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Research Article

Docking-Based Screening of *Momordica charantia* Compounds Against Diabetes-Related Targets

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ABSTRACT

The use of natural compounds has become increasingly preferred for mitigating severe complications associated with diabetes mellitus, owing to their low cost and minimal side effects. The present study aims to evaluate the in vitro α-amylase inhibitory activity and examine the molecular interactions of various phytocompounds present in the seeds of Momordica charantia Linn. These compounds include 15-Demethyl plumieride, Ellagic Acid, 3,4-Dihydroxybenzoic Acid, Stigmasta-7,25-dien-3beta-ol, D-Galactouranic Acid, Trehalose. Molecular docking studies were performed using the three-dimensional structures of these compounds against the diabetic target protein, α-amylase. Additionally, two-dimensional interactions were analyzed using ligand interaction diagrams. The softwares like PyRx, Biovia Discovery Studio were used. The results indicated that bioactive compounds such as 15-Demethyl plumieride, Ellagic Acid, Stigmasta-7,25-dien-3beta-ol exhibited higher binding affinities (>7.5 kcal/mol) toward the target protein. Furthermore, the α-amylase inhibition assay demonstrated that the seed extract possesses significant antidiabetic potential. These findings suggest that the identified bioactive compounds can be further isolated and investigated through in vivo studies as promising antidiabetic agents.

INTRODUCTION

1.1. DRUG DISCOVERY

Drug discovery is a multifaceted process, which involves identification of a drug chemical therapeutically useful in treating and management of a disease condition. Typically, researchers find out new drugs through new visions into a disease process that permit investigator to design a medicine to stopover or contrary the effects of the disease. The process of drug discovery includes the identification of drug candidates, synthesis,

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characterization, screening, and assays for therapeutic efficacy. When a molecule avails its satisfactory results in these investigations, it will commence the process of drug development subsequent to clinical trials. Drug discovery and development is an expensive process due to the high budgets of R&D and clinical trials. It takes almost 12-15 years to develop a single new drug molecule from the time it is discovered when it is available in market for treating patients. These statistics challenge imagination, but a brief understanding of the R&D process can explain why so many compounds don't make it and why it takes such a large, lengthy effort to get one medicine to patients. The Success requires immense resources the best scientific and logical minds, highly sophisticated laboratory and technology; and multifaceted project management. It also takes persistence and good fortune. Eventually, the process of drug discovery brings hope, faith and relief to billions of patients[32].

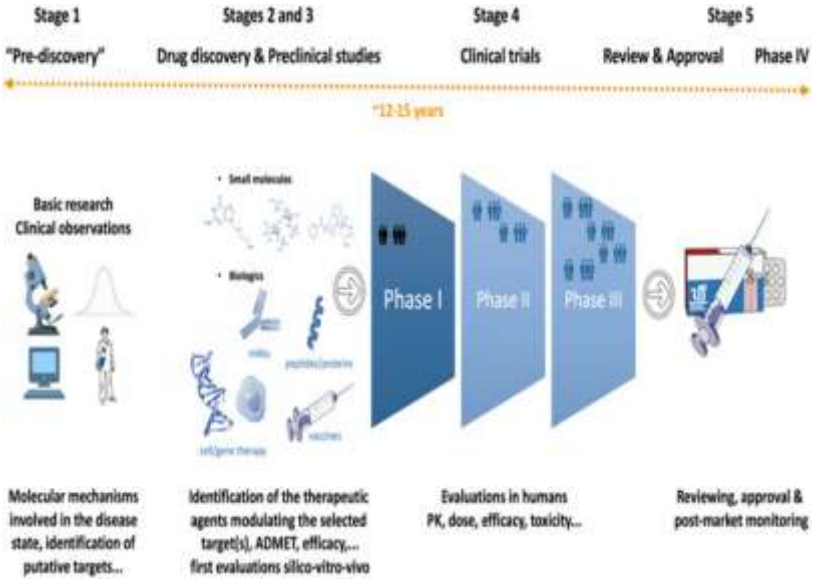


Figure 1: Drug Discovery and Development

1.2. SCREENING AND DESIGN

1. Structure-based drug design (SBDD)

Structure-based drug design is the technique to be used in drug design. Structure-based drug design helps in the discovery process of new drugs. SBDD, or direct drug design, relies on knowledge of the 3D structure of the biological target (protein) obtained through methods such as x-ray crystallography or NMR spectroscopy Flow chart of CADD processes. Structure of target protein Information of target protein structures Information of the structure of ligands Structure based drug design Ligand based drug design Ligand docking De novo design MD Pharmacophore modeling QSAR Pharmacophore modeling Ligand based virtual screening Propose new lead or optimize existing lead Drug to start the paradigm of SBDD structure. The crystal structure should be well defined, with a resolution of at least 2.5 Å typically considered to be necessary.

In cases in which the 3D structure of the target is not available, a virtual model can be generated by homology modeling of the nearest target related protein for which the 3D structure is known and available. However, unless there is very high conservation of receptor site residues, the use of homology models of virtual screening is much riskier than using solved structures.[32]

