responsibility for carbohydrate digestion. Some other important mechanism is alpha-glucosidase, which also catalyses the crucial stages of glucose metabolism, primarily starch, by functioning on 1,4-alpha bonds as well as being able to produce glucose as the end product. Large molecules, such as starch, cannot pass the barrier of blood-to-brain because glucose must enter the bloodstream; to resolve this issue, alpha-amylase causes a conformational change in the large starch molecules down into smaller fragments of glucose to go through the barrier of blood-to-brain. When there is an additional transformation of starch to sugars, the blood sugar level will rise, and insulin will take some action by instructing cells to metabolise the excess sugar moieties and store them as sources of energy, i.e. glycogen. In a healthy individual, this cycle continues indefinitely (Agarwal and Gupta, 2016). Furthermore, type two diabetes could be ended up causing mostly by impairment of insulin-producing pancreatic beta cells, which may be triggered by such an abundance of lipids through the digestive system. Pancreatic lipase is indeed the main enzyme in digestion and absorption, willing to take responsibility for high fat absorption via the breakdown of triacylglycerols in the intestinal epithelium into free monoglycerides and fatty acid. Pancreatic lipase inhibitors have recently attracted the attention of researchers due to their obesity-fighting action by delaying pancreatic lipase operation. One such activity might reduce cholesterol digestion and therefore prevent the adrenal glands, restoring regular insulin sensitivity from beta cells (Tushuizen *et al*. 2007).

Table 1: The molecular structure, the molecular formula and spectrum of the active compounds of the leaves of ethyl acetate extract of *Trigonella foenum-graecum* of Anand city

Sr.No	Name of the Compound	RT	Molecular Formula	Molecular structure	Spectrum
1	1,2-epoxyhexadecane	18.550	C16H32O		
2	Carbonic acid, 2-ethylhexyl octyl ester	24.872	C17H34O3		
3	13-Tetradecen-1-ol acetate	25.647	C16H30O2		
4	9H-Fluorene-9-carboxylic acid, tridecyl ester	27.673	C27H36O2		
5	26-hydroxy-cholesterol	30.014	C27H46O2		
6	Citronellyl isobutyrate	34.001	C14H26O2		

Interleukin-6 is a cytokine of proinflammatory that helps promote the formation of insulin resistance as well as the pathophysiology of type two diabetes by attempting to control differentiation, migration, multiplication, and death of cells (Rehman *et al*. 2017). Tumor necrosis factor-alpha is a powerful marker of inflammation and antimutagenic generated by activated phagocytes, macrophages, CD4+ immune cells, t lymphocytes, white blood cells, plasma cells, granulocytes, and nerve cells. It plays a role in several metabolic diseases, including Type two diabetes and obesity. It inhibits the action of insulin, resulting in insulin sensitivity. Tumor necrosis factor-alpha serum concentrations are enhanced in patients through type 2 diabetes, which is connected to reduced glucose tolerance, higher insulin resistance, islet impairment, as well as increased type two diabetes mellitus threat. Diabetes people through disease have also considerably higher serum tumor necrosis-alpha levels than healthy volunteers (Shi *et al*. 2019). It is traditionally defined as employing blood serum glucose levels as well as postprandial plasma levels. The mode of operation of such an anti-hyperglycemic representative is really to reduce endogenous glucose production as well as intestinal glucose absorption while raising peripheral uptake of

glucose. Oral glucose - lowering representatives significantly decrease blood sugar levels. People are frequently employed in the dealing ofdiabetes. Acarbose reduces hepatic gluconeogenesis, decreases gastro - intestinal absorption of glucose, as well as increases sensitivity to insulin through target cells (Rehani *et al.,* 2019).

The three-dimensional formation of six selected ligands was downloaded in structure data format from the Pubchem database and transformed into a protein data bank for adhesion with protein targets. Molecular docking in this research was conducted using the CB-dock2 docking operating systems. The particularly emphasized molecule compounds were docked against every antidiabetic protein target in CB-dock operating system to understand better the treatment strategies (Figure 1, 2, 3, 4, 5, 6).

According to the finding, anand city substances derived from *Trigonella foenum-graecum* leaves 26-hydroxy-cholesterol and 13-Tetradecen-1-ol acetate docked all six receptor sites. But according to best binding effectiveness 26-hydroxy-cholesterol found best compounds. Out of six ligands four ligands did not demonstrate binding affinity to specific receptors, which might be because that particular compound did not bind to that receptor site (Table 2).

Table 2: Receptors -Ligands docking study of of *Trigonella foenum-graecum*

Sr. No.	Name of ligand	Name of protein receptor	Docked binding energy (Kcal/mol)
1	1,2-epoxyhexadecane	Alpha-amylase	NA
		Alpha-glucosidase	-4.9
		Interleukin 6	-4.2
		Tumor necrosis factor-α	-5.0
		Beta-glucosidase	NA
		Pancreatic lipase	NA
2	Carbonic acid, 2-ethylhexyl octyl ester	Alpha-amylase	-5.2
		Alpha-glucosidase	-5.1
		Interleukin 6	-4.6
		Tumor necrosis factor-α	NA
		Beta-glucosidase	NA
		Pancreatic lipase	-5.5
3	13-Tetradecen-1-ol acetate	Alpha-amylase	-5.2
		Alpha-glucosidase	-5.4
		Interleukin 6	-4.2
		Tumor necrosis factor-α	-5.0
		Beta-glucosidase	-6.3
		Pancreatic lipase	-5.6
4	9H-Fluorene-9-carboxylic acid, tridecyl ester	Alpha-amylase	-7.0
		Alpha-glucosidase	-6.1
		Interleukin 6	-5.2
		Tumor necrosis factor-α	-7.5
		Beta-glucosidase	NA
		Pancreatic lipase	NA
5	26-hydroxy-cholesterol	Alpha-amylase	-7.1
		Alpha-glucosidase	-7.4
		Interleukin 6	-6.3
		Tumor necrosis factor-α	-9.2
		Beta-glucosidase	-10.6
		Pancreatic lipase	-7.5
6	Citronellyl isobutyrate	Alpha-amylase	NA
		Alpha-glucosidase	-6.1
		Interleukin 6	-5.0
		Tumor necrosis factor-α	-5.4
		Beta-glucosidase	NA
		Pancreatic lipase	-5.9

NA=Not Applicable

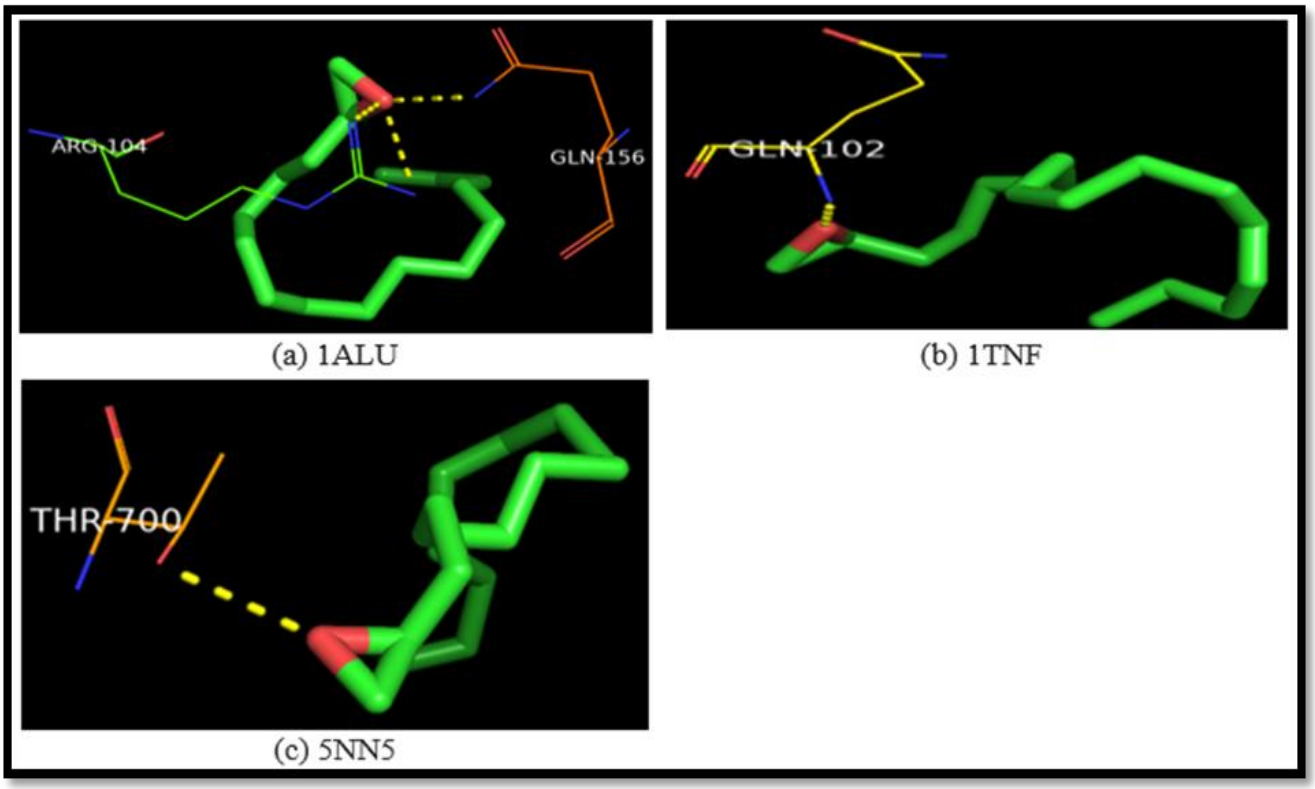


Figure 1: 3D structure of receptors 1ALU, 1TNF , 5NN5 and ligand 1,2-Epoxyhexadecane interaction with amino acids