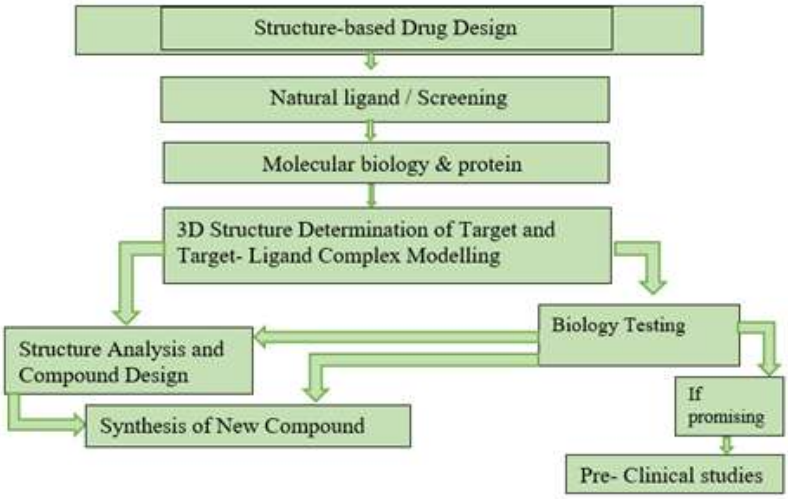


Figure 2: Structure based Drug Design

2. Ligand-Based Drug Design (LBDD)

Ligand-based drug design, or indirect drug design, relies on knowledge of other known active molecules with the potential against biological targets of interest. Pharmacophore models are derived from these known molecules to define the necessary structural characteristics to enable binding to the biological target. Alternatively, in quantitative structure-activity relationship (QSAR), we derive the correlation between the calculated molecular properties of a compound and their experimentally determined biological activity. These predicated QSAR correlations may in turn be used to predict the activity of novel analogs. The ligand-based drug design approach involves the analysis of ligands known to interact with a target. These methods use a set of reference structure collected from compounds known to interact with the target of interest and analysis their 2D or 3D structure. In some cases, usually in which data pertaining to the 3D structure of a target protein are not available, drug design can instead be based on process using the known ligands of a target protein as the starting point. This approach is known as "ligand-based drug design".[33]

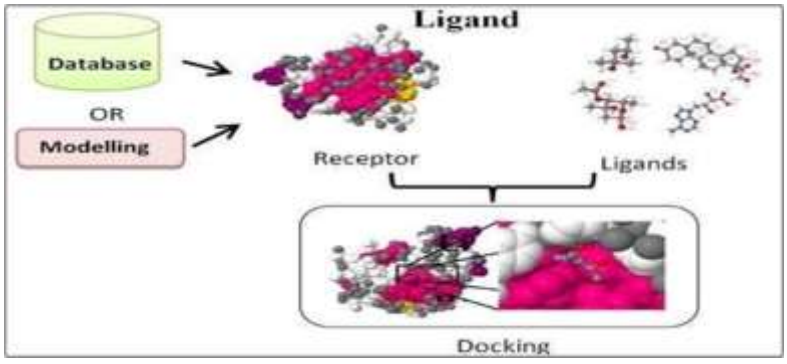


Figure 3: Ligand based Drug Design

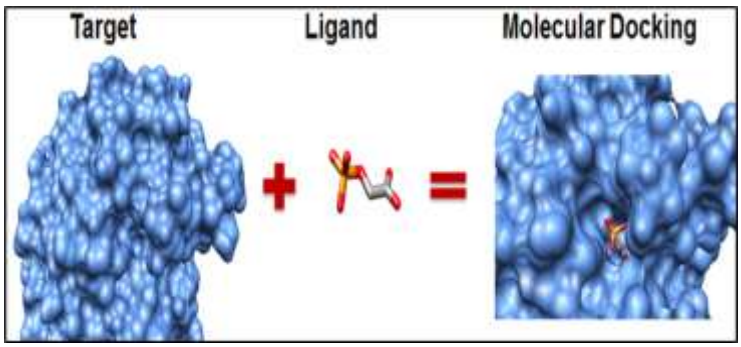


Figure 4: Molecular docking

3. Molecular Docking

Molecular docking is the computational modeling of the structure of complexes formed by two or more interacting molecules. The goal of molecular docking is the prediction of the three-dimensional structure. Docking plays an important role in the rational design of drugs. The aim of molecular docking is to achieve an optimized conformation for both the protein and ligand so and relative orientation between protein and ligand so that the free energy of the overall system is minimized. Molecular recognition plays a key role in promoting fundamental biomolecular events such as enzyme-substrate, drug-protein and drug-nucleic acid interaction.

Docking theory: The following docking theory topics are available:

1. CDOCKER : Uses a random preliminary ligand placement and full CHARMm forcefield based docking.

2. LibDock: Fast docking-based on binding site features ('hotspots').

3. LigandFit: Docking-based on an initial shape match to the binding site.

4. MCSS: Uses CHARMm to dock fragments by using a unique computationally efficient Multiple Copy Simultaneous Search algorithm.

Drug-receptor interactions occur on atomic scales. To form a deep understanding of how and why drug compounds bind to protein targets, we must consider the biochemical and biophysical properties of both the drug itself and its target at an atomic level. Swiss PDB (protein data bank) is an excellent tool for doing this.

It can predict key physicochemical properties, such as hydrophobicity and polarity that have a profound influence on how drugs bind to proteins[31].

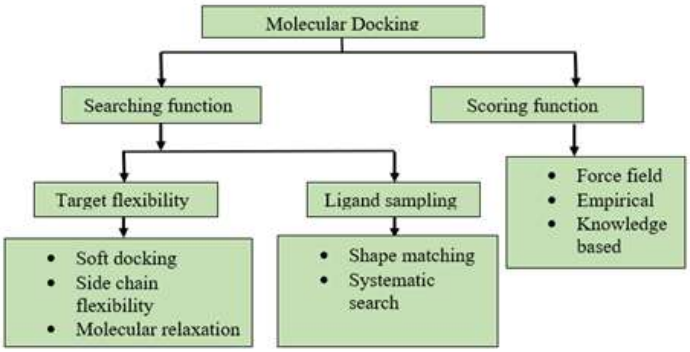


Figure 5: Method used for protein ligand docking

Applications and importance of molecular docking:

The uses of docking programs to indicate the nature of the atoms and functional groups present in the 3D (three-dimensional) structures also enable to examine the binding of a drug to its target site.

4. Quantitative Structure Activity Relationship (QSAR)

Quantitative structure-activity relationship (QSAR) modeling pertains to the construction of predictive models of biological activities as a function of structural and molecular information of a compound library. The concept of QSAR has typically been used for drug discovery and development and has gained wide applicability for correlating molecular information with not only biological activities but also with other physicochemical properties, which has therefore been termed quantitative structure-property relationship (QSPR). Typical molecular parameters that are used to account for electronic properties, hydrophobicity, steric effects, and topology can be determined empirically through experimentation or theoretically via computational chemistry. A given set of data sets is then subjected to data pre-processing and data modeling through the uses of statistical or machine learning techniques. This review aims to cover the essential concepts and techniques that are relevant for performing QSAR/QSPR studies through the uses of selected examples from our previous work.