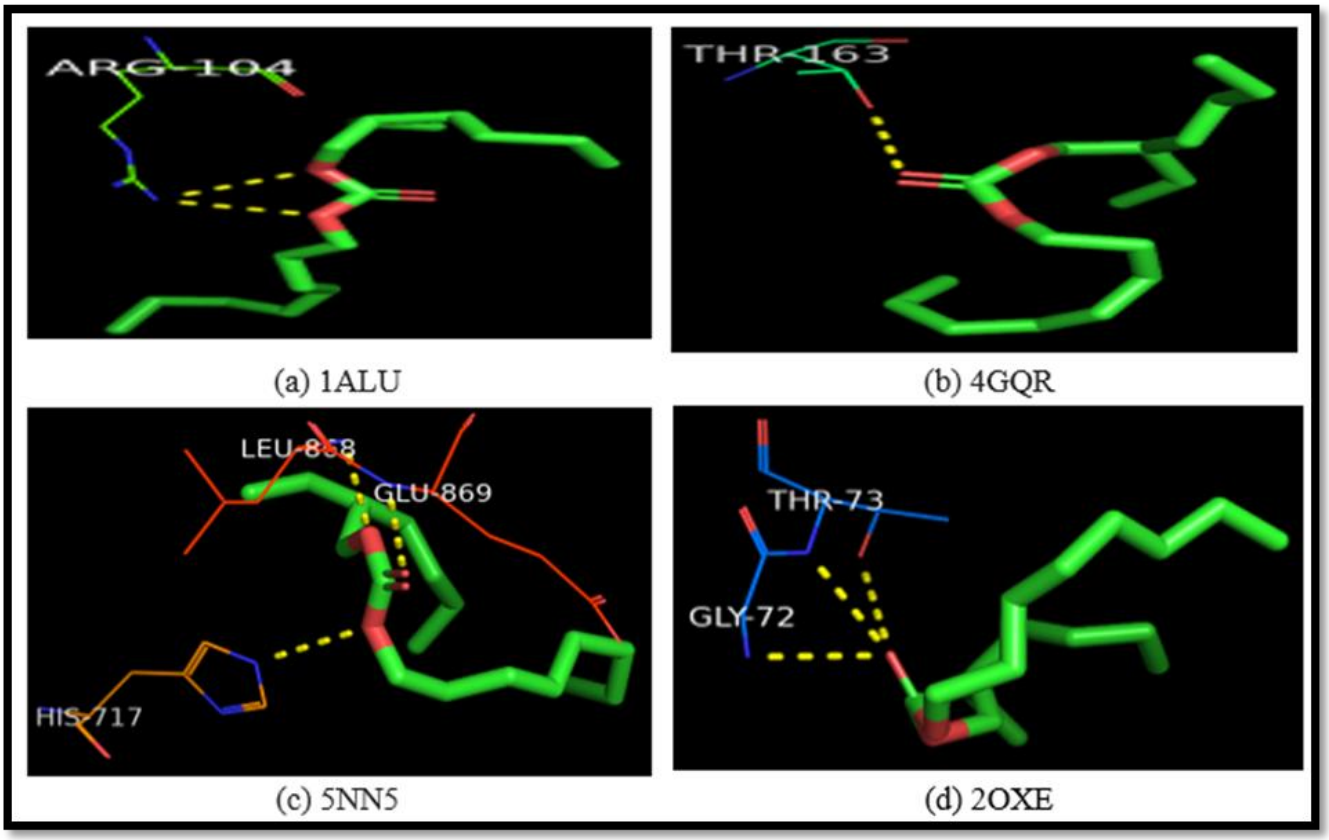


Figure 2: 3D structure of receptors 1ALU, 4GQR , 5NN5 ,2OXE and ligand 1 Carbonic acid, 2-ethylhexyl octyl ester interaction with amino acid

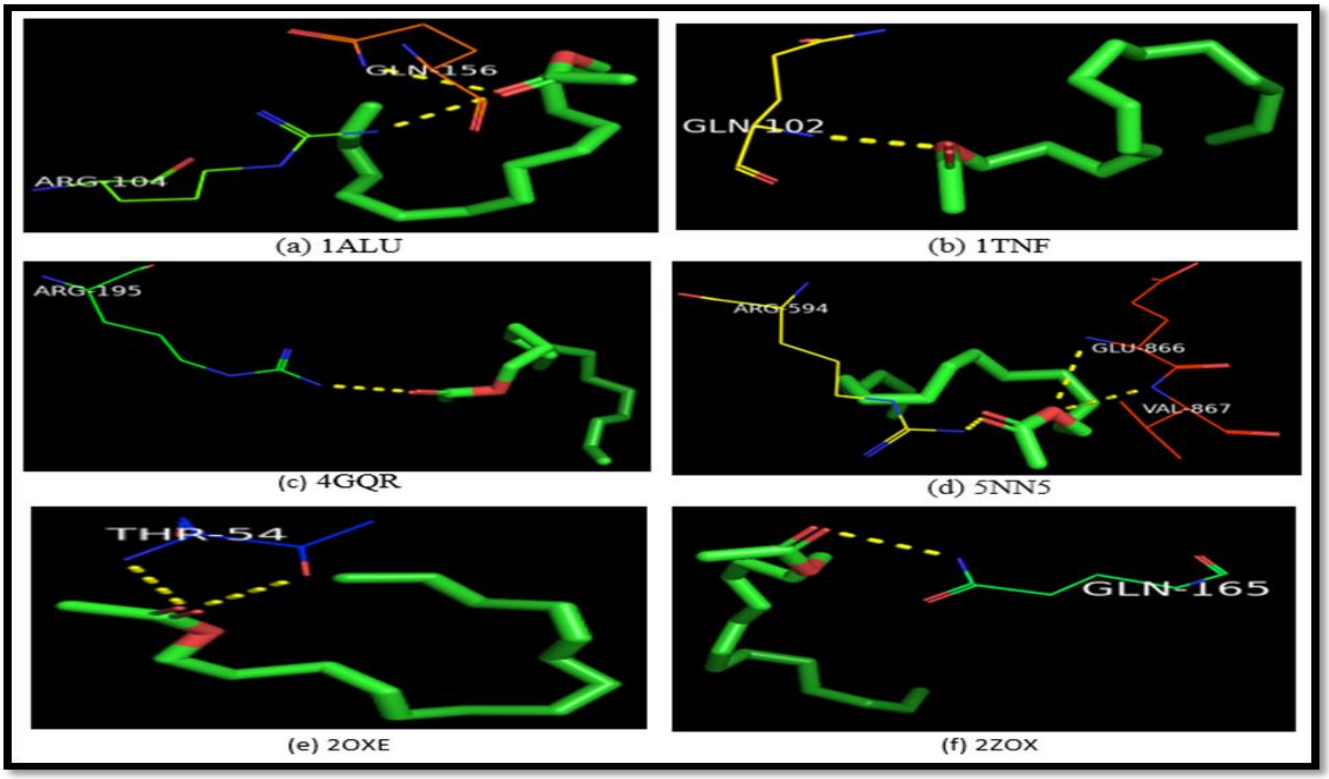


Figure 3: 3D structure of receptors 1ALU, 1TNF,4GQR , 5NN5 ,2OXE,2ZOX and ligand 13-Tetradecen-1-ol acetate interaction with amino acids

In literature survey 1, 2-Epoxyhexadecane found in through gc-ms for antibacterial activities of *Moringa oleifera* leaf extracts (Enerijiofi *et al*. 2021). 13-Tetradecen-1-ol acetate which have antioxidant and antitumor acrivity in many sources (Chun *et al*. 2010). 26-hydroxycholesterol can inhibit both cholesterol synthesis and low density lipoprotein (LDL) receptor activity and can useful in Alzheimer's disease prevention or slowing down its progression (Javitt, 1990). Citronellyl isobutyrate is a capable therapeutic representative in the dealing of type II diabetes in addition its associated complications (Atere *et al.,* 2017). So, we found many compounds which have along with antidiabetics, also have many therapeutic applications. That proved that this plant has many medicinal properties.

In silico drug-likeness, medicinal chemistry and toxicity prediction

Drug-likeness quantifies a likelihood of a compound becoming an oral medication. Structure, as well as physical and chemical inspections of development compounds, advanced sufficiently to be evaluated oral drug applicants revealed drug-likeness. The above concept is frequently utilised in filter chemical libraries in order for excluding compounds with characteristics that are most likely incompatible with such an acceptable oral bioavailability characteristic. One such category of SwissADME provides a variety of rule-based filters to varying distances of characteristics in which the compound is identified as drug-like. Such filters are frequently derived from analysis performed by major pharmaceutical corporations through order to enhance the quality of their proprietary chemical libraries. Multiple estimations enable the majority view or even the choice of approaches better suited to the end-specific user's specifications in terms of the drug molecule or project-related requirements. Whatever violation in any of the specific set of circumstances is here highlighted with in performance panel (Ani *et al*. 2020). Predicted drug-likeness parameters all six compounds show promising follow Lipinski rules but in veber rule alert except 26-hydroxy-cholesterol and Citronellyl isobutyrate, all four compounds follow this rule. Also, all the compounds show promising bioavailability Scores (Table 3).

Table 3**:** Predicted drug-likeness parameters of the screened compounds

Compounds	Lipinski rules					Veber rules		Veber #Violation	Bioavailability Score
	MW < 500	HBA <10	HBD <5	MLogP <4.15	Lipinski #Violation	nRB <10	TPSA Å <140		
1,2-epoxyhexadecane	240.42	1	0	4.06	Yes #0	13	12.53	No#1	0.55
Carbonic acid, 2-ethylhexyl octyl ester	286.45	3	0	3.96	Yes #0	15	35.53	N0 #1	0.55
13-Tetradecen-1-ol acetate	254.41	2	0	4.09	Yes #0	14	26.30	No#1	0.55
9H-Fluorene-9-carboxylic acid, tridecyl ester	392.57	2	0	5.68	Yes #1	14	26.30	No#1	0.55
26-hydroxy-cholesterol	402.65	2	2	5.41	Yes #1	6	40.46	Yes #0	0.55
Citronellyl isobutyrate	226.36	2	0	3.58	Yes #0	8	26.30	Yes #0	0.55

The goal of in medicinal Chemistry is really to assist medicinal chemists through there own frequent drug development activities. Two important information processing techniques can be used to evaluate potential troubling fragments. PAINS (pan assay interference compounds, also known as common hitters as well as promiscuous substances) are molecules with substructures that exhibit powerful reaction through assays regardless of a target protein. One of the crucial components actions is assisting in the choice among the most viable virtual molecules to be synthesised as well as evaluated in biochemical assays or even other experimental research. In the this screening process, syntheticaccessibility is an essential aspect to consider. Undoubtedly, medicinal chemists are indeed the greatest at determining Synthetic accessibility for just a sensible number of compounds (Daina *et al*. 2017). In addition, the compounds were evaluated for BRENK as well as PAIN alerts. Irrespective of a targeted protein becoming studied, such structural fragments as well as elements have been well-known to generate false-positive responses in in-silico assay methods. Such warnings must be looked at with caution.BRENK alerts, on the other side, illustrate fragments of various hazardous, reactive chemical, as well as metabolic processes instability substances. A Syntheticaccessibility Scoring system has been mainly based on the hypothesis that regularity of functional monomers in really obtainable compounds strongly correlated to synthesised comfort. A fragmental input to Syntheticaccessibility should be positive for commonly used chemical moieties as well as negative for rare moieties. Whenever there are too many small molecules formations to evaluate, in silico prediction can be employed for pre-filtering. A syntheticaccessibility score that ranges from one (extremely easy) to ten (extremely difficult) (Bakchi *et al.,* 2020). Predicted medicinal chemistry parameters all four compounds show no PAIN alert but in Brenk alert some compounds like 1,2-Epoxyhexadecane, 13-Tetradecen-1-ol acetate, 26-hydroxy-cholesterol and Citronellyl isobutyrate predicted a this alert. Throughout this research, none of the compounds tested positive for PAIN. This clearly shows that no structurally promiscuous moiety exists (otherwise known as frequent litters). Also all the compounds show promising Syntheticaccessibility Score (Table 4).