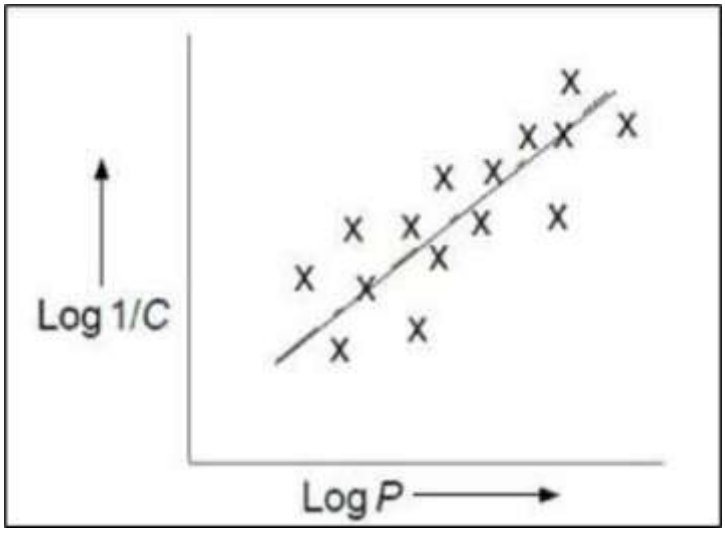


Figure 6: A hypothetical plot of the activity (Log1/C) of a series of compounds against the logarithm of partition coefficient parameter's (LogP).

Regression analysis is a group of mathematical methods of QSAR used to obtain mathematical equations relating different sets of data that have been obtained from experimental work or calculated using theoretical study. The data are fed into a suitable computer program, which, on execution, produces an equation that represents the line that is the best fit for those data. Regression analysis would calculate the values of m and c that gave the line of best fit to the data.

1.3. COMPUTER AIDED DRUG DESIGN

The development of new drugs is no longer a process of trial and error or strokes of luck in the field of research, it has become a delicate process depends mainly on the overlapping medical and pharmaceutical science and informatics. The explosive development of computer technology and methodologies to calculate molecular properties have increasingly made it possible to

use computer technique to aid the drug discovery process.

Computer-aided drug design is a pc era that designs a product and files the design's technique. CADD can also facilitate the manufacturing system through shifting unique diagrams of a products materials, methods, tolerances and dimensions with unique conventions for the product in query. It can be used to supply both two-dimensional or 3-dimensional diagrams, that can then when rotated to be considered from any attitude, even from the inside searching out. The channel of drug discovery from concept to marketplace includes seven fundamental steps: ailment choice, target selection, lead compound identification, lead optimization, pre-medical trial trying out, medical trial checking out and pharmacogenomic optimization. In practice, the closing five steps required to skip again and again.

The compounds for trying out may be obtained from herbal supply (Plants, animals, microorganisms) and by using chemical synthesis. These compounds can be rejected as perspectives owing to absence or low hobby, life of toxicity or carcinogenicity, complexity of synthesis, inadequate performance etc. As a result, simplest one of a hundred thousand investigated compounds may be delivered to the market and one average fee of improvement of latest drug rose as much as 800 million bucks. The discount of time-ingesting and value of the last ranges of drug trying out is not likely due to strict kingdom popular on their cognizance. Therefore, essential efforts to increasing performance of development of medicine are directed to levels of discovery and optimization of ligands.[34]

ADVANTAGES OF CADD:

- Less Time requires
- Accuracy
- information about the disease
- Increase productivity & higher quality designs.
- screening is reduced
- Database screening & optimization
- less manpower is required
- CADD gives valuable information about target molecules,

The latest advancements like QSAR, combinatorial chemistry different databases & available new software tools provide a basis for designing of ligands & inhibitors that require specificity.

APPLICATION OF CADD:

- Determine the lowest free energy structures for the receptor-ligand complex Search database and rank hits for lead generation.
- Calculate the differential binding of a ligand to two different macromolecular receptors. Study the geometry of a particular complex Propose modification of a lead molecules to optimize potency or other properties de novo design for lead generation.
- Library design.
- Design Review and Evaluation. Review and Evaluation is checking whether the designed part has been designed properly.[34]

BENEFITS OF CADD:

CADD methods and bioinformatics tools offer significant benefits for drug discovery programs.

- Cost Savings: - The Tufts Report suggests that the cost of drug discovery and development has reached $800 million for each drug successfully brought to market. Many biopharmaceutical companies now use computational methods and bioinformatics tools to reduce this cost burden. Virtual screening, lead optimization and predictions of bioavailability and bioactivity can help guide experimental research. Only the most promising experimental lines of inquiry can be followed and experimental dead-ends can be avoided early based on the results of CADD simulations.

- Time-to-Market: - The predictive power of CADD can help drug research programs choose only the most promising drug candidates. By focusing drug research on specific lead candidates and avoiding potential "dead-end" compounds, biopharmaceutical companies can get drugs to market more quickly.

- Drug Development: - Researchers in Germany report an advance toward the much-awaited era in which scientists will discover and design drugs for cancer, arthritis, AIDS and other diseases almost entirely on the computer, instead of relying on the trial-and error methods of the past. In the report, Michael C. Hutter12 and colleagues note that computer-aided drug design already is an important research tool. The method involves using computers to analyze the chemical structures of potential drugs and pinpoint the most promising candidates. Existing computer programs check a wide range of chemical features to help distinguish between drug-like and nondrug materials. These programs usually cannot screen for all features at the same time, an approach that risks overlooking promising drug-like substances. In the new study, researchers describe a more gradual and efficient system. Their new program uses an initial quick screen for drug-like features followed immediately by a second, more detailed screen to identify additional drug -like features. They applied this new classification scheme to a group of about 5,000 molecules that had previously been screened for drug-like activity. The new strategy was more efficient at identifying drug-like molecules "whereby up to 92 percent of the non-drugs can be sorted out without losing considerably more drugs in the succeeding steps," the researchers say.[34]