Table 4: Predicted medicinal chemistry parameters of the screened compounds

Compounds	PAINS #alerts	Brenk #alerts	Synthetic accessibility
1,2-epoxyhexadecane	0	1	2.86
Carbonic acid, 2-ethylhexyl octyl ester	0	0	3.67
13-Tetradecen-1-ol acetate	0	1	2.50
9H-Fluorene-9-carboxylic acid, tridecyl ester	0	0	3.84
26-hydroxy-cholesterol	0	1	6.09
Citronellyl isobutyrate	0	1	2.93

Estimation of chemical toxicity is indeed an essential step in the drugdiscovery progression. Computational toxicology guesstimates not only are quicker than animal hazardous dose determinations, but they may furthermore assist to decrease the number of

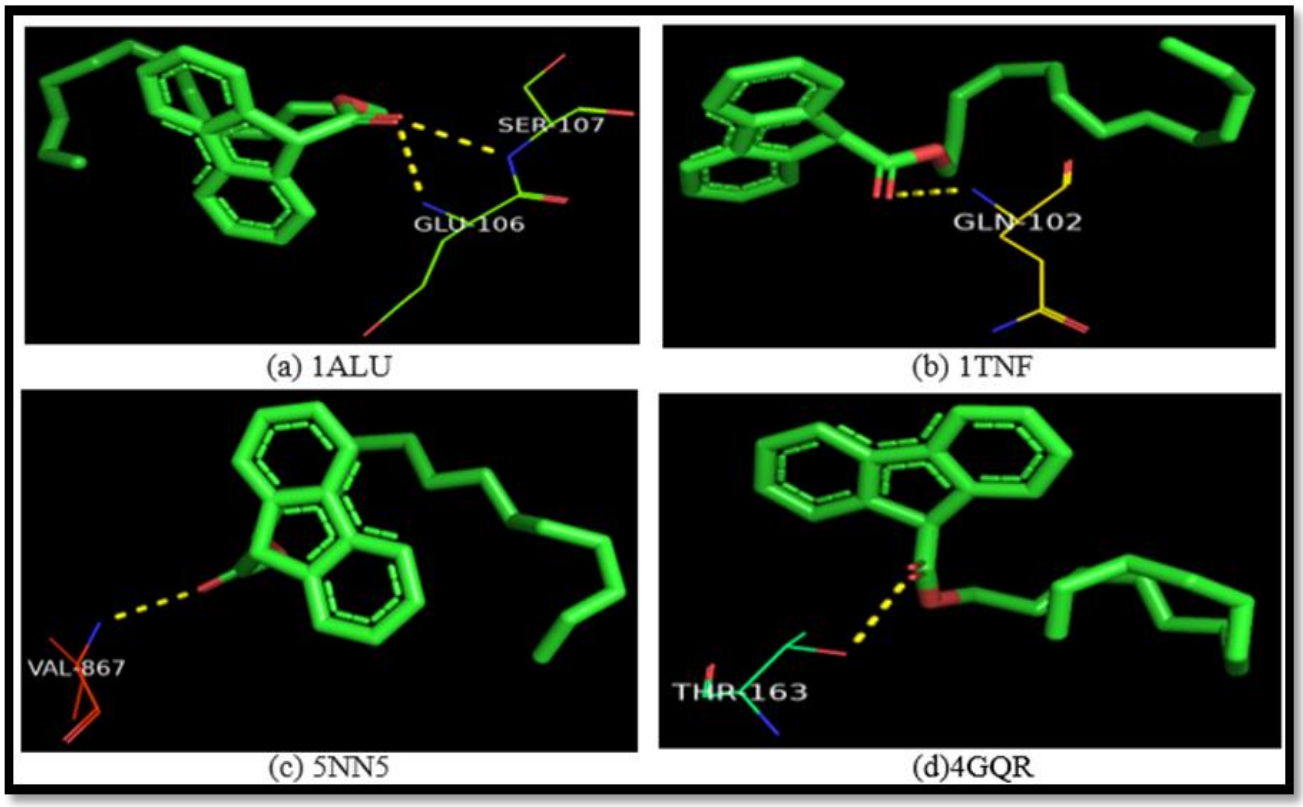


Figure 4: 3D structure of receptors 1ALU, 1TNF, 5NN5, 4GQR and ligand 9H-Fluorene-9-carboxylic acid, tridecyl ester interaction with amino acids