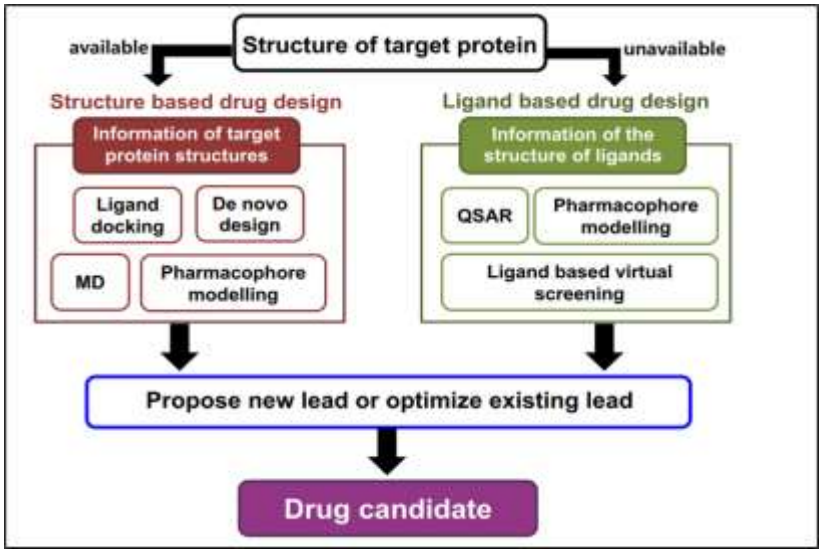


Figure 7: Flow chart of CADD process

1.4. VIRTUAL SCREENING

Virtual screening is a computational method where large libraries of compounds are assessed for their potential to bind specific sites on target molecules such as proteins and well-compounds tested. Virtual screening is a computational technique used in drug discovery research. By using computers, it deals with the quick search of large libraries of chemical structure in order to identify those structures which are most likely to bind to a drug target, typically a protein receptor or enzyme. Virtual screening has become an integral part of the drug target, typically a protein receptor or enzyme. Virtual screening has become an integral part of the drug discovery process. Related to the more general and longer pursued concept of database searching, the term "virtual screening" is relatively new. Virtual screening has largely been a numbers game focusing on questions like how can we filter down the enormous chemical space of over 1060 conceivable compounds to a manageable number that can be synthesized, purchased and tested. Although filtering the entire chemical universe might be a fascinating question, more practical virtual screening scenarios focus on designing and optimizing targeted combinatorial libraries and enriching libraries of available compounds from in-house compound repositories or vendor offerings. It is less expensive than high-throughput screening, faster than conventional screening, scanning a large number of potential drugs like molecules in very less time.

Virtual screening can be used to:

− Select compounds for screening from in-house database.

− Choose compounds to purchase from external suppliers.

− Decide which compounds to synthesize next.

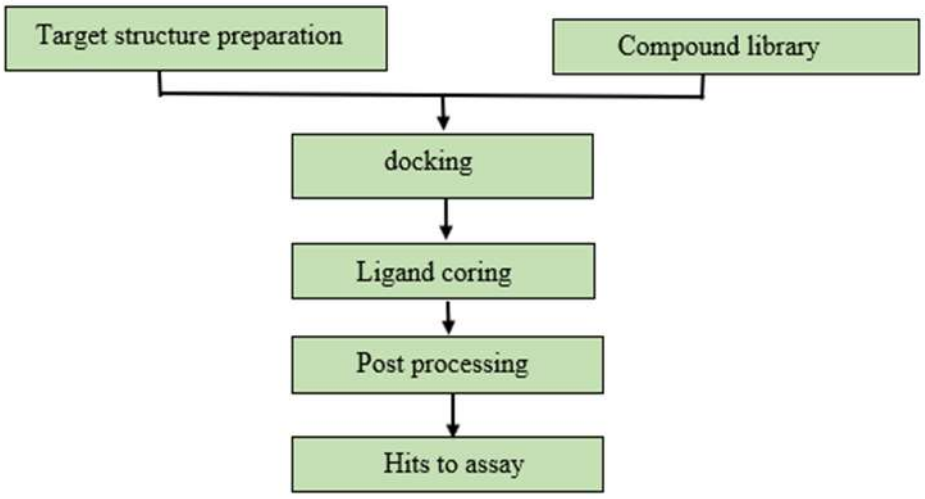


Figure 8: Virtual Screening

1.5 DIABETES MELLITUS

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia (high blood glucose levels) resulting from defects in insulin secretion, insulin action, or both. Insulin is a vital anabolic hormone responsible for regulating the metabolism of carbohydrates, lipids, and proteins, and any disturbance in its function leads to metabolic imbalance. The condition primarily affects key tissues such as the liver, skeletal muscles, and adipose tissue, causing impaired glucose utilization and increased blood sugar levels. The severity and presentation of symptoms

vary depending on the type and duration of the disease; some individuals may experience excessive thirst, frequent urination, increased appetite, weight loss, and blurred vision, while others, especially in early stages of type 2 diabetes, may remain asymptomatic. If left uncontrolled, diabetes can lead to serious acute and chronic complications such as diabetic ketoacidosis, cardiovascular diseases, kidney failure, neuropathy, and retinopathy. Over the past decades, diabetes has emerged as a major global public health concern due to its rapidly increasing prevalence, high morbidity, and associated mortality, making its prevention and management critically important.

CLASSIFICATION

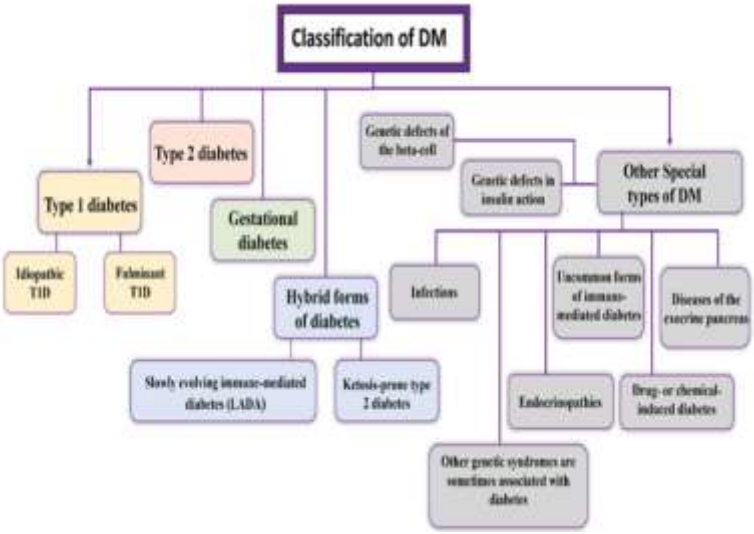


Fig 9:- Classification of Diabetes Mellitus, Represents different types of Diabetes Mellitus

RISK FACTORS

Diabetes mellitus is influenced by several genetic and lifestyle-related factors. A family history of diabetes increases susceptibility, while obesity and a sedentary lifestyle are major contributors to insulin resistance.

Unhealthy dietary habits, particularly high sugar and fat intake, further elevate risk. Advancing age, along with conditions like hypertension, dyslipidemia, and PCOS, also play a significant role. Additionally, a history of gestational diabetes, chronic stress, and environmental factors can increase the likelihood of developing diabetes.

Key Points:

- Family history
- Obesity
- Physical inactivity
- Unhealthy diet
- Age
- Hypertension & PCOS
- Gestational diabetes
- Stress & environment

PREVENTION

Diabetes mellitus can be prevented and managed through healthy lifestyle practices and appropriate medical care. Prevention focuses on maintaining a healthy weight, following a balanced diet, and engaging in regular physical activity to improve

insulin sensitivity. Early monitoring of blood glucose levels helps in timely detection.

Treatment includes lifestyle management along with medications such as oral antidiabetic drugs or insulin therapy, depending on the condition.

Key Points:

- Healthy diet and weight management
- Regular physical activity
- Routine blood glucose monitoring
- Avoid sedentary lifestyle
- Use of antidiabetic medications/insulin
- Management of comorbid conditions
- Stress control and regular medical check-ups

1.6. ANTI-DIABETIC DRUG

Diabetes is widespread worldwide, and there is concern that the mortality rate due to diabetes will increase. Until now, various antidiabetic drugs have been used to improve the pathological condition in diabetes patients. It has been reported that some antidiabetic drugs not only improve blood glucose levels but may prolong life. Antidiabetic drugs include acarbose, metformin, and sodium-glucose cotransporter 2 (SGLT2) inhibitors, which are considered as types of drugs that can induce direct glucose excretion from the body. The mechanism underlying the effect of these drugs is expected to involve a calorie restriction-mimicking effect by direct glucose excretion, and not just an effect whereby the disease state is improved. From the latest findings, it has become clear that these antidiabetic drugs have many health benefits not limited to the treatment of diabetes, i.e., these drugs may extend the life of not only diabetes patients but also those without diabetes.

1. BITTER MELON

Bitter melon (Momordica charantia) is a tropical vine widely cultivated in Asia, Africa, and the Caribbean for its nutritional and medicinal value. It belongs to the gourd family and is easily recognized by its rough, elongated fruit and distinctly bitter taste. The plant is rich in vitamins such as vitamin C and bioactive compounds that contribute to its antioxidant properties. In culinary practices, it is commonly used in stir-fries, curries, and traditional dishes despite its bitterness. Bitter melon also holds an important place in traditional healing systems like Ayurveda. It is especially studied for its potential role in managing Type 2 Diabetes and improving metabolic health.

TAXONOMICAL CLASSIFICATION

Kingdom: Plantae

Phylum: Tracheophyta

Order: Cucurbitales

Family: Cucurbitaceae

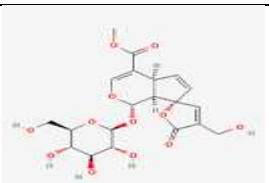
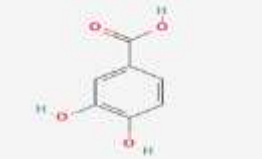
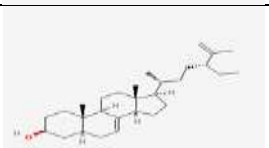
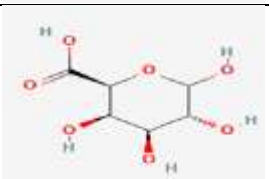
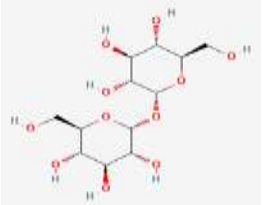
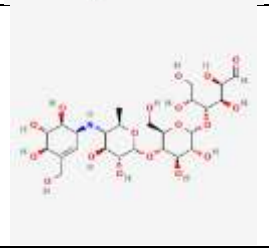
Genus: Momordica L

Species: Momordica charantia

BIOLOGICAL SOURCE

It is the fresh or dried unripe fruit, leaves, and seeds of the tropical vine Momordica charantia Linn.. It belongs to the family Cucurbitaceae

Table 1: Chemical Constituents of Bitter Melon with their structure

Sr. No.	Ligands	IUPAC Name	2D Structure
1	15-Demethyl plumieride	methyl (1*S*,4*aS*,7*R*,7*aS*)-4'-(hydroxymethyl)-5'-oxo-1-[(2*S*,3*R*,4*S*,5*S*,6*R*)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxyspiro[4*a*,7*a*-dihydro-1*H*-cyclopenta[c]pyran-7,2'-furan]-4-carboxylate	
2	Ellagic acid	6,7,13,14-tetrahydroxy-2,9-dioxatetracyclo[6.6.2.04,16.011,15]hexadeca-1(15),4,6,8(16),11,13-hexaene-3,10-dione	
3	Protocatechuic Acid	3,4-dihydroxybenzoic acid	
4	Stigmasta-7,25-dien-3beta-ol	(3*S*,5*S*,9*R*,10*S*,13*R*,14*R*,17*R*)-17-[(2*R*,5*R*)-5-ethyl-6-methylhept-6-en-2-yl]-10,13-dimethyl-2,3,4,5,6,9,11,12,14,15,16,17-dodecahydro-1*H*-cyclopenta[a]phenanthren-3-ol	
5	D-Galacturonic Acid	(2*S*,3*R*,4*S*,5*R*)-3,4,5,6-tetrahydroxyoxane-2-carboxylic acid	
6	Trehalose	(2*R*,3*S*,4*S*,5*R*,6*R*)-2-(hydroxymethyl)-6-[(2*R*,3*R*,4*S*,5*S*,6*R*)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxyoxane-3,4,5-triol	
7	Acarbose (Standard)	(2*R*,3*R*,4*R*,5*R*)-4-[(2*R*,3*R*,4*R*,5*S*,6*R*)-5-[(2*R*,3*R*,4*S*,5*S*,6*R*)-3,4-dihydroxy-6-methyl-5-[[(1*S*,4*R*,5*S*,6*S*)-4,5,6-trihydroxy-3-(hydroxymethyl)cyclohex-2-en-1-yl]amino]oxan-2-yl]oxy-3,4-dihydroxy-6-(hydroxymethyl)oxan-2-yl]oxy-2,3,5,6-tetrahydroxyhexanal	

USES

1. Antidiabetic Activity:

One of the most studied effects is its ability to lower blood glucose levels, making it beneficial in managing Type 2 Diabetes by improving insulin sensitivity and glucose uptake.