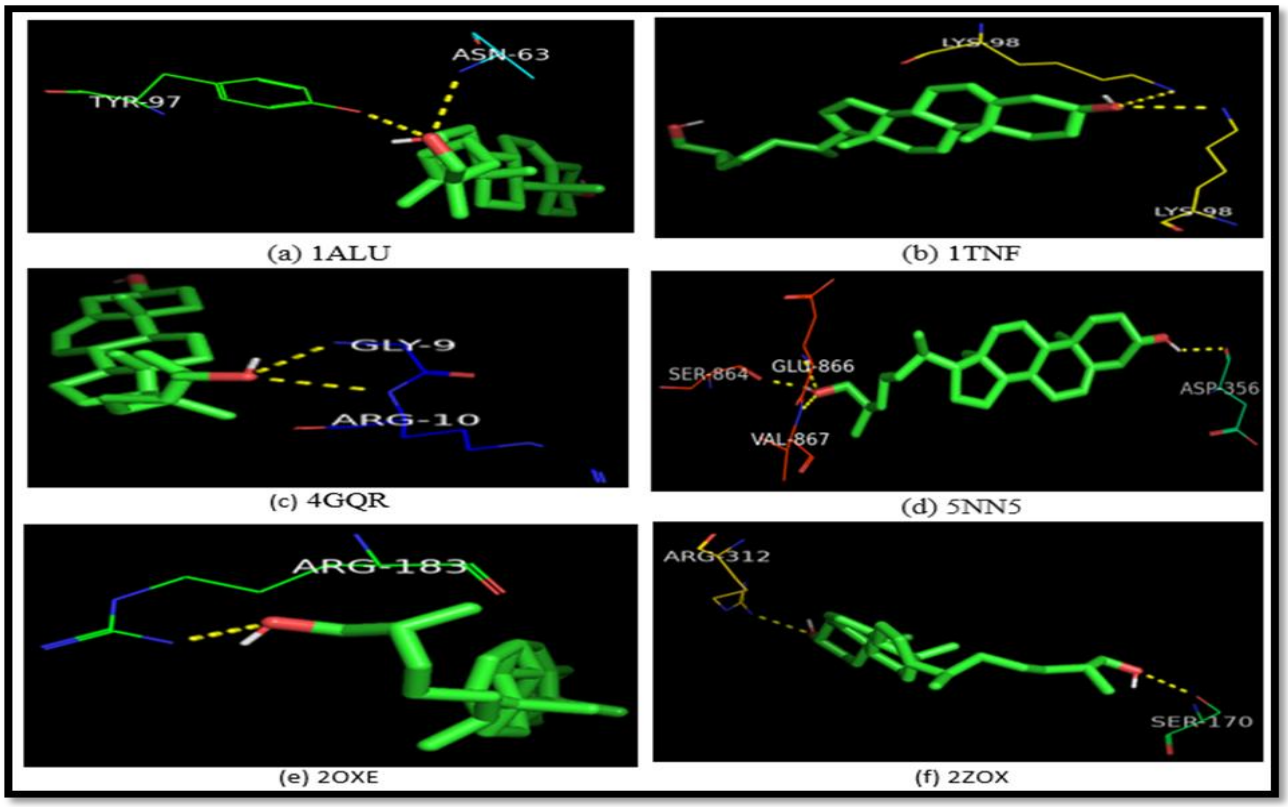


Figure 5: 3D structure of receptors 1ALU, 1TNF, 5NN5, 4GQR,2OXE,2ZOX and 26-hydroxy-cholesterol interaction with amino acids

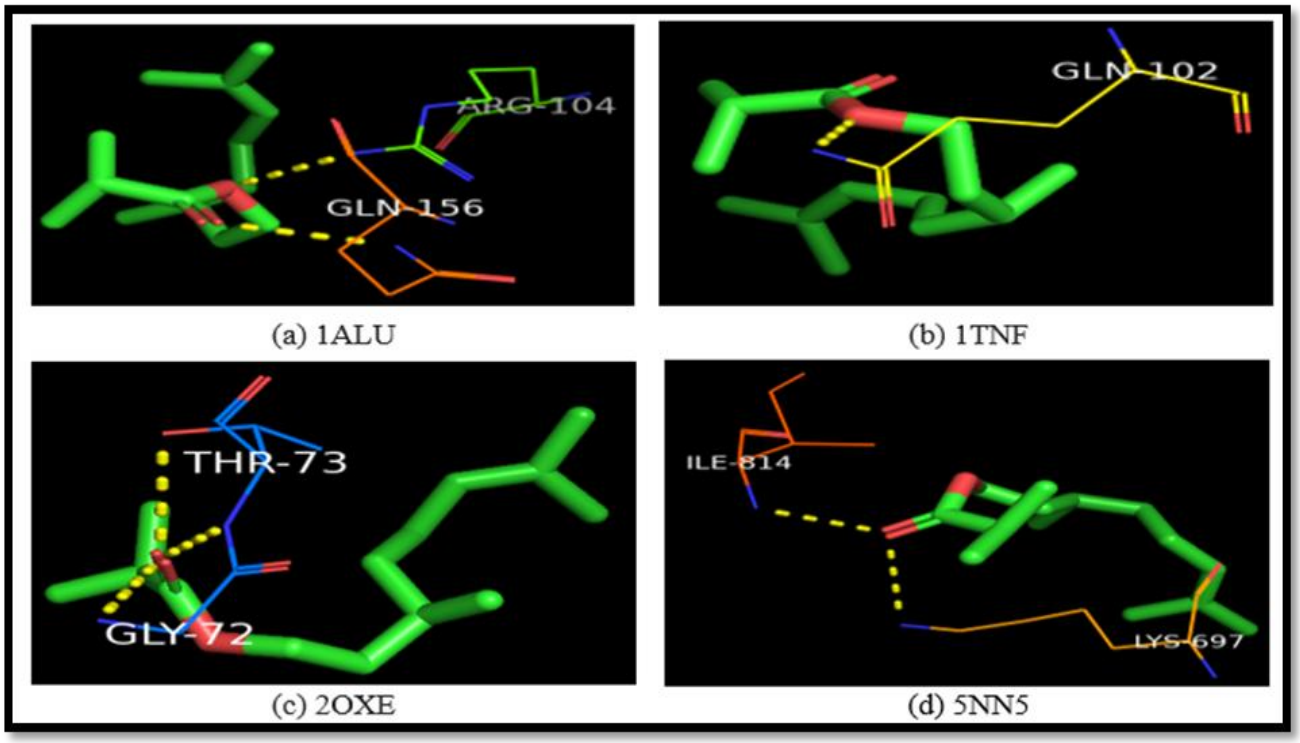


Figure 6: 3D structure of receptors 1ALU, 1TNF, 2OXE, 5NN5 and Citronellyl isobutyrate interaction with amino acids