2. Antioxidant Activity:

It contains phenolic compounds and flavonoids that help neutralize free radicals, thereby reducing oxidative stress in the body.

3. Anti-inflammatory Activity:

Bitter melon shows the ability to reduce inflammation by inhibiting pro-inflammatory mediators, which may help in chronic inflammatory conditions.

4. Antimicrobial Activity:

Extracts of the plant demonstrate activity against various bacteria, viruses, and fungi, supporting its traditional use in treating infections.

5. Anticancer Activity:

Preliminary studies suggest that it may inhibit the growth of certain cancer cells by inducing apoptosis and preventing tumor proliferation.

6. Hypolipidemic Activity:

It helps in lowering cholesterol and triglyceride levels, contributing to cardiovascular health.

7. Immunomodulatory Activity:

Bitter melon can enhance immune response by stimulating immune cells and improving overall immunity.

2. AIM AND OBJECTIVE

AIM

To perform Docking-Based Screening of Momordica charantia Compounds Against Diabetes-Related Targets

OBJECTIVE

- Draw structure of phytoconstituents of *Momordica Charantia Linn*
- Study of physiochemical property of phytoconstituents
- Study of ADME
- Study of toxicity
- Molecular docking of phytoconstituents on the 1HNY receptor (The structure of human pancreatic alpha-amylase).

3. EXPERIMENTAL WORK

3.1 DOWNLOADING SOFTWARE PROGRAM

PYRX

PyRx is open-source virtual screening software used in Computer-Aided Drug Design for molecular docking and analysing ligand-protein interactions. It has a user-friendly graphical interface that includes tools like AutoDock and AutoDock Vina for docking simulations.

PyRx allows researchers to import protein and ligand structures, prepare molecules, and perform energy minimisation before docking. The software is popular for virtual screening of large compound libraries to find potential drug candidates..

BIOVIA-DISCOVERY STUDIO

BIOVIA Discovery Studio is widely used in Computer-Aided Drug Design (CADD) to study interactions between ligands (drug molecules) and biological targets such as proteins and enzymes. It allows researchers to visualize molecular structures in three dimensions and analyzed binding interactions at the atomic level.

AVAGADRO

It is an open-source molecular modeling and visualization tool used in chemistry, pharmacology, and Computer-Aided Drug Design (CADD). It is designed to build, edit, and visualize molecular structures in three-dimensional (3D) form.

CHEMSKETCH

ACD/ ChemSketch is a chemical drawing and molecular modeling software developed by Advanced Chemistry Development (ACD/Labs). It is widely used in chemistry, pharmacology, and Computer-Aided Drug Design (CADD) for drawing chemical structures and predicting basic molecular properties.

3.2 SWISS ADME

This website allows you to compute physicochemical descriptors as well as to predict ADME parameters, pharmacokinetic properties, drug like nature and medicinal chemistry friendliness of one or multiple small molecules to support drug discovery**.**

3.3. TOXICITY PREDICTION

Determining the toxicity of chemicals is necessary to identify their harmful effects on humans, animals, plants, or the environment. It is also one of the main steps in drug design.

3.4. PREPARATION OF LIGAND

The major active phytoconstituents from selected plants were identified, and their SMILES notations were retrieved from PubChem. Using ChemSketch, 2D structures were drawn and saved as .mol files. All ligands were imported into Avogadro, optimized using the UFF force field, and prepared by detecting torsion roots, correcting torsion angles, assigning charges, and converting them into .pdb format for further use.

3.5. PREPARATION OF RECEPTOR

The structure of human pancreatic alpha-amylase (PDB ID: 1HNY) was retrieved from the Protein Data Bank. This Enzyme catalyzes the hydrolysis of starch (a polysaccharide) into smaller units such as maltose and dextrins. This process is essential for carbohydrate digestion and energy production.. The structure was visualized in Discovery Studio, with unnecessary chains removed, and prepared for docking using AutoDock in PyRx. The final structure was saved in .pdb format.

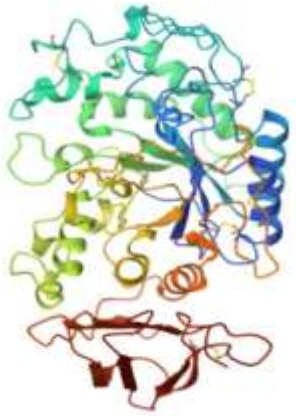


Figure 10: 3D Structure of 1HNY receptor

3.6. MOLECULAR DOCKING :-

Computational chemistry is the mathematical description or chemistry data used to analyze the interaction between drug molecules and targeted molecules of microbial, cancer cell etc. molecular docking is a powerful approach to detecting new structure-based drugs. molecular docking studies can be done at minimum cost, save time, and produce fast result in computational studies, which are used to predict the active sites, binding angle, binding targeted protein.

4. RESULT AND DISCUSSION

4.1. DRUG LIKELINESS STUDY: The results of Drug Likeliness study given in table 2.

Table 2: Drug Likeliness Study Results

Sr. No.	Chemical Constituents	Molecular Weight	Rotatable Bond	H-bond Acceptor (HBA)	H-Bond Donor (HBD)	LogP	Follow Lipinski Rule	Violations
1	15-Demethyl plumieride	456.4 g/mol	6	12	5	-2.77	Yes	HBA>10
2	Ellagic acid	302.19 g/mol	0	8	4	1.31	Yes	0
3	3,4-Dihydroxybenzoic acid	154.12 g/mol	1	3	3	0.8	Yes	0
4	Stigmasta-7,25-dien-3beta-ol	412.7 g/mol	6	1	1	7.94	Yes	Log p >5
5	D-Galacturonic Acid	194.14 g/mol	1	6	5	-3.13	Yes	0
6	Trehalose	342.3 g/mol	4	11	8	-5.4	No	HBA>10 HBD>5
7	Acarbose (Standard)	645.6 g/mol	13	19	14	-8.8	No	MW>500 HBA>10 HBD>5

DISCUSSION BASED ON DRUG LIKENESS STUDY:

The drug-likeness evaluation based on Lipinski's Rule of Five indicates that most of the selected compounds possess favorable properties for oral bioavailability. Compounds such as Ellagic acid and 3,4-Dihydroxybenzoic acid fully comply with the rule, suggesting good permeability and absorption. In contrast, Acarbose and trehalose show multiple violations, indicating poor absorption, which aligns with their known limited bioavailability. Some compounds exhibit minor deviations, such as high lipophilicity or hydrogen bonding capacity, but still remain potential candidates. Overall, the results suggest that certain phytochemicals may serve as better drug-like candidates compared to the standard drug, especially for targeting Human alpha-amylase, though further pharmacokinetic and experimental validation is required.

4.2. TOXICITY STUDIES: The results Toxicity study given in table 3.

Table 3: Toxicity Studies

Sr no.	Phytochemical name	Predicted toxicity	Predicted LD50	Carcino-genicity	Immuno-toxicity	Hepato-toxicity	Nephro-toxicity
1	15-Demethyl plumieride	4	2000 mg/kg	Inactive	Active	Inactive	Active
2	Ellagic acid	4	2991 mg/kg	Active	Inactive	Inactive	Active
3	3,4-Dihydroxybenzoic acid	4	2000 mg/kg	Active	Inactive	Inactive	Active
4	Stigmasta-7,25-dien-3beta-ol	4	2000 mg/kg	Inactive	Active	Inactive	Inactive
5	D-Galacturonic Acid	6	1000 mg/kg	Inactive	Inactive	Inactive	Active
6	Trehalose	6	29700 mg/kg	Inactive	Inactive	Inactive	Active
7	Acarbose (Standard)	4	2000 mg/kg	Inactive	Active	Active	Active

DISCUSSION BASED ON TOXICITY STUDY:

Among the tested compounds, most phytochemicals exhibit moderate to low toxicity with acceptable LD_{50} values, indicating relatively safe profiles. Compounds such as Ellagic acid show higher LD_{50} values, suggesting lower toxicity, while D-Galacturonic acid demonstrates comparatively higher toxicity. Most compounds are predicted to be non-hepatotoxic and non-carcinogenic, although some show carcinogenic or nephrotoxic tendencies. The standard drug Acarbose exhibits multiple toxicity concerns, including hepatotoxicity and nephrotoxicity. Overall, several phytoconstituents display safer toxicity profiles than the standard drug and may serve as promising alternatives, though further experimental validation is required to confirm their safety and therapeutic potential

4.3. ADME STUDY: The results ADME Study given in table 4.

Table 4: ADME Study Result

Ligands	GI Absorption	BBB Permeation	P-gp Substrate	CYPIA2 Inhibitor	CYP2D6 Inhibitor	CYP3A4 Inhibitor	Log Kp
15-Demethyl plumieride	Low	No	No	No	No	No	-10.23 cm/s
Ellagic acid	High	No	No	Yes	No	No	-7.36 cm/s
3,4-Dihydroxybenzoic acid	High	No	No	No	No	Yes	-6.42 cm/s
Stigmasta-7,25-dien-3beta-ol	Low	No	No	No	No	No	-2.42 cm/s
D-Galacturonic Acid	Low	No	Yes	No	No	No	-9.15 cm/s
Trehalose	Low	No	Yes	No	No	No	-11.36 cm/s
Acarbose (Standard)	Low	No	Yes	No	No	No	-16.5 cm/s

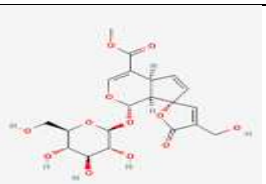
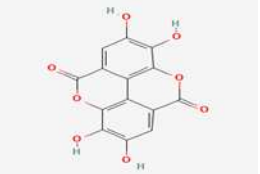
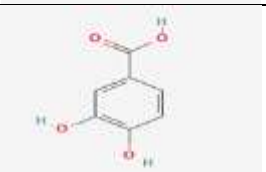
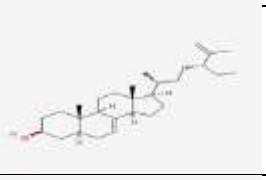
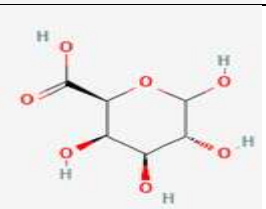
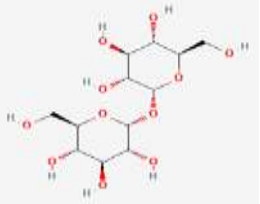
DISCUSSION BASED ON ADME STUDY:

The ADME analysis indicates that compounds such as Ellagic acid and 3,4-Dihydroxybenzoic acid exhibit favorable pharmacokinetic properties, particularly high gastrointestinal absorption, suggesting good oral bioavailability. In contrast, most other compounds show low absorption and no blood–brain barrier permeation, indicating limited distribution to the central nervous system. Some compounds, including D-Galacturonic acid and Acarbose, are identified as P-glycoprotein substrates, which may reduce their intracellular retention. Minimal inhibition of cytochrome P450 enzymes is observed overall, suggesting a lower risk of metabolic drug interactions, although specific compounds show selective inhibition. Additionally, low skin permeability across all compounds indicates poor transdermal absorption. Overall, a few phytochemicals demonstrate promising ADME profiles, while others may require optimization to improve their pharmacokinetic properties.

4.4. BINDING AFFINITY OF DIFFERENT CHEMICAL CONSTITUENTS.: The results

Binding Affinity of different Chemical Constituents given in table 4.

Tabel No. 5: Binding Affinity of different Chemical Constituents.

Ligands	2D Structure	BINDING AFFINITY
15-Demethyl plumieride		-7.5
Ellagic acid		-8.1
Protocatechuic Acid		-5.9
Stigmasta-7,25-dien-3beta-ol		-8.8
D-Galacturonic Acid		-5.9
Trehalose		-6.2
Acarbose (Standard)		-9

DISCUSSION BASED ON BINDING AFFINITY OF DIFFERENT CHEMICAL CONSTITUENTS:

The docking study revealed varying binding affinities among the tested ligands, indicating differences in their interaction with the target

receptor. Stigmasta-7,25-dien-3β-ol showed the highest binding affinity (−8.8 kcal/mol), closely comparable to the standard Acarbose (−9 kcal/mol), suggesting strong inhibitory potential. Ellagic acid also exhibited good binding (−8.1 kcal/mol), supporting its effectiveness. 15-Demethyl plumieride showed moderate affinity (−7.5 kcal/mol), indicating stable interaction.