animal research (Raies and Bajic,2016). Predictions of organ toxicity as well as three toxic effects endpoints including such cytotoxicity, mutagenicity, as well as immunotoxicity are discussed here. Hepatotoxicity is defined as liver failure as well as damage caused by an excess of prescription medications as well as foreign substances. A variety of factors can develop liver cell damage, which include drugs, toxic metabolites, medicinal herbs as well as nutritional probiotics, or other agents. Compounds which alter an individual's genetic information, generally DNA, have been classified as mutagens, and also the negative impacts are referred to as mutagenicity. Immunotoxins are substances that, when exposed, change the immune system function, as well as immunotoxicity is an adverse impact. The existing immunotoxicity prototype has been based on the inhibition of B cellular metabolism. Poisonous doses have been frequently expressed as LD50 value systems in mg/kg body mass. The median lethaldose (LD50) is indeed the dosage during which 50% of test group end up dying after being exposed to the a compound. Toxic effects groups are identified by the nationally and internationally harmonised system of substances labeling classification(Banerjee *et al*. 2018).

Each toxic effect, such as mutagenicity, cytotoxicity, and Immunotoxicity has a link to diabetes. Diabetes could be ended up caused by missense mutations inside the insulin receptor, which result in the making of mechanically irregular insulins to lowered biological processes as well as binding properties. Monogenicdiabetes mentions diabetes caused by mutations as well as alterations in a single gene. A genetic component causes type 2 diabetes (Nishi and Nanjo,2011). Immunotoxicity and diabetes are linked; Type 1 diabetes is indeed an autoimmune disorder. A body's immune system mistakenly targets pancreatic cells, destroying their capacity to produce insulin, a hormone that enables the body to control levels of blood sugar (DiMeglio *et al*. 2018). Through terms of cytotoxicity, reactive hypoglycemia in diabetes is thought to result in innate immunity dysfunction that also fails to control the dissemination of foreign microbes through diabetics (Berbudi, et al. 2020). In predicted toxicity, only 26-hydroxy-cholesterol shows toxicity inimmunotoxicityy.Others all five compounds are nontoxic compounds with high predicted Probability. (Table 5).

Table 5 Predicted toxicity parameters of the screened compounds

Compounds	Hepato toxicity #Probability	Immuno toxicity #Probability	Muta genicity #Probability	Cyto toxicity #Probability	Toxicity class	LD_{50} (mg/kg)
1,2-epoxyhexadecane	Inactive #0.84	Inactive #0.79	Inactive #0.99	Inactive #0.79	5	5000
Carbonic acid, 2-ethylhexyl octyl ester	Inactive #0.83	Inactive #0.99	Inactive #0.95	Inactive #0.83	5	2470
13-Tetradecen-1-ol acetate	Inactive #0.76	Inactive #0.98	Inactive #0.77	Inactive #0.77	5	5000
9H-Fluorene-9-carboxylic acid, tridecyl ester	Inactive #0.72	Inactive #0.92	Inactive #0.71	Inactive #0.77	6	6170
26-hydroxy-cholesterol	Inactive #0.77	Active #0.99	Inactive #0.85	Inactive #0.94	4	890
Citronellyl isobutyrate	Inactive #0.72	Inactive #0.99	Inactive #0.99	Inactive #0.81	5	5000

Therefore, it can be concluded from the results that from Anand city of medicinal plant *Trigonella foenum-graecum* leaves 1,2-Epoxyhexadecane , Carbonic acid, 2-ethylhexyl octyl ester, 13-Tetradecen-1-ol acetate, 9H-Fluorene-9-carboxylic acid, tridecyl ester, 26-hydroxy-cholesterol and Citronellyl isobutyrate compounds were identified by gas-chromatography– mass spectrometry analysis. In the current *in silico* docking study, results clearly demonstrated that all six compounds have antidiabetic potential but among the compounds, 26-hydroxy-cholesterol is the most efficient through antidiabetic activity. Furthermore, all six compounds have promising drug-likeness properties. In medicinal chemistry, all six compounds have not shown any PAIN alert but for BRENK alert some compounds show this alert. Also in toxicity, except 26-hydroxy-cholesterol compounds, all other five compounds are predicted as nontoxic compounds. Based on the present research work findings, it was identified that medicinal plant *Trigonella foenum-graecum* leaves have effective in antidiabetic action. All these plant leaves possessed significant antidiabetic activity may be due presence of compounds. There are very few studies on these plant leaves for anti-diabetic properties. Therefore, the current study has presented helpful information on the quality of these herbal materials to verify the authenticity, safety, and efficacy before commercial interest in both research institutes and pharmaceuticals companies for the manufacturing of newdrugs for the dealing of various diseases specifically diabetes mellitus by using an in silico pharmacoinformatic approach with a view to validate and prioritize promising compounds for further studies.

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REFERENCES

Abubakar, A., and Haque, M. (2020) Preparation of medicinal plants: Basic extraction and fractionation procedures for experimental purposes. *Journal of pharmacy & bioallied sciences*, **12**(1): 1.

Agarwal, P. and Gupta, R. (2016) Alpha-amylase inhibition can treat diabetes mellitus. *Res. Rev. J. Med. Health Sci*, **5**(4): 1-8

Ani, R. S., Anand, B., and Deepa, O. S. (2020) In Silico Prediction Tool for Drug-likeness of Compounds based on Ligand Based Screening. *International Journal of Research in Pharmaceutical Sciences***, 11**: 6273-6281 Doi:

Atere, T. G., Akinloye, O. A., Ugbaja, R. N., Ojo, D.A., and Metibemu, D.S. (2017) Molecular interactions and docking studies of the phytochemical constituents of costus afer against therapeutic targets of type 2 diabetes. *Journal of Applied Bioinformatics & Computational Biology*, **6**(2):

Bakchi, B., Krishna, A. D., Sreecharan, E., Ganesh, V. B. J., Niharika, M., Maharshi, S., Puttagunta ,S. B., Sigalapalli,D.K., Bhandare ,R. R. and Shaik, A. B. (2022) An Overview on Applications of SwissADME Web Tool in the Design and Development of Anticancer, Antitubercular and Antimicrobial agents: A Medicinal Chemist's Perspective. *Journal of Molecular Structure*, **1259**: 132712.