Lower binding affinities were observed for Trehalose (−6.2 kcal/mol), Protocatechuic acid, and D-Galacturonic acid (−5.9 kcal/mol each), suggesting weaker interactions. Overall, compounds with more complex structures demonstrated better binding efficiency. These findings highlight the potential of selected ligands as promising candidates for further study.

4.5. 2D STRUCTURE OF LIGAND INTERACTION WITH RECEPTOR 1HNY

1. 15-Demethyl plumieride

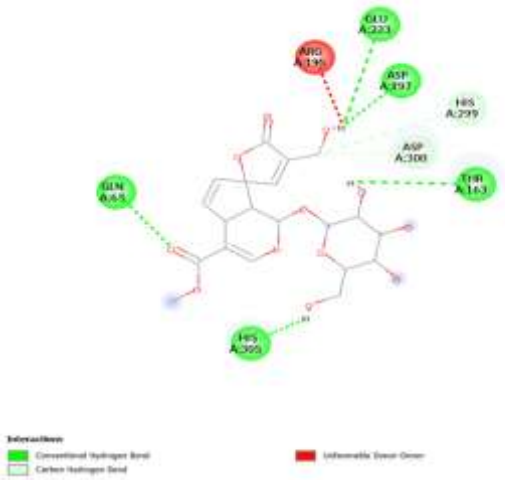


Fig11:- 2D Structure of Interaction of 15-Demethyl plumieride with 1HNY Receptor

2. Ellagic acid

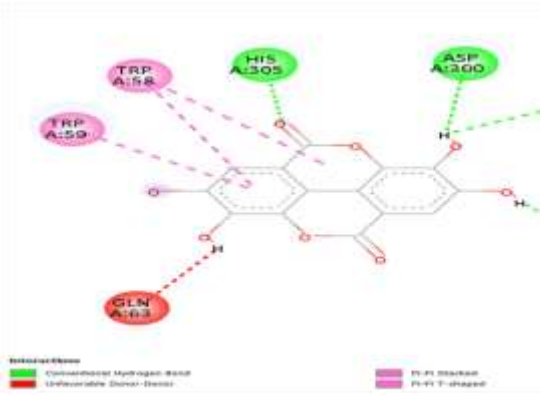


Fig12:- 2D Structure of Interaction of Ellagic acid with 1HNY Receptor

3. Protocatechuic Acid

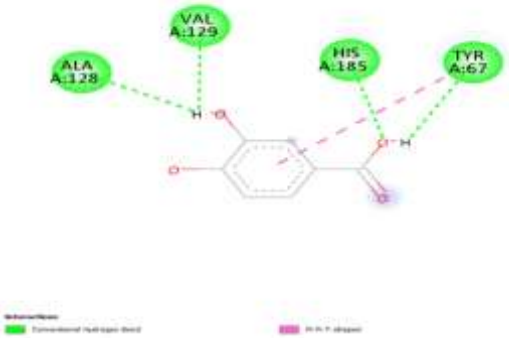


Fig13:- 2D Structure of Interaction of Protocatechuic Acid with 1HNY Receptor

4. Stigmasta-7,25-dien-3beta-ol

Fig14:- 2D Structure of Interaction of Stigmasta-7,25-dien-3beta-ol with 1HNY Receptor

5. D-Galacturonic Acid

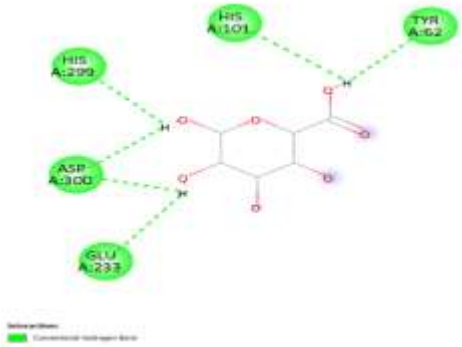


Fig15:- 2D Structure of Interaction of D-Galacturonic Acid with 1HNY Receptor

6. Trehalose

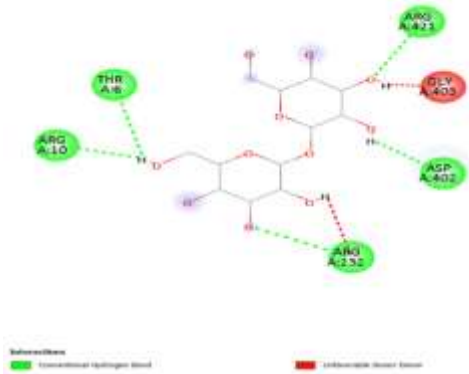


Fig16:- 2D Structure of Interaction of Trehalose with 1HNY Receptor

7. Acarbose

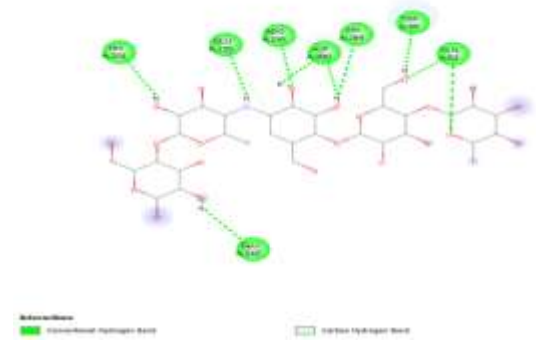


Fig17:- 2D Structure of Interaction of Acarbose with 1HNY Receptor

5. CONCLUSION

This study demonstrated that phytoconstituents of Momordica charantia have potential antidiabetic activity using molecular docking against the α-amylase receptor (1HNY). Compounds like Stigmasta-7,25-dien-3β-ol and Ellagic acid showed strong binding affinity comparable to Acarbose, indicating good inhibitory potential.

Drug-likeness, toxicity, and ADME studies suggested that several compounds possess favorable pharmacokinetic properties and relatively safe profiles. Overall, these findings highlight Momordica charantia as a promising source of antidiabetic agents. However, further experimental validation is required to confirm these results

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