Banerjee, P., Eckert, A. O., Schrey, A. K., and Preissner, R. (2018) ProTox-II: a webserver for the prediction of toxicity of chemicals. *Nucleic acids research*, **46**(W1): W257-W263

Berbudi, A., Rahmadika, N., Tjahjadi, A. I., and Ruslami, R. (2020) Type 2 diabetes and its impact on the immune system. *Current diabetes reviews*, **16**(5): 442

Branch, S. (2013). Fenugreek (*Trigonella foenum-graecum* L.) as a valuable medicinal plant. *International Journal of Advanced Biological and Biomedical Research*, **1**: 922-931.

ChunYan, H., Hong, P., ZhenYu, Z., and Jing, S. (2010) Evaluation of antioxidant and antitumour activities of lemon essential oil. *J Med Plant Res*, **4**: 1910-5.

Daina, A., Michielin, O., and Zoete, V. (2017) SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. *Scientific reports*, **7**(1): 1-13

DiMeglio, L. A., Evans-Molina, C., and Oram, R. A. (2018) Type 1 diabetes. *The Lancet*, **391**(10138): 2449-2462.

Drwal, M. N., Banerjee, P., Dunkel, M., Wettig, M. R. and Preissner, R. (2014) ProTox: a web server for the in silico prediction of rodent oral toxicity. *Nucleic acids research*, **42**(W1): W53-W58

Enerijiofi, K. E., Akapo, F. H., and Erhabor, J. O. (2021) GC–MS analysis and antibacterial activities of Moringa oleifera leaf extracts on selected clinical bacterial isolates. *Bulletin of the national research centre*, **45**: 1-10

Ferreira, L. G., and Ricardo, N. (2015) Dos Santos, Glaucius Oliva, and Adriano D. Andricopulo. *Molecules*, **20**, 13384-13421

Gupta, K., and Mamidi, P. (2020) Mumurshiyam of Bhela Indriya Sthana: An explorative study. *Journal of Integrated Health Sciences*, **8**: 109-17

Javitt, N. B. (1990) 26-Hydroxycholesterol: synthesis, metabolism, and biologic activities. *Journal of Lipid research*, **31**(9): 1527-1533.

Koria, B., Kumar, R., Nayak, A., and Kedia, G. (2013) Prevalence of diabetes mellitus in urban population of Ahmadabad city, Gujarat. *National Journal of Community Medicine*, **4**(03), 398-401.

Lipinski C.A., Lombardo F., Dominy B.W. and Feeney P.J. (2001) Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. *Adv. Drug. Deliv. Rev*. **46**: 3–26.

Nishi, M., and Nanjo, K. (2011). Insulin gene mutations and diabetes. *Journal of diabetes investigation*, **2**(2): 92-100

Ononamadu, C. J., and Ibrahim, A. (2021) Molecular docking and prediction of ADME/drug-likeness properties of potentially active antidiabetic compounds isolated from aqueous-methanol extracts of Gymnema sylvestre and Combretum micranthum. *BioTechnologia. Journal of Biotechnology Computational Biology and Bionanotechnology*, **102**(1): 85-99.

Padma, M., Ganesan, S., Jayaseelan, T., Azhagumadhavan, S., Sasikala, P., Senthilkumar, S., and Mani, P. (2019) Phytochemical screening and GC–MS analysis of bioactive compounds present in ethanolic leaves extract of Silybum marianum (L). *Journal of drug delivery and therapeutics*, **9**(1): 85-89.

Raies, A. B., and Bajic, V. B. (2016). In silico toxicology: computational methods for the prediction of chemical toxicity. *Wiley Interdisciplinary Reviews: Computational Molecular Science*, **6**(2): 147-172.

Rehani, P. R., Iftikhar, H., Nakajima, M., Tanaka, T., Jabbar, Z. and Rehani, R. N. (2019) Safety and mode of action of diabetes medications in comparison with 5-aminolevulinic acid (5-ALA). *Journal of Diabetes Research*, **2019**:10.

Rehman, K., Akash, M.S.H., Liaqat, A., Kamal, S., Qadir, M.I. and Rasul, A. (2017) Role of interleukin-6 in development of insulin resistance and type 2 diabetes mellitus. *Critical Reviews in Eukaryotic Gene Expression*, **27**(3).

Shi, J., Fan, J., Su, Q. and Yang, Z. (2019) Cytokines and abnormal glucose and lipid metabolism. *Frontiers in endocrinology*, **10**: 703.

Tushuizen, M.E., Bunck, M.C., Pouwels, P.J., Bontemps, S., Van Waesberghe, J.H.T., Schindhelm, R.K., Mari, A., Heine, R.J. and Diamant, M. (2007) Pancreatic fat content and β-cell function in men with and without type 2 diabetes. *Diabetes care*, **30**(11): 2916-2921.

Veber D.F., Johnson S.R., Cheng H.Y., Smith B.R., Ward K.W. and Kopple K.D. (2002) Molecular properties that influence the oral bioavailability of drug candidates. *J. Med. Chem.* **45**(12): 2615–2623.